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Jardel Corrêa de Oliveira

FREQUÊNCIA DE EVENTOS ADVERSOS NAS MULHERES COM HIV/AIDS EM TERAPIA ANTIRRETROVIRAL: UMA REVISÃO SISTEMÁTICA E METANÁLISE

Sorocaba/SP
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Dissertação apresentada à Banca Examinadora do Programa de Pós-Graduação em Ciências Farmacêuticas da Universidade de Sorocaba, como exigência parcial para obtenção do título de Mestre em Ciências Farmacêuticas.

Orientador: Profa. Dra. Luciane Cruz Lopes

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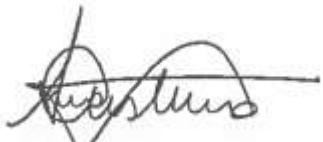
BANCA EXAMINADORA:

Profa. Dra. Luciane Cruz Lopes
Universidade de Sorocaba

Prof. Dr. Haliton Alves de Oliveira Júnior
Hospital Alemão Oswaldo Cruz



Profa. Dra. Ana Cristina Garcia Ferreira
Fiocruz Brasília/Ministério da Saúde

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RESUMO

Antecedentes: A terapia antirretroviral (TARV) é recomendada para todas as pessoas com HIV/Aids e como qualquer tratamento de uso crônico, apresenta efeitos adversos. Pouco se sabe sobre esses efeitos em mulheres vivendo com HIV/AIDS. **Objetivo:** Determinar a incidência de eventos adversos em mulheres com HIV/AIDS em terapia antirretroviral. **Métodos:** Revisão sistemática que incluiu ensaios clínicos controlados e randomizados que avaliaram eventos adversos em mulheres em uso de qualquer TARV, com pelo menos 12 semana de seguimento. Desfechos foram o número de mulheres com eventos adversos clínicos e/ou laboratoriais relacionado ou não a TARV, descontinuação do tratamento, eventos adversos graves (grau 3 e/ou 4) e sérios, eventos adversos sobre o aparelho reprodutor feminino e a saúde óssea e o número de morte por todas as causas e relacionadas à TARV. Foram excluídos estudos de profilaxia pré e pós-exposição ao HIV, de mulheres grávidas ou amamentando, de coinfecção com tuberculose, hepatite B ou C, análises post hoc, extensões abertas sem comparador, e com TARV ou doses não utilizadas na prática clínica. Não houve limitação ao *status* de publicação, período de condução do estudo e idioma. A busca se deu no *Medline*, *Embase*, *Cochrane Library*, *Epistemonikos*, Lilacs, *Who Index* e em portais de registros de ensaios clínicos. A equipe selecionou, em pares e de forma independente, todas as citações, resumos e artigos de texto completo; conflitos foram resolvidos por consenso ou por um terceiro revisor. Para o risco de viés utilizou-se a ferramenta RoB2 da Cochrane. Estimou-se a taxa de incidência de eventos por 1000 pessoas-ano, ajustada por tempo e perda de seguimento. **Resultados:** Foram identificados 21.238 estudos para triagem, dos quais 10 (n=4.716 pessoas; 2.871 mulheres) atenderam ao critério de elegibilidade. Sete estudos incluíram apenas mulheres. A maioria (80%) não teve cegamento. Quatro tiveram uma quantidade de perdas de seguimento que poderiam interferir nos seus resultados. Seis eram da indústria farmacêutica e três tiveram financiamento misto. Nove tiveram alto risco de viés. A descontinuação do tratamento por qualquer evento adverso variou entre diferentes esquemas ARV, sendo que a análise combinada de todos as TARV mostrou uma taxa de incidência média de descontinuação do tratamento de 20,78 eventos por 1000 pessoas-ano (ICr 95% 5,58-57,31). A descontinuação por eventos adversos relacionados a TARV de todos os tratamentos agregados ocorreu em uma média de 4,31 por 1000 pessoas-ano (ICr 95% 0,13-54,72). Nenhum dos estudos avaliou eventos adversos no sistema reprodutor feminino. Apenas um estudo analisou a ocorrência de osteoporose. **Conclusão:** A escassez de informações sobre eventos adversos da TARV especificamente em mulheres, aliado ao alto risco de viés da quase totalidade dos estudos

existentes, grande parte deles com participação da indústria farmacêutica, não permite que se estabeleçam conclusões sobre esquemas preferenciais para uso em mulheres com HIV/Aids. Novos estudos são necessários, com desenho metodológico e qualidade científica adequados para avaliar os eventos adversos da TARV em mulheres, de maneira a subsidiar uma abordagem centrada nas pessoas, capaz de manejar oportunamente tais eventos adversos e garantir ao máximo a adesão ao tratamento.

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Palavras-chave: HIV. Síndrome de Imunodeficiência Adquirida. Antirretrovirais. Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos. Mulheres.

ABSTRACT

Background: Antiretroviral therapy (ART) is recommended for all people with HIV/AIDS and like any chronic treatment, it has adverse effects. Little is known about these effects in women living with HIV/Aids. **Objective:** To determine the incidence of adverse events in women with HIV/AIDS on ART. **Methods:** Systematic review that included randomized controlled trials that evaluated adverse events in women using any ART, with at least 12 weeks of follow-up. Outcomes were the number of women with clinical and/or laboratory adverse events related or not to ART, treatment discontinuation, severe (grade 3 and/or 4) and serious adverse events, adverse events on the female reproductive system and bone health, and number of deaths from all causes and related to ART. Studies of pre- and post-exposure prophylaxis, pregnant or breastfeeding women, of co-infection with tuberculosis, hepatitis B and C, post hoc analyses, open-label extensions without comparator, and with ART or doses not used in clinical practice were excluded. There wasn't limitation on publication status, study period and language. The search was carried out on Medline, Embase, Cochrane Library, Epistemonikos, Lilacs, Who Index and on clinical trial registry portals. The team independently selected all citations, abstracts and full-text articles in pairs; conflicts were resolved by consensus or by a third reviewer. Cochrane's RoB2 tool was used for risk of bias. The incidence rate of events per 1000 person-years, adjusted for time and loss to follow-up, was estimated. **Results:** 21.238 studies were identified for screening, of which 10 (n=4.716 people; 2.871 women) met the eligibility criteria. Seven studies included only women. Most (80%) were not blinded. Four had a number of losses to follow-up that could interfere with their results. Six were from the pharmaceutical industry and three had mixed funding. Nine had a high risk of bias. Treatment discontinuation for any adverse event varied between different ARV regimens, with the combined analysis of all ART showing a mean incidence rate of treatment discontinuation of 20.78 events per 1000 person-years (95% CrI 5.58-57.31). Discontinuation for ART-related adverse events from all pooled treatments occurred at a mean of 4.31 per 1000 person-years (95% CrI 0.13-54.72). None of the studies evaluated adverse events in the female reproductive system. Only one study looked at the occurrence of osteoporosis. **Conclusion:** The scarcity of information on adverse events of ART specifically in women, combined with the high risk of bias in almost all existing studies, most of them with the participation of the pharmaceutical industry, does not allow conclusions to be drawn about preferential regimens for use in women with HIV/AIDS. New studies are needed, with adequate methodological design and scientific quality, to assess adverse events of ART in women, in order to support a people-centered approach, capable of

managing such adverse events in a timely manner and ensuring maximum adherence to treatment.

PROSPERO: CRD42021251051

Keywords: HIV. Acquired Immunodeficiency Syndrome. Anti-Retroviral Agents. Drug-Related Side Effects and Adverse Reactions. Women.

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LISTA DE ABREVIATURAS E SIGLAS

Aids (AIDS) – Síndrome da imunodeficiência adquirida

ARV – Antirretorival(is)

CCR5 – Receptor CC-quimiocina 5

DMO – Densidade mineral óssea

ECCR – Ensaio(s) clínico(s) controlado(s) e randomizado(s)

GRADE - *Grading of Recommendations, Assessment, Development and Evaluations*

HBsAg – Antígeno de superfície da hepatite B

HCV – Vírus da hepatite C

HIV – Vírus da imunodeficiência humana

ICr (CrI) – Intervalo de credibilidade

IQR – Intervalo interquartil

NR – Não reportado

NRTI – Inibidor(es) da transcriptase reversa nucleosídeos e nucleotídeos

NNRTI – Inibidor(es) da transcriptase reversa não nucleosídeos

OMS (WHO) – Organização Mundial da Saúde

Rob2 – Risco de viés 2

SD – Desvio padrão

TARV (ART) – Terapia antirretroviral

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1 INTRODUÇÃO

Estima-se que 84,2 milhões de pessoas no mundo já tenham se infectado com o vírus da imunodeficiência humana (HIV) desde o início da pandemia. Dessas, 38,4 milhões de pessoas ainda viviam com o vírus em 2021, sendo que 650.000 faleceram naquele ano de doenças relacionadas a síndrome da imunodeficiência adquirida (Aids) (UNAIDS, 2022).

Inicialmente, o HIV/Aids predominava na população masculina. No entanto, esse cenário se modificou ao longo dos anos. Em 2021, 54% das pessoas no mundo com HIV eram mulheres ou garotas. Quase metade (49%) dos novos casos mundiais de infecção pelo vírus em 2021 ocorreram em pessoas do sexo feminino. Na África subsaariana, esse percentual chegava a 63%, sendo que seis de cada sete casos novos de infecção entre adolescente de 15 a 19 anos eram em mulheres e o risco da infecção se apresentava duas vezes maior naquelas entre 15 e 24 anos (UNAIDS, 2022).

No Brasil, entre 2007 e 2021, houve 381.793 notificações de casos de infecção por HIV, sendo 32.701 somente em 2020. Nesse ano, a razão entre os sexos foi de 2,8 homens para cada mulher, permanecendo uma proporção maior de homens com o vírus na realidade brasileira. De 1980 até 2021, o Brasil contabilizou 1.045.355 casos de Aids, com uma queda no número de novos casos por ano desde 2013. A taxa de detecção de Aids em mulheres reduziu 50% entre 2010 e 2020, de 16 casos/100.000 habitantes para 8 casos (BRASIL, 2021).

No final de 2021, 28,7 milhões de pessoas no mundo estavam em uso de terapia antirretroviral. Das mulheres com 15 anos ou mais, 80% tinham acesso ao tratamento (UNAIDS, 2022). No Brasil, no mesmo ano, as estimativas apontavam que o país tinha cerca de 920 mil pessoas vivendo com HIV, das quais 77% estavam em tratamento com antirretroviral. Dessas em tratamento, 94% não transmitiam o vírus por estarem com a carga viral indetectável (BRASIL, 2022).

Atualmente, o protocolo brasileiro para tratamento de pessoas vivendo com HIV/Aids, guias de prática clínica de outros países e da Organização Mundial da Saúde recomendam o tratamento de todas as pessoas diagnosticadas com o vírus, independentemente de terem a doença (BRASIL, 2018a; EUROPEAN AIDS CLINICAL SOCIETY, 2021; NATIONAL INSTITUTE OF HEALTH, 2019; WORLD HEALTH ORGANIZATION, 2016). Todos esses documentos reforçam a importância da adesão ao tratamento para que se consiga obter os objetivos de tornar a carga viral indetectável e reduzir a morbimortalidade da doença e o risco de transmissão do vírus.

Manter a adesão à terapia, ainda mais considerando o caráter crônico do HIV/Aids, implica em monitorar e manejar possíveis efeitos adversos da terapia antirretroviral. No entanto, apesar das mulheres representarem pouco mais de metade das pessoas vivendo com o vírus no mundo, revisão sistemática identificou que a mediana de participação delas nos ensaios clínicos da terapia é de apenas 19% (CURNO *et al*., 2016). Isso faz com que as recomendações de tratamento sejam extrapoladas de estudos em que predominam os homens. Em 2005, um estudo já chamava a atenção para possíveis diferenças na toxicidade dos antirretrovirais entre os sexos, que poderia ser maior nas mulheres, em virtude da maior concentração dos medicamentos que elas demonstraram em estudos de farmacocinética (CLARK; SQUIRES, 2005).

Estudos observacionais sugerem possíveis consequências do uso de antirretrovirais sobre os hormônios sexuais femininos, o que pode impactar negativamente na vida reprodutiva e na saúde óssea das mulheres. Um estudo transversal sugeriu aumento de anormalidades menstruais (VALIAVEETTIL *et al*., 2019), o que não foi confirmado por outro estudo de coorte (MASSAD *et al*., 2006). Metanálise (KING; ALBERT; MURRAY, 2019) de seis estudos observacionais mostrou aumento de amenorreia, que pode estar relacionado com menor densidade mineral óssea (DMO). As pesquisas são contraditórias quanto ao efeito da terapia antirretroviral (TARV) ou da própria infecção pelo HIV sobre os ossos. Revisão sistemática (CARVALHO *et al*., 2010) com um ensaio clínico e quatro estudos transversais mostrou que mulheres em uso de inibidores da protease, uma classe de antirretrovirais, apresentaram diferença de mais de 3% de perda na DMO no colo do fêmur. Outra revisão (CEZARINO *et al*., 2018), de estudos principalmente transversais, associou a redução da DMO em mulheres com a infecção pelo HIV, concluindo que novas pesquisas são necessárias para estabelecer o efeito da terapia sobre essa questão.

Compreender as diferenças na ocorrência de eventos adversos entre os sexos, em especial nas mulheres, e o efeito dos antirretrovirais sobre os hormônios femininos é fundamental para o manejo e a adesão ao tratamento. Esta revisão visa descrever a incidência dos eventos adversos nas mulheres com HIV/Aids em uso de TARV nas diferentes faixas etárias.

2 REVISÃO DE LITERATURA

2.1 Classificação dos eventos adversos de acordo com a gravidade

Algumas terminologias, como a *Common Terminology Criteria for Adverse Events* (CTCAE), que teve sua quinta edição em 2017 (U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; NATIONAL INSTITUTES OF HEALTH; NATIONAL CANCER INSTITUTE, 2017), foram estabelecidas para padronizar a descrição dos eventos adversos, tanto clínicos como laboratoriais. Elas são organizadas conforme a gravidade de tais eventos, indo do grau 1, que são os mais leves, até o grau 5, os mais graves.

De forma geral, a divisão em graus segue as seguintes definições:

- Grau 1: leve – sintomas leves, causando nenhuma ou mínima interferência com as atividades sociais e diárias usuais, que não necessitam de intervenção.
- Grau 2: moderado – eventos que precisam de intervenções locais, mínimas ou não invasivas, que podem limitar as atividades instrumentais da vida diária esperadas para a idade, como preparar refeições, comprar alimentos ou roupas, usar telefone, manejar dinheiro etc.
- Grau 3: graves – eventos que causam prejuízo funcional, como limitação para as atividades de auto cuidado da vida diária (tomar banho, vestir-se, comer, usar o banheiro e tomar medicamentos), exigindo intervenção, hospitalização ou prolongamento do tempo de internação, mas que não chegam a causar risco de vida imediato.
- Grau 4: eventos adversos com potencial risco de vida, que necessitam de intervenções urgentes para prevenir dano permanente, perda funcional persistente ou morte.
- Grau 5: Morte relacionada a eventos adversos.

Um outro exemplo, organizado especificamente para descrever os eventos adversos da TARV, foi a Tabela de Graduação da Gravidade dos Eventos Adversos em Adultos e Crianças da divisão de AIDS (DAIDS) do Instituto Nacional de Saúde (NIH) dos Estados Unidos (US DEPARTMENT OF HEALTH AND HUMAN SERVICES *et al*., 2017), cuja versão mais atual é de julho de 2017.

Os protocolos de ensaios clínicos e os estudos publicados também costumam reportar os eventos adversos como sérios, que correspondem a uma definição com fins regulatórios. São

eventos de interesse analisados pelas agências reguladoras no processo de autorização para comercializar os medicamentos e para monitorar o seu uso pós-comercialização. De acordo com *Food and Drug Administration* (FDA) dos Estados Unidos (U.S. FOOD & DRUG ADMINISTRATION; OFFICE OF THE COMMISSIONER, 2020), quando tais eventos afligem uma pessoa, devem ser relatados e abrangem:

- Morte;
- Risco de vida;
- Hospitalização ou prolongamento do tempo de internação;
- Dano ou perda de função significante, persistente ou permanente, que afeta as atividades normais da vida, a qualidade de vida ou a função/estrutura do corpo;
- Anomalias congênitas e defeitos de nascimento;
- Necessidade de intervenções médicas ou cirúrgicas para prevenir algum dos desfechos anteriores.

2.2 A influência dos efeitos adversos na adesão ao tratamento

Com o avanço das opções terapêuticas para HIV/Aids, que permitiram o controle da infecção, essa se tornou uma condição crônica. Isso ressalta a importância de se trabalhar a adesão ao tratamento, ainda mais com as recomendações atuais de tratar todas as pessoas com o vírus, visando manter a carga viral indetectável e impedir sua transmissão.

O manual de adesão ao tratamento para pessoas vivendo com HIV e Aids do Ministério da Saúde (BRASIL *et al*., 2018a) cita os efeitos adversos entre os fatores que dificultam a adesão à TARV. Esse documento recomenda que os profissionais de saúde orientem sobre a possibilidade de reações adversas e verifiquem sua ocorrência em todos os atendimentos.

Em 2007, uma revisão (BONOLO; GOMES; GUIMARÃES, 2007) de 56 artigos científicos identificou os efeitos adversos como um dos fatores independentemente associados com a descontinuação da TARV no início do tratamento. Os estudos demonstraram que esquemas ARV com menos efeitos adversos contribuem com a adesão.

Um estudo (PADOIN *et al*., 2013) de adultos com HIV/Aids atendidos em um Hospital Universitário do Sul do Brasil descreveu fatores associados com a não adesão ao tratamento. Dentre as pessoas incluídas nesse estudo, 44% foram classificadas como não aderentes, sendo que os efeitos adversos foram a segunda principal causa de descontinuação da terapia (26%).

Outras duas pesquisas (COUTINHO; O'DWYER; FROSSARD, 2018; PASCHOAL *et al*., 2014) realizadas no Rio de Janeiro confirmaram o impacto negativo dos efeitos adversos na adesão. Uma delas (PASCHOAL *et al*., 2014) avaliou pessoas com HIV/Aids acompanhadas no ambulatório de um hospital público. Realizou uma análise qualitativa, em que o fator que dificulta a adesão à TARV mais citado foram os efeitos adversos. A outra (COUTINHO; O'DWYER; FROSSARD, 2018), conduzida em um Centro de Saúde da Fundação Oswaldo Cruz, buscou avaliar a influência da depressão na adesão de pessoas com HIV/Aids atendidas na atenção primária à saúde. Não encontrou relação com a depressão, mas identificou os efeitos adversos como um dos aspectos mencionados pelos participantes que afetam a adesão.

Um estudo de caso-controle (LIMA, 2019) analisou a frequência dos eventos adversos e suas implicações na TARV em pessoas com HIV atendidas no Instituto de Medicina Integral de Recife-PE. Concluiu que a maioria das pessoas em uso da terapia convive com efeitos adversos, que têm potencialmente levado a alterações nos esquemas ARV, sendo um dos principais problemas que dificultam a adesão.

Outra revisão mais recente (SANTOS *et al*., 2018) incluiu 16 estudos que avaliaram fatores desfavoráveis à adesão a TARV. Identificou três fatores principais, sendo um deles a ocorrência de efeitos adversos que afetam a qualidade de vida das pessoas.

Todos esses achados reforçam a importância de se estar atento a ocorrência de eventos adversos em pessoas vivendo com HIV/Aids desde o início do tratamento. Nesse sentido, é fundamental manter um acompanhamento regular, com orientação sobre as reações adversas que podem ocorrer com o esquema ARV em uso e como se deve manejá-las, incluindo em quais situações a pessoa deve retornar ao sistema de saúde ou procurar um serviço de emergência.

2.3 A replicação do HIV

Inicialmente, o HIV se liga e se funde as células CD4. Como é um vírus RNA, ele precisa transformar seu material genético para DNA para que possa se integrar a célula hospedeira. Nessa etapa, o vírus utiliza a sua enzima transcriptase, que converte o RNA em DNA. Em seguida, uma outra enzima viral, chamada de integrase, junta o DNA viral ao da célula CD4, o que se mantém pelo resto da vida da célula hospedeira. Depois de estabelecida essa ligação, o CD4 começa a codificar novos RNA virais, que produzem cadeias longas de proteínas e enzimas que irão compor os novos vírus. Em um formato ainda imaturo, as novas partículas virais deixam as células CD4. Uma vez fora da célula hospedeira, uma terceira

enzima, a protease, transforma as cadeias proteicas longas em proteínas menores e funcionais, que levam ao amadurecimento do vírus (FLETCHER, 2022).

Os antirretrovirais atuam em diferentes etapas do ciclo de replicação do HIV. Atualmente, existem oito classes desses medicamentos: 1) antagonistas do correceptor de quimiocina 5 (CCR5); 2) inibidores de fusão; 3) inibidores de ligação; 4) inibidores da transcriptase reversa nucleosídeos e nucleotídeos (NRTI); 5) inibidores da transcriptase reversa não nucleosídeos (NNRTI); 6) inibidores da integrase; 7) inibidores da protease; 8) inibidores pós-ligação (FLETCHER, 2022).

2.4 Classes de antirretrovirais

2.4.1 Antagonistas de CCR5

Para o HIV entrar na célula CD4, ele precisa se ligar ao receptor CD4 e um de seus correceptores: CCR5 ou correceptor de quimiocina CXC 4 (CXCR4). Os medicamentos dessa classe bloqueiam o CCR5, inibindo a entrada dos vírus com tropismo por esse correceptor. Para que possam ser usados, é necessário antes testar o tropismo do HIV, pois se o vírus tiver tropismo pelo CXCR4 ou duplo (para ambos os correceptores), o medicamento não será útil (FLETCHER, 2022).

Atualmente, existe apenas o fármaco maraviroc aprovado para uso nessa classe (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022). Outros estão em desenvolvimento, como vicriviroc, cenicriviroc e leronlimab (HIV.GOV; NATIONAL INSTITUTE OF HEALTH, 2022; WISHART *et al*., 2018).

2.4.2 Inibidores de fusão

Esses medicamentos inibem a fusão do HIV à célula CD4, ao se ligar ao envelope de glicoproteína 41 do vírus. Enfuvirtida é o único fármaco em uso dessa classe (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022).

2.4.3 Inibidores de ligação

Fostemsavir é o fármaco que representa essa classe. Seu metabólito ativo se liga ao envelope de glicoproteína 120 do HIV, impedindo sua ligação às células CD4, consequentemente evitando a entrada do vírus nessas células (FLETCHER, 2022).

2.4.4 Inibidores da transcriptase reversa nucleosídeos e nucleotídeos

Esses medicamentos sofrem fosforilação intracelular por meio de várias enzimas do hospedeiro, formando trifosfatos ativos, que interferem na integração do DNA formado pela enzima transcriptase reversa. Ao se ligar à cadeia de DNA da célula CD4, o trifosfato impede o alongamento da cadeia pela incorporação de DNA produzido pela enzima do vírus. Os NRTI são utilizados normalmente em pares (FLETCHER, 2022).

São representantes em uso dessa classe: abacavir, didanosina (usado atualmente apenas em crianças), entricitabina, lamivudina (esses dois últimos são considerados citosinas análogas), estavudina, fumarato de tenofovir desoproxila, tenofovir alafenamida e zidovudina (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022). Há três novos fármacos em desenvolvimento: azvudina, censavudina e fozivudina (WISHART *et al*., 2018).

2.4.5 Inibidores da transcriptase reversa não nucleosídeos

Um NNRTI costuma ser utilizado em esquemas com dois NRTI. Essa classe interfere na ação da transcriptase reversa, impedindo-a de adicionar novos nucleotídeos à cadeia de DNA da célula CD4. Eles tornam a enzima menos flexível e inibem a polimerização do DNA, reduzindo o alongamento da cadeia de DNA e, consequentemente, a replicação viral. Eles são ativos contra o HIV1, mas não contra HIV2 (FLETCHER, 2022).

Doravirina, efavirenz, elsulfavirina, etravirina, nevirapina e rilpivirina pertencem a essa classe (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022).

2.4.6 Inibidores da integrase

Esses medicamentos inibem a atuação da enzima viral integrase, responsável por integrar o DNA produzido pela transcriptase reversa à cadeia de DNA da célula CD4

(FLETCHER, 2022). São representantes dessa classe: bictegravir, cabotegravir, dolutegravir, elvitegravir e raltegravir (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022).

2.4.7 Inibidores da protease

Eles são geralmente utilizados com dois NRTI, mas também podem ser empregados em esquemas que poupem o uso de nucleosídeos e nucleotídeos. Comumente são administrados com agentes de reforço (*"booster"*), como ritonavir ou cobicistate (inibidor do citocromo P450 3A). Atuam inibindo competitivamente a clivagem das cadeias proteicas longas em proteínas menores e funcionais, promovida pela enzima viral protease. Com isso, interferem no processo de maturação viral, produzindo vírus imaturos e não infecciosos (FLETCHER, 2022).

Fazem parte dessa classe: atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir e tipranavir (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022).

2.4.8 Inibidores pós-ligação

Essa classe é representada pelo ibalizumabe, um anticorpo monoclonal que se liga ao CD4. O fármaco não impede a ligação do HIV à célula hospedeira, mas bloqueia a entrada do vírus (BMJ GROUP, 2020; BRASIL *et al*., 2018a; FLETCHER, 2022; TSIBRIS, 2022).

3 OBJETIVOS

3.1 Objetivo geral

- Determinar a incidência de eventos adversos em mulheres com HIV/Aids em uso de TARV.

3.2 Objetivos específicos

- Descrever a incidência de eventos adversos no sistema reprodutor feminino, incluindo atraso na puberdade, menopausa precoce, fogachos, amenorreia e outras irregularidades menstruais;

- Estimar a incidência de eventos adversos para saúde óssea das mulheres, abrangendo osteopenia, osteoporose, fraturas gerais, vertebrais, não vertebrais, de punho e de quadril por osteoporose;

- Determinar a frequência de descontinuação da TARV por eventos adversos em mulheres;

- Descrever o número de mulheres com qualquer evento adverso e com eventos graves e sérios, gerais e relacionados a TARV;

- Estimar as hospitalizações por eventos adversos (gerais e relacionadas a TARV), a morte por todas as causas e as mortes por eventos adversos da TARV em mulheres.

4 MÉTODOS

Essa revisão sistemática e metanálise foi realizada de acordo com o *Cochrane Handbook for Intervention Reviews* (25). Os métodos foram descritos previamente no protocolo: “Sex differences and adverse events of antiretrovirals in people living with HIV/AIDS: a systematic review and meta-analysis protocol”, publicado no BMJ Open e disponível no APÊNDICE A.

Este estudo foi registrado também no PROSPERO (número de registro CRD42021251051). Esta versão sofreu modificações durante a elaboração do protocolo final publicado pelo BMJ Open, sendo solicitadas alterações na versão do PROSPERO (APÊNDICE B), que foram aceitas e publicadas em 27 de setembro de 2022.

4.1 Critérios de elegibilidade

A questão de pesquisa, com os critérios de inclusão, foi elaborada de acordo com o acrônimo inglês PICOTS.

4.1.1 População

Mulheres vivendo com HIV/Aids em uso de terapia antirretroviral, independentemente da idade.

4.1.2 Intervenção

Qualquer esquema antirretroviral contendo fármacos em doses ainda utilizados na prática clínica, conforme descrito no item 4.8.

4.1.3 Comparador

Qualquer esquema antirretroviral contendo fármacos em doses ainda utilizados na prática clínica, desde que inclua algum medicamento ou dose ou esquema de administração diferente da intervenção.

4.1.4 Desfechos de interesse

O protocolo previa a avaliação da frequência de eventos adversos nos sistemas reprodutivo e ósseo feminino. No entanto, tais desfechos não foram abordados ou foram pouco relatados nos estudos. Por isso, optamos por incluir nesse estudo sobre a frequência de eventos adversos em mulheres também os desfechos previstos para o outro objetivo descrito no nosso protocolo, que pretende comparar os eventos adversos entre os sexos.

Outra mudança que adotamos em relação ao protocolo foi a descrição de eventos adversos clínicos (sinais e sintomas), laboratoriais e totais (clínicos e laboratoriais), uma vez que os estudos costumavam apresentar os resultados dessa forma. Também separamos os eventos adversos graves em graus 3 ou 4, grau 3, grau 4 e sérios, conforme definição utilizada pelos autores dos estudos.

Os desfechos utilizados nessa revisão, considerando o número de mulheres acometidas em cada braço dos estudos, estão descritos no Quadro 1.

Os estudos não costumam descrever as mortes como relacionadas a eventos adversos, exceto quando decorrentes da TARV, ou não o fazem de forma uniforme, utilizando diferentes maneiras de descrevê-las. Por vezes, incluem como eventos adversos as mortes decorrentes de complicações da Aids, como infecções oportunistas, e as relacionadas à terapia. Porém, em geral, relatam o número total de mortes como um dos motivos de perda de seguimento, sem separar quais são por eventos relativos à Aids daquelas por causas desconhecidas, causas externas ou outras comorbidades. Algumas mortes, por exemplo, são por doenças cardiovasculares e os estudos habitualmente não definem se estão associadas com a Aids, que aumenta o risco desse tipo de doenças, ou se decorrem de efeitos adversos da terapia. Por isso, optamos em coletar o número de morte por todas as causa e aquelas definidas pelos estudos como relacionadas à TARV.

4.1.5 Tempo de seguimento

Estudos com pelo menos 12 semanas de seguimento.

4.1.6 Tipos de estudos

Nós incluímos apenas ensaios clínicos controlados randomizados (ECCR). Estudos observacionais podem ter amostras maiores e tempo de seguimento mais longo que os ECCR e

coletar informações sobre eventos adversos raros ou de longo prazo. No entanto, tais estudos, por não serem randomizados, têm maior risco de viés, produzindo resultados de comparação entre diferentes TARV menos confiáveis para nortear a prática clínica. Além disso, os ECCR costumam coletar eventos adversos de forma mais controlada, padronizada e monitorada do que os estudos observacionais.

Quadro 1 – Desfechos primários e secundários avaliados nessa revisão

Desfechos primários
Número de participantes com qualquer evento adverso e de participantes com eventos adversos relacionados a TARV (conforme definido nos estudos): - Descontinuação do tratamento; - Eventos adversos clínicos e/ou laboratoriais; - Eventos adversos clínicos; - Eventos adversos laboratoriais.
Desfechos secundários
Número de participantes com qualquer evento adverso e de participantes com eventos adversos relacionados a TARV (conforme definido nos estudos): - Eventos adversos clínicos e/ou laboratoriais de graus 3 e/ou 4; - Eventos adversos clínicos de graus 3 e/ou 4; - Eventos adversos laboratoriais de graus 3 e/ou 4; - Eventos adversos clínicos e/ou laboratoriais de grau 3; - Eventos adversos clínicos de grau 3; - Eventos adversos laboratoriais de grau 3; - Eventos adversos clínicos e/ou laboratoriais grau 4; - Eventos adversos clínicos de grau 4; - Eventos adversos laboratoriais de grau 4; - Eventos adversos clínicos e/ou laboratoriais sérios; - Eventos adversos clínicos sérios; - Eventos adversos laboratoriais sérios; - Atraso na puberdade; - Amenorreia; - Irregularidade menstrual; - Menopausa precoce; - Total com fogachos; - Total com fogachos graves (ou severos); - Total com fogachos moderados; - Total com fogachos leves; - Total com fogachos graves/moderados; - Total com fogachos moderados/leves; - Osteopenia; - Osteoporose; - Fraturas gerais por osteoporose; - Fraturas vertebrais por osteoporose; - Fraturas não vertebrais por osteoporose; - Fraturas de punho por osteoporose; - Fraturas de quadril por osteoporose; - Hospitalização por eventos adversos. Morte por todas as causas; Morte relacionada a TARV.

Fonte: Elaboração própria

4.1.7 Critérios de exclusão

Excluímos estudos de profilaxia pré (PREP) e pós-exposição (PEP) ao HIV, de mulheres grávidas ou amamentando, com foco em coinfecção com tuberculose, hepatite B ou C, bem como, análises post hoc ou secundárias e extensões abertas, sem comparador. Estudos com ARV ou doses não mais utilizados na prática clínica ou com ARV em fase de desenvolvimento, ainda não aprovados para uso, também foram excluídos.

Além dos motivos de exclusão acima, descritos no protocolo do BMJ Open, excluímos adicionalmente braços dos estudos que utilizaram múltiplos esquemas antirretrovirais. Isso, pois mesmo medicamentos de uma mesma classe estão associados a diferentes efeitos adversos e não seria possível atribuir os eventos adversos descritos nos estudos a um esquema antirretroviral específico.

4.2 Fontes de informação

Essa revisão abrange os resultados das buscas, realizadas no final de maio de 2021, nas seguintes fontes: MEDLINE via Pubmed, Embase via Elsevier, *Cochrane Central Register of Controlled Trials* (Central), *Latin American and Caribbean Health Sciences Literature* (Lilacs) via Biblioteca Virtual em Saúde (BVS), Epistemonikos e *Global Index Medicus*.

Adicionalmente, fizemos uma busca por ensaios clínicos registrados no ClinicalTrials.gov.

4.3 Estratégia de busca

A estratégia de busca utilizou Descritores em Ciências da Saúde/*Medical Subject Headings* (DeCS/MeSH), sinônimos e termos correlatos, adaptados de acordo com cada base de dados (APÊNDICE C, Quadro 5). Ela foi conduzida por uma bibliotecária experiente e revisada por outra profissional bibliotecária, conforme *Peer Review of Electronic Search Strategies* (Press) (MCGOWAN *et al*., 2016). Não houve nenhuma limitação quanto ao status e ano de publicação e idioma. Um serviço de tradução profissional seria acessado, se necessário.

4.4 Processo de seleção

Inicialmente, foi realizada uma calibração para seleção por títulos e resumos. Depois, utilizamos o site Covidence ("Covidence - Better systematic review management", [s.d.]), sendo que cada estudo foi avaliado em duplicata de forma independente. As divergências foram resolvidas por consenso ou por um terceiro pesquisador, se necessário.

Para seleção por texto completo, utilizamos uma planilha de Excel (https://1drv.ms/x/s!AkzxfYpR4grGgf54jHaTbpl4uUov8g?e=wapKHf). Todos os pesquisadores que contribuíram nessa etapa passaram por uma calibração. Na sequência, a seleção se deu em duplas de maneira independente, seguida por consenso e, quando preciso, resolução das divergências por um terceiro pesquisador.

4.5 Extração dos dados

A extração dos dados iniciou com uma etapa de calibração com todos os pesquisadores envolvidos. Depois, foi conduzida de forma independente e em duplas. As divergências foram resolvidas por consenso ou com um terceiro pesquisador. Os estudos elegíveis que se referiam aos mesmos participantes foram agrupados sob um único número de identificação, incluindo os protocolos de registro e os dados postados, quando disponíveis. Os materiais suplementares dos estudos também foram consultados.

Os dados extraídos foram as características dos estudos (primeiro autor, período de condução do estudo, ano de publicação, financiador, países e número de locais onde foi realizado, número de registro, duração do seguimento, tempo de medida dos desfechos em semanas) e dos participantes (critérios de inclusão, idade, exposição prévia a TARV – virgens ou experenciados –, número total de participantes randomizados e em cada braço do estudo, número de participantes em cada braço que recebeu pelo menos uma dose da TARV, número e percentual de mulheres, esquema ARV utilizado em cada braço, duração do tratamento, nível de CD4, comorbidades e outras intervenções realizadas além da TARV), os eventos adversos reportados pelos estudos conforme os desfechos de interesse dessa revisão (número de participantes que tiveram cada desfecho) e o método de coleta dos eventos adversos (se os pesquisadores monitoraram ativamente, se foi por relato espontâneo ou ambos). Também obtivemos informações sobre o cegamento e o sigilo de alocação. Utilizamos uma planilha do Excel (https://1drv.ms/x/s!AkzxfYpR4grGgoBPZMih_fpyLV-HRQ?e=yaNVc4).

Nos estudos agrupados sob um mesmo número de identificação que tiveram resultados publicados com diferentes durações de seguimento, os eventos adversos foram extraídos para cada tempo em que foram reportados.

4.6 Avaliação do risco de viés

A qualidade dos estudos foi determinada por meio da ferramenta de avaliação do risco de viés para ECCR da Cochrane, versão 2 (RoB2) (COCHRANE, 2019). O risco foi julgado de acordo com cinco domínios: processo de randomização, desvios da intervenção pretendida, dados de desfecho perdidos, medição dos desfechos e seleção no reporte dos resultados. As perguntas dentro de cada domínio foram avaliadas de forma independente por dois pesquisadores, que atribuíram como respostas: ‘definitivamente sim’, ‘provavelmente sim’, ‘provavelmente não’, ‘definitivamente não’ ou ‘não informado’. As divergências foram resolvidas por consenso ou, se necessário, por um terceiro revisor. De acordo com essas respostas, o risco de viés foi definido como ‘baixo risco’, ‘alguma preocupação com risco de viés’ ou ‘alto risco’. O viés de publicação foi avaliado por meio do gráfico de funil (EGGER *et al*., 1997) para cada desfecho.

4.7 Análise estatística

O protocolo previa a descrição da prevalência dos eventos adversos nas mulheres. No entanto, optamos por estimar a taxa de incidência de eventos por 1000 pessoas-ano, uma vez que permite o ajuste das análises pelas perdas e pelo tempo de seguimento, o qual variou consideravelmente entre os estudos. A seguir, descrevemos em detalhes em que se basearam e como foram realizadas as análises estatísticas.

4.7.1 Notação

Sem perda de generalidade, o número de eventos adversos de um determinado tipo (p.e., hospitalização) é denotado por y para y = 0,1, …, M. Assumiu-se que um mesmo estudo pode contribuir com estimativas diferentes para diferentes grupos de tratamento, que são considerados independentes e indexados por i para i = 1,2,…, k.

4.7.2 Aproximação do número de pessoas-ano de exposição

Tipicamente, o tempo de seguimento nos estudos foi relatado em semanas. Contudo, a interpretação clínica é facilitada pelo emprego de pessoas-ano acompanhadas (GORDIS, 2013). Dessa maneira, para cada grupo de tratamento i, a soma total do número de anos que os participantes randomizados estiveram sob observação foi aproximada por:

$$T_i = \frac{\text{seguimento}_i \times n_i - (\text{seguimento}_i \times p_i \times 0.5)}{52.143} \tag{1}$$

onde seguimento_i representa o tempo de seguimento em semanas, n_i denota o número de participantes analisados e p_i representa o número de participantes que descontinuaram ou que foram perdidos durante o seguimento no estudo i. Com base na equação (1), é possível depreender que a premissa é que os participantes perdidos ao longo do tempo contribuíram com metade do tempo total de seguimento.

4.7.3 Modelo

A distribuição de Poisson é a escolha natural para modelar dados em forma de contagens. Dessa maneira, um modelo metanalítico Bayesiano foi implementado assumindo uma distribuição de Poisson e efeitos aleatórios. Assumindo que os grupos de tratamento são independentes, o número de eventos adversos no grupo de tratamento i, y_i, durante o tempo total de seguimento em pessoas-ano, T_i, para i = 1, 2, …, k foi considerado como:

$$y_i \sim \text{Poisson}(\lambda_i) \tag{2}$$

$$\lambda_i = \theta_i \times T_i \tag{3}$$

$$\log(\theta_i) \sim \text{N}(d, \tau^2) \tag{4}$$

onde λ_i é a média da distribuição e θ_i é a taxa de incidência no i-ésimo estudo. Como pode ser visto na equação (4), o modelo assume que as taxas de incidência (na escala log) são amostras aleatórias de uma distribuição normal, cuja média verdadeira é d com variância τ^2. Tanto d como τ^2 são entidades desconhecidas, e precisam ser estimadas com base nos dados observados. Do ponto de vista da metanálise, as estimativas de d e τ^2 representam o logaritmo da taxa de incidência sumária ao longo dos grupos de tratamento (modelo de efeitos aleatórios) e a variância intergrupos de tratamentos, respectivamente.

O modelo foi especificado com distribuições a priori não-informativas:

$$d \sim \text{N}(0, 10^4)$$

$$\tau \sim \text{Unif}(0, 5)$$

Para facilitar a interpretação, os resultados sumários foram mostrados como $\hat{d} \times 1000$, denotando a taxa de incidência sumária por 1000 pessoas-ano.

4.7.4 Implementação

Os parâmetros do modelo foram estimados pelo método de Monte Carlo acoplado a cadeias de Markov (MCMC) por meio do amostrador de Gibbs implementado no programa MultiBUGS (GOUDIE *et al*., 2020). As primeiras 50.000 simulações foram descartadas (*burn-in period*) e o modelo foi continuado por mais 166.667 iterações por meio de três cadeias independentes, totalizando 500.000 simulações. A convergência e autocorrelação foram verificadas graficamente no programa Stata (versão 16, StataCorp,Texas, EUA) como descrito por Thompson; Palmer; Moreno (THOMPSON; PALMER; MORENO, 2006). Os resultados sumários das metanálises foram calculados pela mediana da distribuição posterior, e os intervalos de credibilidade de 95% pelos percentis 2,5 e 97,5 das distribuições posteriores.

4.8 Antirretrovirais incluídos na revisão

Inicialmente, fizemos um levantamento dos fármacos antirretrovirais utilizados pelo programa brasileiro de HIV/Aids (BRASIL *et al*., 2018a, 2018b). Adicionalmente, verificamos os fármacos descritos na ATC da WHO, incluindo aqueles que não eram utilizados no Brasil (WORLD HEALTH ORGANIZATION; WHO COLLABORATING CENTRE FOR DRUG STATISTICS METHODOLOGY, 2022). Depois, fizemos uma reunião com um infectologista que atuava no programa de HIV/Aids do Ministério da Saúde do Brasil para checar quais dos antirretrovirais da lista ainda estavam em uso na prática clínica.

Na etapa de seleção de títulos e resumos, coletamos o nome de outros antirretrovirais que não haviam sido identificados nas etapas anteriores. Como os critérios de exclusão previam a retirada de estudos com TARV não mais utilizada na prática clínica ou em doses diferentes das recomendadas atualmente, checamos as doses em diferentes fontes: UpToDate, PCDT adulto, PCDT infantil, BNF, BNF Children, Micromedex/Dynamed (BMJ GROUP, 2019, 2020; BRASIL *et al*., 2018a, 2018b; FLETCHER, 2022; TSIBRIS, 2022). Elaboramos uma tabela com a descrição das doses encontradas. Antirretrovirais que não tinham doses descritas nessas fontes foram avaliados para determinar se tinham sido descontinuados ou se estavam em fase de desenvolvimento (HIV.GOV; NATIONAL INSTITUTE OF HEALTH, 2022;

NATIONAL INSTITUTE OF HEALTH; NATIONAL LIBRARY OF MEDICINE; NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION, 2022; WISHART *et al*., 2018).

Os antirretrovirais considerados nessa revisão, com as respectivas classes e doses utilizadas em adultos e crianças, estão descritos no Quadro 2.

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continua)

Antirretroviral	Classe farmacológica	Adulto	Criança
Abacavir	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	300 mg 12/12h 600 mg/d	Crianças >= 3 meses 1) Por peso (mg/kg) 8 mg/kg/dose 12/12h 16-20 mg/kg/dose/d 2) Por faixa de peso 14 - <20 kg 150 mg 12/12h; 300 mg/d 20 - <25 kg 150/manhã e 300 mg/tarde; 450 mg/d >= 25 kg 300 mg 2x/d; 600 mg/d ou 14 - 20 kg 150 mg 12/12h; 300 mg/d 21 - 29 kg 150/manhã e 300 mg/tarde; 450 mg/d >= 30 kg 300 mg 2x/d; 600 mg/d
Atazanavir	Inibidores da protease	300 mg/d com ritonavir ou cobicistate 400 mg/d sem ritonavir 400 mg/d com ritonavir se uso concomitante de efavirenz ou tenofovir	1) Pó oral >= 3 meses com ritonavir ou cobicistate 5 - <15 kg 200 mg/d (se intolerância a esta dose, 150 mg/d) 15 - <25kg 250 mg/d >=25 kg 300 mg/d 2) cápsula para >= 6 anos e >= 15 kg com ritonavir ou cobicistate 15 - <35 kg 200 mg/d >= 35 kg 300 mg/d ou 15kg-20kg 150 mg/d 20kg-40kg 200 mg/d ≥40 kg 200-300 mg/d 3) sem ritonavir ou cobicistate >6 - <13 anos 520 mg m^2/dose/d 13 - <18 anos 620 mg m2/dose/d
Bictegravir	Inibidores da integrase	50 mg/d	14- <25 kg 30 mg/d ≥25 kg 50 mg/d

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Cabotegravir	Inibidores da integrase	1) oral 30 mg/d com rilpivirina 2) injetável (IM) dose inicial 600 mg com rilpivirina dose de manutenção 400 mg/mês com rilpivirina	-
Cobicistate	Inibidor do citocromo P450 3A	150 mg/d	1) com elvitegravir >= 25 kg 150 mg/d 2) com atazanavir >= 35 kg 150 mg/d 3) com darunavir >= 40 kg 150 mg/d
Darunavir	Inibidores da protease	800 mg/d 600 mg 12/12h	Criança >=3 anos 1) Dose por peso 10-15 kg: 20 mg/kg/2x/d 2) Dose por faixa de peso: 10 - <11kg 200 mg 2x/d; 350 mg/d 11 - <12kg 220 mg 2x/d; 385 mg/d 12 - <13 kg 240 mg 2x/d; 420 mg/d 13 - <14 kg 260 mg 2x/d; 455 mg/d 14 - < 15 kg 280 mg 2x/d; 490 mg/d 15 - <30 kg 375 mg 2x/d; 600 mg/d 30 - <40 kg 450 mg 2x/d; 675 mg/d >= 40 kg 600 mg 2x/d; 800 mg/d ou 20-30kg 375mg 12/12h 30-40kg 450mg 12/12h ≥40kg 600mg 12/12h ou (para >= 12 anos) 30 - <40 kg 400 mg 2x/d 675 mg/d >= 40 kg 800 mg/d 600 mg 2x/d
Didanosina	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	não mais usado em adultos	1) pó para solução oral <60 kg 125 mg 12/12h; 250 mg/d >= 60 kg 200 mg 12/12h; 400 mg/d ou Crianças 1-7 meses 50-100 mg/m2/dose 12/12h Crianças 8 meses-17 anos 120-240 mg/m2/dose/d 2) cápsula de liberação retardada 20 - <25 kg 200 mg/d 25 - <60 kg 250 mg/d >= 60 kg 400 mg/d

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Dolutegravir	Inibidores da integrase	50 mg/d 50 mg 12/12h (se resistência ou risco de interação)	1) comprimidos solúveis para solução oral 3 - <6 kg 5 mg/d 6 - <10 kg 15 mg/d 10 - <14 kg 20 mg/d 14 - < 20 kg 25 mg/d >= 20 kg 30 mg/d 2) comprimidos 14 - <20 kg 40 mg/d >= 20 kg 50 mg/d; 50 mg 12/12h (se resistência ou risco de interação)
Doravirina	Inibidores da transcriptase reversa não nucleosídeos	100 mg/d	-
Efavirenz	Inibidores da transcriptase reversa não nucleosídeos	600 mg/d Em algumas fontes, se usada em combinação com tenofovir e lamivudina ou tenofovir e entricitabina: 400 mg/d	1) Crianças de 3 meses a <3 anos Metabolizadores extensivos 3 - <5 kg 200 mg/d 5 - <7 kg 300 mg/d 7 - <14 kg 400 mg/d 14 - <17 kg 500 mg/d >= 17 kg 600 mg/d Metabolizadores lentos 3 - <7 kg 50 mg/d 7 - <14 kg 100 mg/d >= 14 kg 150 mg/d Outro esquema 3,5 - < 5 kg 100 mg/d 5 - <7,5 kg 150 mg/d 7,5 - <15 kg 200 mg/d 15 - <20 kg 250 mg/d 2) crianças >3 anos e adolescentes 10 - <15 kg 200 mg/d 15 - <20 kg 250 mg/d 20 - <25 kg 300 mg/d 25 - <32,5 kg 350 mg/d 32,5 - <40 kg 400 mg/d >= 40 kg 600 mg/d Por superfície corporal 367 mg/m^2/dose/dia
Elsulfavirina	Inibidores da transcriptase reversa não nucleosídeos	Aprovado somente na Rússia	Aprovado somente na Rússia

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Elvitegravir	Inibidores da integrase	85 mg/d com ritonavir associado a atazanavir ou lopinavir 150 mg/d com ritonavir associado a darunavir ou fosamprenavir 150 mg/d com cobicistate	Criança 6-11 anos >= 25 kg 150 mg/d Criança 12-17 anos >=35 kg 150 mg/d
Entricitabina	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	cápsula 200 mg/d solução 240 mg/d	1) Criança 1 - <3 meses 3 mg/kg/dose/dia 2) Criança >= 3 meses solução oral <33 kg 6 mg/kg/dose/dia >= 33 kg 240 mg/d cápsula >= 25 kg 200 mg/d
Enfuvirtida	Inibidores de fusão	90 mg subcutâneo 2x/dia	Crianças 6-16 anos (>= 11 kg) 1) Por peso 2 mg/kg/dose 2 x/dia 2) Por faixa de peso 11 - 15,5 kg 27 mg 2x/d 15,6 - 20 kg 36 mg 2x/d 21,1 - 24,5 kg 45 mg 2x/d 24,6 - 29 kg 54 mg 2x/d 29,1 - 33,5 kg 63 mg 2x/d 33,6 - 38 kg 72 mg 2x/d 38,1 - 42,5 kg 81 mg 2x/d >= 42,6 kg 90 mg 2x/d
Estavudina	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	<60 kg 30 mg 12/12h >= 60 kg 40 mg 12/12h	< 30 kg 1 mg/kg/dose 12/12h 30 - <60 kg 30 mg 12/12h >= 60 kg 40 mg 12/12h
Etravirina	Inibidores da transcriptase reversa não nucleosídeos	200mg 2x/dia	Crianças >=2 anos (>= 10 kg) 10 - <20 kg 100 mg 12/12h 20 - < 25 kg 125 mg 12/2h 25 - <30 kg 150 mg 12/12h >= 30 kg 200 mg 12/12h
Fosamprenavir	Inibidores da protease	Com ritonavir: 700 mg 12/12h 1400 mg/d Sem ritonavir: 1400 mg 12/12h	Com ritonavir: <11 kg 45 mg/kg/dose 12/12h 11 - <15 kg 30 mg/kg/dose 12/12h 15 - <20 kg 23 mg/kg/dose 12/12h 20 - <40 kg 18 mg/kg/dose 12/12h >= 40 kg 700 mg 12/12h Sem ritonavir: >= 2 anos 30 mg/kg/dose 12/12h >= 47 kg 1400 mg 12/12h
Fostemsavir	Inibidores de fusão	600 mg 12/12h	-

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Ibalizumabe	Inibidores pós-ligação	dose inicial 2 g IV manutenção 800 mg IV a cada 14 d	-
Indinavir	Inibidores da protease	800 mg 8/8h 800 mg 12/12h com ritonavir	350 a 500 mg/m^2/dose 8/8h 400 mg/m2/dose 12/12h com ritonavir
Lamivudina	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	150 mg 12/12h 300 mg/d	1) Dose por peso (mg/kg) <3 meses 4 mg/kg/dose 12/12h >=3 meses 5 mg/kg/dose 12/12h >= 3 anos 8-10 mg/kg/dose/dia 2) Dose por faixa de peso 3 - <6 kg 30 mg 12/12h 6 - <10 kg 40 mg 12/12h 10 - <14 kg 60 mg 12/12h 14 - <20 kg 75 mg 12/12h; 150 mg/d 20 - <25 kg 75 mg/manhã e 150 mg/noite; 225 mg/d >=25 kg 150 mg 12/12h; 300 mg/d ou 14 - 21 kg 75 mg 12/12h; 150 mg/d 21 - 29 kg 75 mg/manhã e 150 mg/noite; 225 mg/d >=30 kg 150 mg 12/12h; 300 mg/d

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Lopinavir	Inibidores da protease	400 mg 12/12h 800 mg/d Se em combinação com efavirenz, nelfinavir ou nevirapina: solução 520 mg 12/12h comprimido 500 mg 12/12h	Criança >= 14 dias 1) Por peso (mg/kg) 16 mg/kg/dose 12/12h 2) Por faixa de peso <15 kg 12 mg/kg/dose 12/12h 15-40 kg 10 mg/kg/dose 12/12h >40 kg 400 mg 12/12h ou comprimido: >= 15 kg - 25 kg 200 mg 12/21h >25 - 35 kg 300 mg 12/12h >35 kg 400 mg 12/12h 3) Por superfície corporal 230 ou 300 mg/m2/dose 12/12h ≥0,6 - <0,9 m2 200 mg 12/12h ≥0,9 - <1,4 m2 300 mg 12/12h ≥1,4 m2 400 mg 12/12h ou Criança 14 dias-5 meses 3,75 mL/m^2 12/12h Criança 6 meses-17 anos 2,9 mL/m^2 12/12h Criança 2-17 anos 0,5 - 0,7 m^2 200 mg 12/12h 0,8 - 1,1 m^2 300 mg 12/12h ≥1,2 m^2 400 mg 12/12h 4) Situações especiais *Se experenciado no uso de ARV ou com diminuição da sensibilidade a lopinavir: <15 kg 13 mg/kg/dose 12/12h 15-45 kg 11 mg/kg/dose 12/12h >45 kg 400 mg 12/12h ou comprimido: >= 15 kg - 20 kg 200 mg 12/21h >20 - 30 kg 300 mg 12/12h >30 kg 400 mg 12/12h *Se em combinação com efavirenz, nelfinavir ou nevirapina: 300 mg/m2/dose 12/12h ≥0,6 - <0,8 m2 200 mg 12/12h ≥0,8 - <1,2 m2 300 mg 12/12h ≥1,2 - <1,7 m2 400 mg 12/12h ≥1,7 m2 500 mg 12/12h <15 kg 13 mg/kg/dose 12/12h 15-45 kg 11 mg/kg/dose 12/12h > 45 kg solução 520 mg 12/12h ou comprimido: >= 15 kg - 20 kg 200 mg 12/21h >20 - 30 kg 300 mg 12/12h >30 - 45 kg 400 mg 12/12h > 45 kg 500 mg 12/12h

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Maraviroc	Antagonistas de CCR5	1) com medicamentos sem interação: 300 mg 12/12h 2) com interação: 150 mg 12/12h ou 600 mg 12/12h	1) com medicamentos sem interação: 2 - <4 kg 30 mg 12/12h 4 - <6 kg 40 mg 12/12h 6 - <10 kg 100 mg 12/12h 10 - <14 kg 150 mg 12/12h 14 - <30 kg 200 mg 12/12h ≥30 kg 300 mg 12/12h 2) com interação: comprimidos 10 - <20 kg 50 mg 12/12h 20 - <30 kg 75 mg 12/12h 30 - < 40 kg 100 mg 12/12h >=40 kg 150 mg 12/12h solução oral 10 - <20 kg 50 mg 12/12h 20 - <30 kg 80 mg 12/12h 30 - < 40 kg 100 mg 12/12h >=40 kg 150 mg 12/12h
Nelfinavir	Inibidores da protease	750 mg 8/8h 1250 mg 12/12h	Crianças >= 2 anos 1) Por peso (mg/kg) 45 - 55 mg/kg/dose 12/12h 25 - 35 mg/kg/dose 8/8h 2) Por faixa de peso 10 - <13 kg 500 mg 12/12h ou 250 mg 8/8h 13 - <19 kg 750 mg 12/12h ou 500 mg 8/8h 19 - <21 kg 1000 mg 12/12h ou 500 mg 8/8h ≥21 kg 1000 - 1250 mg 12/12h ou 750 mg 8/8h
Nevirapina	Inibidores da transcriptase reversa não nucleosídeos	Inicial: 200 mg/d/14d Manutenção: 200 mg 12/12h 400 mg/d (liberação estendida)	1) Crianças <8 anos 200 mg/m2/dose/dia por 14 dias, depois de 12/12h ou 200 mg/m2/dose 12/12h 2) Crianças >= 8 anos 120 - 150 mg/m2/dose/ dia por 14 dias, depois de 12/12h 3) Crianças >=6 anos capazes de ingerir comprimido de liberação estendida 0,58 - 0,83 m2: 200 mg/d 0,84 - 1,16 m2: 300 mg/d ≥1,17 m2: 400 mg/d 4) Adolescente = adulto

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Raltegravir	Inibidores da integrase	400 mg 12/12h 1200 mg/d	1) suspensão oral Por peso 6 mg/kg/dose 12/12h Por faixa de peso 3 - <4 kg 25 mg 12/12h 4 - <6 kg 30 mg 12/12h 6 - <8 kg 40 mg 12/12h 8 - <11 kg 60 mg 12/12h 11 - <14 kg 80 mg 12/12h 14 - <20 kg 100 mg 12/12h 2) comprimidos mastigáveis Por peso 6 mg/kg/dose 12/12h 3 - <6 kg 25 mg 12/12h 6 - <10 kg 50 mg 12/12h 10 - <14 kg 75 mg 12/12h 14 - <20 kg 100 mg 12/12h 20 - <28 kg 150 mg 12/12h 28 - <40 kg 200 mg 12/12h ≥40 kg 300 mg 12/12h 3) comprimidos revestidos >= 25 kg 400 mg 12/12h >= 40 kg 400 mg 12/12h ou 1200 mg/d
Rilpivirina	Inibidores da transcriptase reversa não nucleosídeos	>= 35 kg 25 mg/d	>= 12 anos e >= 35 kg 25 mg/d
Ritonavir	Inibidores da protease	Isolado: 300 mg 12/12h, aumentado em 100 mg 12/12h a cada 2-3 dias, até 600 mg 12/12 Em associação com outro inibidor de protease: - Com atazanavir 100 mg/d - Com darunavir 100-200 mg/d - Com lopinavir 200 mg/d - Com tipranavir 400 mg/d 100 - 400 mg/d em 1-2 doses	1) Criança >1 mês 250 mg/m2/dose 12/12h, aumentado em 50 mg/m2/dose 12/12h a cada 2-3 dias até 350 mg/m2/dose 12/12h 2) Com atazanavir 15-19 kg 80-100 mg/d >= 20 kg 100 mg/d 3) Com darunavir 15-29 kg 50 mg 12/12h 30-39 kg 60 mg 12/12h >= 40 kg 100 mg 12/12h 12-17 anos com darunavir em dose única >=40 kg 100 mg/d 3) Com fosamprenavir 25-32 kg 3 mg/kg/dose 12/12h >= 33 kg 100 mg 12/12h 4) Com tipranavir Criança 2-11 anos 150 mg/m2/dose 12/12h Criança 12-17 anos 200 mg 12/12h
Saquinavir	Inibidores da protease	500 mg 12/12h/7 dias, depois 1000 mg 12/12h	Crianças >= 2 anos 5 - <40 kg 50 mg/kg/dose 12/12h >= 40 kg 1000 mg 12/12h

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (continuação)

Antirretroviral	Classe farmacológica	Adulto	Criança
Tenofovir alafenamida	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	25 mg/d com bictegravir e entricitabina; ou rilpivirina e entricitabina 10 mg/d com elvitegravir, cobicistate e entricitabina; ou darunavir, cobicistate e entricitabina	1) Criança 12-17 kg >= 35 kg 25 mg/d 2) Com bictegravir e entricitabina >= 25 kg 25 mg/d 3) Com rilpivirina e entricitabina >= 35 kg 25 mg/d 4) Com elvitegravir, cobicistate e entricitabina >= 25 kg 10 mg/d 5) Com darunavir, cobicistate e entricitabina >= 40 kg 10 mg/d
Fumarato de tenofovir desoproxila	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	245 mg/d ou 300 mg/d	Crianças >= 2 anos 1) Por peso (mg/kg) >= 10kg 8 mg/kg/dose/d ou 6,5 mg/Kg/d 2) Pó oral 10 - <12 kg 80 mg/d 12 - <14 kg 100 mg/d 14 - <17 kg 120 mg/d 17 - <19 kg 140 mg/d 19 - <22 kg 160 mg/d 22 - <24 kg 180 mg/d 24 - <27 kg 200 mg/d 27 - <29 kg 220 mg/d 29 - <32 kg 240 mg/d 32 - <34 kg 260 mg/d 34 - <35 kg 280 mg/d ≥35 kg 300 mg/d 3) comprimido 17 - <22 kg 123 ou 150 mg/d 22 - <28 kg: 163 ou 200 mg/d 28 - <35 kg: 204 ou 250 mg/d ≥35 kg: 245 ou 300 mg/d
Tipranavir	Inibidores da protease	500 mg 12/12h (usado em associação com ritonavir 200 mg 12/12h)	Crianças >= 2 anos Por peso 14 mg/kg/dose 12/12h Por superfície corporal 375 mg/m^2/dose 12/12h Com ritonavir: 6 mg/kg/dose 12/12h

Quadro 2 – Antirretrovirais incluídos nessa revisão com as respectivas classes e doses (conclusão)

Antirretroviral	Classe farmacológica	Adulto	Criança
Zidovudina	Inibidores da transcriptase reversa nucleosídeos e nucleotídeos	250-300 mg 12/12h	1) Por peso (mg/kg) <9 kg 12 mg/kg/dose 12/12h; 8 mg/kg/dose 8/8h 9 - <30 kg 9 mg/kg/dose 12/12h; 6 mg/kg/dose 8/8h ≥30 kg 300 mg 12/12h; 200 mg 8/8h 2) Por faixa de peso 8-13 kg 100 mg 12/12h 14-20 kg 100 mg/manhã e 200 mg/noite 21-27 kg 200 mg 12/12h 28-29 kg 200-250 mg 12/12h >= 30 kg 250-300 mg 12/12h 3) Por superfície corporal 160 ou 180 ou 240 mg/m^2/dose 12/12h

Fonte: Elaboração própria

5 RESULTADOS

5.1 Seleção dos estudos

As buscas, realizadas até 30 de maio de 2021, encontraram 35.772 estudos. Com a retirada de 14.534 duplicatas, restaram 21.238 artigos. Excluímos 19.190 na seleção por título e resumo, permanecendo 2.048 estudos, que tiveram o texto completo analisado de acordo com os critérios de elegibilidade, sendo excluídos 2.037. Os motivos de exclusão dos estudos estão descritos na Figura 1, elaborada de acordo com o PRISMA (HADDAWAY; MCGUINNESS; PRITCHARD, 2021), e a lista dos estudos excluídos no APÊNDICE D.

Incluímos 12 publicações para extração dos resultados. Os estudos de Campbell *et al.* e Firnhaber *et al.* (CAMPBELL *et al*., 2012; FIRNHABER *et al*., 2015) continham os mesmos participantes e estavam vinculados a um mesmo protocolo, sendo agrupados sob um único número de identificação. Isso foi similar com os estudos de Eron *et al.* e Rashbaum *et al.* (ERON *et al*., 2018; RASHBAUM *et al*., 2019). Outros dois estudos (LOCKMAN *et al*., 2010, 2012), apesar de terem um protocolo em comum, avaliaram diferentes participantes, sendo considerados em separado. Portanto, tivemos 10 estudos incluídos para análise dos resultados.

5.2 Características dos estudos

As características gerais dos estudos incluídos estão descritas no Quadro 3 e dos braços de cada estudo utilizado nessa revisão no Quadro 4. Em geral, eles foram multicêntricos. Só dois ocorreram em um país único, um na África do Sul (NAICKER *et al*., 2017) e outro na Inglaterra (IBRAHIM *et al*., 2020).

5.2.1 Participantes

Os 10 estudos tiveram 4.716 pessoas randomizadas, das quais 4.693 receberam pelo menos uma dose do tratamento. Sete estudos incluíram apenas mulheres (IBRAHIM *et al*., 2020; KITYO *et al*., 2019; LOCKMAN *et al*., 2010, 2012; NAICKER *et al*., 2017; ORRELL *et al*., 2017; SQUIRES *et al*., 2016). Nos outros três (FIRNHABER *et al*., 2015; HUHN *et al*., 2019; RASHBAUM *et al*., 2019), o percentual de participação delas variou de 11% a 46%. Essa revisão incluiu um total de 2.871 mulheres que tomaram pelo menos uma dose da TARV, com faixa etária mediana entre 28 (IQR 25-33 em um braço e 26-30 em outro) e 46 (mínimo 19,

máximo 75) anos em cinco estudos (HUHN *et al*., 2019; KITYO *et al*., 2019; NAICKER *et al*., 2017; RASHBAUM *et al*., 2019; SQUIRES *et al*., 2016) e média de idade entre 30 (DP 5) e 50,9 (DP 7) anos nos outros cinco (FIRNHABER *et al*., 2015; IBRAHIM *et al*., 2020; LOCKMAN *et al*., 2010, 2012; ORRELL *et al*., 2017). Elas eram virgens de tratamento em sete dos estudos (FIRNHABER *et al*., 2015; LOCKMAN *et al*., 2010, 2012; NAICKER *et al*., 2017; ORRELL *et al*., 2017; RASHBAUM *et al*., 2019; SQUIRES *et al*., 2016), enquanto nos outros três (HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019), já tinham utilizado outros esquemas ARV previamente. A mediana do nível de CD4 variou de 335 (IQR 280-411) a 667 (IQR 532-852) células/mm^3 em sete estudos (HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019; NAICKER *et al*., 2017; ORRELL *et al*., 2017; RASHBAUM *et al*., 2019; SQUIRES *et al*., 2016) e a média de 125 (DP 71) a 385 (DP 210,2) células/mm^3 em quatro estudos (FIRNHABER *et al*., 2015; LOCKMAN *et al*., 2010, 2012; SQUIRES *et al*., 2016). Squires *et al.* (2016) reportou o nível de CD4 em média e mediana. Em seis estudos (FIRNHABER *et al*., 2015; KITYO *et al*., 2019; LOCKMAN *et al*., 2010, 2012; ORRELL *et al*., 2017; SQUIRES *et al*., 2016) havia pessoas com tuberculose, hepatites B e C, o que não excedeu 9% dos participantes em cada braço.

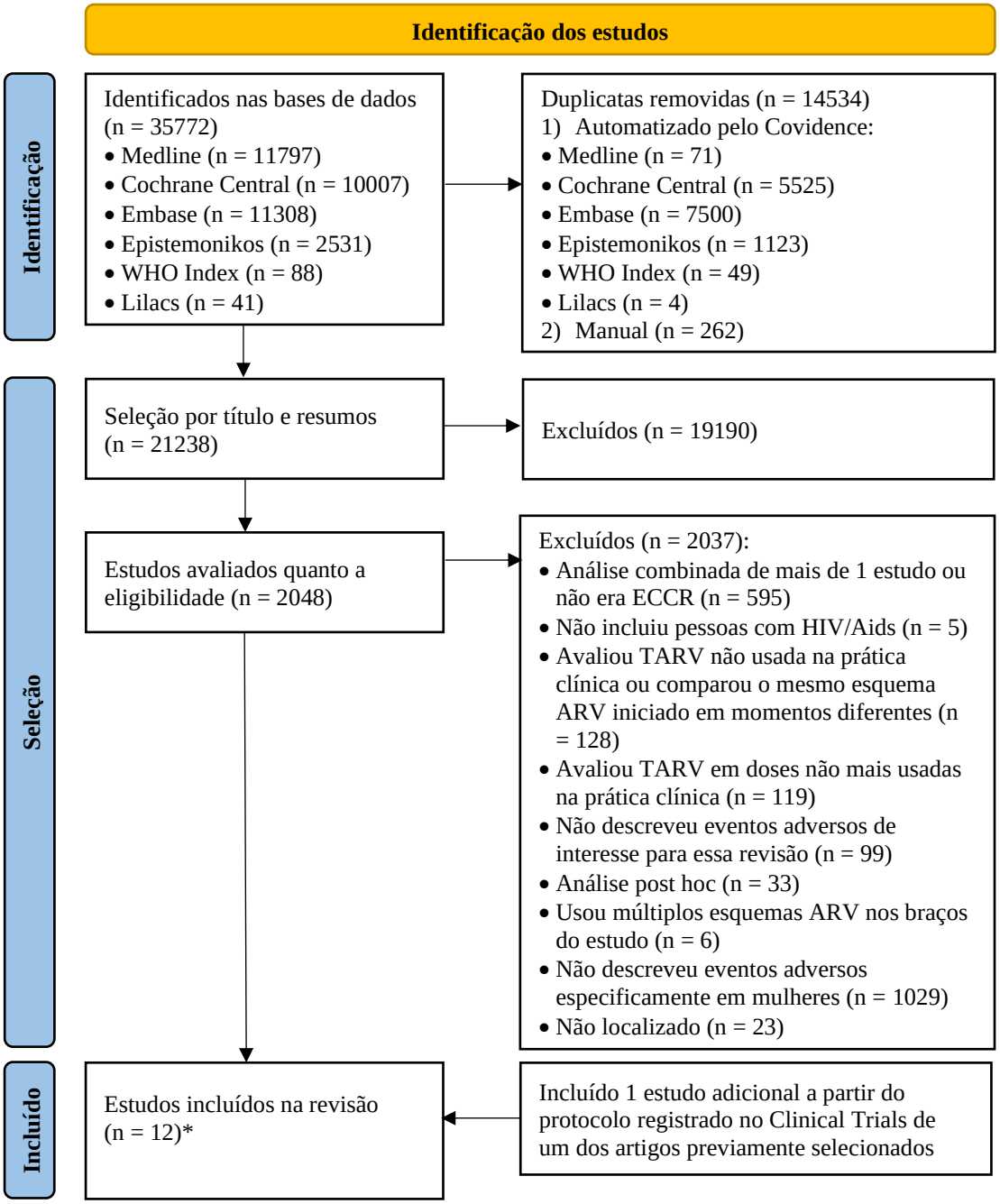
5.2.2 Intervenções e comparadores

Três (HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019) dos 10 estudos contribuíram com informações sobre eventos adversos em mulheres em apenas um braço, totalizando 17 braços, com 11 esquemas antirretrovirais diferentes (Quadro 4).

O estudo de Naicker *et al.* (2017) descreveu que zidovudina foi utilizada de 12 em 12 horas, sem especificar a dose, nem no estudo publicado, nem no protocolo. Como a dose usual desse fármaco, quando usado em conjunto com efavirenz e lamivudina, costuma ser de 300 mg de 12 em 12 horas, assumimos que essa deve ter sido adotada.

O esquema mais avaliado foi atazanavir 300 /dia + ritonavir 100 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia, em dois estudos (ORRELL *et al*., 2017; SQUIRES *et al*., 2016), que incluíram 533 mulheres que receberam pelo menos uma dose desse tratamento. Os menos avaliados foram darunavir/cobicistate 800/150 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia, no braço de um estudo com 41 mulheres (RASHBAUM *et al*., 2019), e efavirenz 600 mg/dia + fumarato de tenofovir desoproxila 300 mg/dia + lamivudina 300 mg/dia, em apenas 29 mulheres (NAICKER *et al*., 2017).

Figura 1 – Fluxograma de seleção dos estudos segundo o PRISMA



*Apesar de serem incluídos individualmente 12 artigos, eles foram avaliados como 10 estudos, pois dois pares pertenciam a um mesmo protocolo, contribuindo com dados sobre os mesmos participantes. ECCR = ensaio clínico controlado randomizado; TARV = terapia antirretroviral; WHO = OMS (Organização Mundial da Saúde)

Fonte: Elaboração própria, adaptado de HADDAWAY; MCGUINNESS; PRITCHARD, 2021

Quadro 3 – Características gerais dos estudos (continua)

Autor, ano	Protocolo	Financiamento	Locais do estudo	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento	Duração do tratamento (em semanas)	Exposição prévia a TARV	Outras intervenções além da TARV e de medidas contraceptivas	Cegamento	Sigilo de alocação
Squires, 2016	NCT01705574	Gilead Sciences	80 serviços hospitalares, ambulatoriais e universitários na Bélgica, República Dominicana, França, Itália, México, Portugal, Porto Rico, Rússia, Tailândia, Uganda, Reino Unido e Estados Unidos	583	575	48	Não	Nenhuma	Duplo-cego	Não descrito
Firnhaber, 2015	NCT00084136	National Institute of Allergy and Infectious Diseases, National Institutes of Health, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Glaxo SmithKline	46 clínicas, universidades, centros de pesquisa e hospitais no Brasil, Haiti, Índia, Malavi, Peru, África do Sul, Tailândia, Zimbábue e Estados Unidos	1045	1042	184	Não	Permitiu mudança do esquema ARV em caso de falência virológica ou eventos adversos graves	Aberto	Não há

Quadro 3 – Características gerais dos estudos (continuação)

Autor, ano	Protocolo	Financiamento	Locais do estudo	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento	Duração do tratamento (em semanas)	Exposição prévia a TARV	Outras intervenções além da TARV e de medidas contraceptivas	Cegamento	Sigilo de alocação
Orrell, 2017	NCT01910402	ViiV Healthcare	86 hospitais, universidades e clínicas na África do Sul, Espanha, Rússia, Argentina, Tailândia, Itália, Reino Unido, França, México, Portugal, Canadá, Estados Unidos e Porto Rico	499	495	48	Não	Nenhuma	Aberto	Não há
Lockman, 2010	NCT00089505	National Institute of Allergy and Infectious Diseases, Abbott, Boehringer Ingelheim, Gilead, Bristol-Myers Squibb, Glaxo SmithKline	hospitais, universidades e centros de pesquisa na África do Sul, Quênia, Zimbábue, Botsuana, Zâmbia, Malavi e Uganda	243	241	153	Não	Permitiu mudança no esquema ARV em caso de intolerância ou ausência de resposta clínica	Aberto	Não há

Quadro 3 – Características gerais dos estudos (continuação)

Autor, ano	Protocolo	Financiamento	Locais do estudo	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento	Duração do tratamento (em semanas)	Exposição prévia a TARV	Outras intervenções além da TARV e de medidas contraceptivas	Cegamento	Sigilo de alocação
Lockman, 2012	NCT00089505	National Institute of Allergy and Infectious Diseases, Abbott, Boehringer Ingelheim, Gilead, Bristol-Myers Squibb, Glaxo SmithKline	hospitais, universidades e centros de pesquisa na África do Sul, Quênia, Zimbábue, Botsuana, Zâmbia, Malavi e Uganda	502	500	168	Não	Permitiu mudança no esquema ARV em caso de intolerância ou ausência de resposta clínica	Aberto	Não há
Rashbaum, 2019	NCT02431247	Janssen	121 locais em 10 países: Estados Unidos, Canadá, Bélgica, França, Alemanha, Itália, Polônia, Rússia, Espanha e Reino Unido	725	725	48	Não	Nenhuma	Duplo-cego	Não descrito
Kityo, 2019	NCT02652624	Gilead Sciences	58 ambulatórios na República Dominicana, Porto Rico, Rússia, Tailândia, Uganda e Estados Unidos	235	234	48	Sim	Não relatado	Aberto	Não há

Quadro 3 – Características gerais dos estudos (continuação)

Autor, ano	Protocolo	Financiamento	Locais do estudo	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento	Duração do tratamento (em semanas)	Exposição prévia a TARV	Outras intervenções além da TARV e de medidas contraceptivas	Cegamento	Sigilo de alocação
Naicker, 2017	NCT01387022	National Institute of Allergy and Infectious Disease (NIAID), National Institutes of Health (NIH), US Department of Health and Human Services (DHHS) e South African Department of Science and Technology	2 cidades de uma província da África do Sul	59	59	156	Não	Outro NRTI foi usado quando havia contraindicação a zidovudina	Aberto	Não há
Huhn, 2019	NCT02269917	Janssen	106 hospitais e clínicas no Canadá, Estados Unidos, Bélgica, França, Polônia, Espanha, Suécia, Suíça e Reino Unido	766	763	48	Sim	Nenhuma	Aberto	Não há

Quadro 3 – Características gerais dos estudos (conclusão)

Autor, ano	Protocolo	Financiamento	Locais do estudo	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento	Duração do tratamento (em semanas)	Exposição prévia a TARV	Outras intervenções além da TARV e de medidas contraceptivas	Cegamento	Sigilo de alocação
Ibrahim, 2020	EudraCT 2015-005297-37	ViiV Healthcare	9 clínicas de HIV em Londres e Brighton, no Reino Unido	59	59	96	Sim	Não relatado	Aberto	Não há

TARV = terapia antirretroviral; ARV = antirretroviral; NRTI = Inibidores da transcriptase reversa nucleosídeos e nucleotídeos
Fonte: Elaboração própria

Quadro 4 – Características dos braços dos estudos (continua)

Autor, ano	Intervenção	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento (Nº de perdas)	Nº de mulheres (%)	Faixa etária	Nível de CD4	Comorbidades
Squires, 2016	elvitegravir/cobicistate/ entricitabina/fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	293	289 (29)	289 (100)	mediana (IQR) 34 (28–43)	mediana (IQR) 344 (246–466) média (SD) 376 (199,6)	HBsAg positivo 9 (4%); anti-HCV positivo 22 (8%); história de IST 76 (26%); história de ansiedade/depressão 51 (18%)
	atazanavir 300 mg/dia + ritonavir 100 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	290	286 (45)	286 (100)	mediana (IQR) 35 (29–42)	mediana (IQR) 370 (244–489) média (SD) 385 (210,2)	HBsAg positivo 7 (3%); anti-HCV positivo 25 (9%); história de IST 80 (28%); história de ansiedade/depressão 60 (21%)
Firnhaber, 2015	efavirenz 600 mg/dia + lamivudina/zidovudina 150/300 mg 12/12h	519	517 (NR)	241 (46)	média (SD) 35 (9)	média (SD) 163 (85)	Tuberculose pulmonar 28, tuberculose extra pulmonar 10, hepatite C crônica 12, hepatite B crônica 3, qualquer infecção 153
	efavirenz 600 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	526	525 (NR)	242 (46)	média (SD) 35 (9)	média (SD) 155 (81)	Tuberculose pulmonar 25, tuberculose extra pulmonar 7, hepatite C crônica 7, hepatite B crônica 4, qualquer infecção 144

Quadro 4 – Características dos braços dos estudos (continuação)

Autor, ano	Intervenção	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento (Nº de perdas)	Nº de mulheres (%)	Faixa etária	Nível de CD4	Comorbidades
Orrell, 2017	dolutegravir/abacavir/ lamivudina 50/600/300 mg/dia	250	248 (42)	248 (100)	média (SD) 38,1 (11,15)	Mediana* 340 (197–4 97,5)	Hepatite C 16 (6%)
	atazanavir 300 mg/dia + ritonavir 100 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	249	247 (55)	247 (100)	média (SD) 37,8 (10,14)	Mediana* 350 (241–487)	Hepatite C 21 (9%)
Lockman, 2010	nevirapina 200 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	123	121 (9)	121 (100)	média (SD) 30 (5)	média (SD) 136 (60)	HBsAg positivo 9 (8%)
	lopinavir/ritonavir 400/100 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	120	120 (2)	120 (100)	média (SD) 31 (5)	média (SD) 135 (61)	HBsAg positivo 18 (7%)

*O estudo não especificou se os valores entre parênteses representavam a variação de mínimo e máximo ou o intervalo interquartil

Quadro 4 – Características dos braços dos estudos (continuação)

Autor, ano	Intervenção	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento (Nº de perdas)	Nº de mulheres (%)	Faixa etária	Nível de CD4	Comorbidades
Lockman, 2012	nevirapina 200 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	251	249 (21)	249 (100)	média (SD) 35 (7)	média (SD) 126 (68)	HBsAg positivo 18 (7%)
	lopinavir/ritonavir 400/100 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	251	251 (21)	251 (100)	média (SD) 35 (8)	média (SD) 125 (71)	HBsAg positivo 17 (7%)
Rashbaum, 2019	darunavir/cobicistate/ entricitabina/tenofovir alafenamida 800/150/200/10 mg/dia	362	362 (NR)	44 (12)	mediana (IQR) 34 (27–42)	mediana (IQR) 461,5 (342–617)	Não relatado
	darunavir/cobicistate 800/150 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia	363	363 (NR)	41 (11)	mediana (IQR) 34 (27–42)	mediana (IQR) 440 (325–594)	Não relatado
Kityo, 2019	bictegravir/entricitabina/ tenofovir alafenamida 50/200/25 mg/dia	235	234 (3)	234 (100)	mediana (mín-máx) 39 (21 – 63)	mediana (IQR) 667 (532 – 852)	Coinfecção com hepatite B/ hepatite C 2 (5%)

Quadro 4 – Características dos braços dos estudos (conclusão)

Autor, ano	Intervenção	Nº total de participantes	Nº que recebeu pelo menos uma dose do tratamento (Nº de perdas)	Nº de mulheres (%)	Faixa etária	Nível de CD4	Comorbidades
Naicker, 2017	efavirenz 600 mg/dia + fumarato de tenofovir desoproxila 300 mg/dia + lamivudina 300 mg/dia	29	29 (1)	29 (100)	mediana (IQR) 28 (25-33)	mediana (IQR) 345 (289-431)	Não relatado
	efavirenz 600 mg/dia + zidovudina 12/12h + lamivudina 300 mg/dia	30	30 (4)	30 (100)	mediana (IQR) 28 (26-30)	mediana (IQR) 335 (280-411)	Não relatado
Huhn, 2019	darunavir/cobicistate/ entricitabina/tenofovir alafenamida 800/150/200/10 mg/dia	766	763 (NR)	140 (18)	mediana (mín-máx) 46 (19–75)	mediana 630 IQR 468–806 mín-máx 111–1921	Não relatado
Ibrahim, 2020	dolutegravir/abacavir/ lamivudina 50/600/300 mg/dia	59	59 (8)	59 (100)	média (SD) 50,9 (7)	mediana (IQR) 612 (454-807)	Diabetes 3 (5,1%), hipertensão 13 (22%), tabagismo 4 (9,8%)

NR = não reportado; IQR = intervalo interquartil; SD = desvio padrão; HBsAg = antígeno de superfície da hepatite B; HCV = vírus da hepatite C
Fonte: Elaboração própria

5.3 Avaliação do risco de viés dos estudos

A maioria dos estudos (80%) não teve cegamento (FIRNHABER *et al*., 2015; HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019; LOCKMAN *et al*., 2010, 2012; NAICKER *et al*., 2017; ORRELL *et al*., 2017). Somente dois foram duplo-cegos (RASHBAUM *et al*., 2019; SQUIRES *et al*., 2016), mas embora tenham realizado a randomização de forma adequada e centralizada, com sequência gerada por computador, não descreveram como se deu o sigilo de alocação. Quatro estudos tiveram uma quantidade de perdas de seguimento que poderiam interferir nos seus resultados, três (FIRNHABER *et al*., 2015; HUHN *et al*., 2019; SQUIRES *et al*., 2016) avaliados com alto risco viés nesse domínio e um (ORRELL *et al*., 2017) com alguma preocupação de viés.

Apenas um estudo contou com financiamento exclusivo de órgãos governamentais (NAICKER *et al*., 2017). Dos demais, seis (HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019; ORRELL *et al*., 2017; RASHBAUM *et al*., 2019; SQUIRES *et al*., 2016) eram da indústria farmacêutica e três (FIRNHABER *et al*., 2015; LOCKMAN *et al*., 2010, 2012) tiveram financiamento misto (órgãos governamentais e indústria). Em um destes três, a indústria contribuiu apenas com o fornecimento dos medicamentos (FIRNHABER *et al*., 2015). Nos outros dois, além de fornecer os fármacos, em um deles a indústria participou do grupo do estudo, mas não da análise dos dados (LOCKMAN *et al*., 2010), e no outro contribuiu com o protocolo e com sugestões sobre o manuscrito (acatadas a critérios dos autores), mas não com a sua escrita, a análise dos dados e a decisão de publicar (LOCKMAN *et al*., 2012).

Realizamos a avaliação de qualidade por protocolo, visto que a maioria dos estudos apresentou os dados e os resultados para população que recebeu pelo menos uma dose do tratamento e não para o total das pessoas randomizadas. Também porque a avaliação de eventos adversos normalmente inclui os participantes que foram expostos à intervenção (no caso, aqueles que tomaram alguma dose do medicamento).

Consideramos preferencialmente o desfecho primário de descontinuação da TARV por qualquer evento adverso, independentemente de sua relação com o tratamento, uma vez que era um dos desfechos primários previstos no nosso protocolo e foi avaliado por nove dos estudos (HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019; LOCKMAN *et al*., 2010, 2012; NAICKER *et al*., 2017; ORRELL *et al*., 2017; RASHBAUM *et al*., 2019; SQUIRES *et al*., 2016). Apenas metade (HUHN *et al*., 2019; KITYO *et al*., 2019; LOCKMAN *et al*., 2012; NAICKER *et al*., 2017; RASHBAUM *et al*., 2019) relatou a descontinuação por eventos adversos causados especificamente pela TARV, o que não permitiu o uso desse dado na

avaliação de viés. Também cogitamos o impacto da ausência de cegamento da maior parte dos estudos nos nossos outros desfechos primários: número total de qualquer evento adverso e número total de eventos adversos relacionados ao tratamento. Apenas no estudo de Firnhaber *et al.* (2015) a referência para análise foi o número total de qualquer evento adverso laboratorial, uma vez que ele só contribuiu para essa revisão com informações sobre esse desfecho.

Nove estudos (FIRNHABER *et al*., 2015; HUHN *et al*., 2019; IBRAHIM *et al*., 2020; KITYO *et al*., 2019; LOCKMAN *et al*., 2010, 2012; NAICKER *et al*., 2017; ORRELL *et al*., 2017; SQUIRES *et al*., 2016) tiveram alto risco de viés pela ferramenta RoB2 da Cochrane (COCHRANE, 2019), enquanto apenas um (RASHBAUM *et al*., 2019) apresentou alguma preocupação com risco de viés, conforme pode ser visto na Figura 2.

5.3.1 Avalição do viés de publicação

O viés de publicação se aplica a estudos comparativos, que utilizam medidas de efeito como risco relativo, razão de chances e diferença de média. Nosso estudo estimou a taxa de incidência média dos eventos por 1000 pessoas-ano, considerando como unidade de análise os braços dos estudos. Além disso, dada a escassez de dados encontrados sobre a ocorrência de eventos adversos em mulheres, os diferentes esquemas ARV se repetiram pouco nos estudos incluídos nessa revisão. Um mesmo esquema foi identificado em no máximo dois braços. Apesar disso, apresentamos os gráficos de funil (*funnel plots)*, utilizando como estimativa sumária a taxa de incidência para os desfechos em que houveram pelo menos 10 braços avaliados com a ocorrência de no mínimo um evento, embora eles representem diferentes esquemas ARV (APÊNDICE E, Figuras 3 e 4). Os gráficos foram obtidos por meio do programa Stata (versão 16, StataCorp,Texas, EUA).

Embora os desfechos de morte por todas as causas e morte por eventos adversos relacionados a TARV tenham sido ambos avaliados em 15 braços, na maioria deles não houve nenhum evento. Portanto, os gráficos referentes a estes desfechos acabam demonstrando a taxa de incidência relativa a menos de 10 braços, pois só aparecem aqueles em que ocorreu algum evento.

Figura 2 – Avaliação do risco de viés pela ferramenta RoB2 da Cochrane

Estudo, ano	Desfecho	D1	D2	D3	D4	D5	Geral
Squires, 2016	Descontinuação da TARV por EA	+	-	-	+	!	-
Firnhaber, 2015	EA laboratoriais	-	-	-	!	+	-
Orrell, 2017	Descontinuação da TARV por EA	-	+	!	+	!	-
Lockman, 2010	Descontinuação da TARV por EA	-	+	+	+	!	-
Lockman, 2012	Descontinuação da TARV por EA	-	+	+	+	!	-
Rashbaum, 2019	Descontinuação da TARV por EA	+	+	+	+	!	!
Kityo, 2019	Descontinuação da TARV por EA	-	+	+	+	!	-
Naicker, 2017	Descontinuação da TARV por EA	-	+	+	+	!	-
Huhn, 2019	Descontinuação da TARV por EA	-	+	-	+	+	-
Ibrahim, 2020	Descontinuação da TARV por EA	-	+	+	+	!	-

\+ Baixo risco

! Alguma preocupação

\- Alto risco

D1 Processo de randomização

D2 Desvios da intervenção pretendida

D3 Dados de desfecho perdidos

D4 Medição dos desfechos

D5 Seleção no reporte dos resultados

Fonte: Elaboração própria, adaptado de COCHRANE, 2019

5.4 Eventos adversos da TARV em mulheres

Os eventos adversos reportados pelos estudos estão descritos na Tabela 1, cuja apresentação dos resultados está agrupada por desfecho, e na Tabela 2 (APÊNDICE F), que foi organizada por esquema ARV. Os eventos cuja incidência foi zero em todos os estudos que os avaliaram não foram incluídos nas tabelas, mas foram descritos no texto.

5.4.1 Eventos adversos do sistema reprodutor feminino

Nenhum dos estudos avaliou eventos adversos no sistema reprodutor feminino de mulheres com HIV/Aids em tratamento ARV. A ocorrência total ou relacionada a TARV de atraso na puberdade, amenorreia, irregularidade menstrual, menopausa precoce, fogachos totais e fogachos graves (ou severos), moderados e leves, não pode ser determinada por meio de ensaios clínicos controlados e randomizados.

5.4.2 Osteopenia, osteoporose e fraturas por osteoporose

Os estudos avaliaram a saúde óssea mais com base no desfecho substituto de variação da densidade mineral óssea, e não como desfechos que importam para as pessoas, como osteopenia, osteoporose e fraturas relacionadas. Apenas um estudo (IBRAHIM *et al*., 2020) analisou a ocorrência de osteoporose, cuja taxa de incidência foi de 6,15 eventos por 1000 pessoas-ano com o esquema dolutegravir/abacavir/lamivudina 50/600/300 mg/dia. No entanto, tal resultado é pouco preciso, pois tem probabilidade de 95% de se situar entre 0,01 e 4037,00 eventos por 1000 pessoas-ano (intervalo de credibilidade – ICr).

Não houve dados sobre osteopenia e somente dois estudos (HUHN *et al*., 2019; RASHBAUM *et al*., 2019), que abrangeram dois esquemas antirretrovirais (darunavir/cobicistate/entricitabina/tenofovir alafenamida 800/150/200/10 mg/dia e darunavir/cobicistate 800/150 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia) reportaram que não ocorreram fraturas por osteoporose.

5.4.3 Descontinuação por eventos adversos

A taxa de incidência de descontinuação do tratamento por qualquer evento adverso variou de zero a 126,40 eventos por 1000 pessoas-ano entre as diferentes TARV. Os esquemas

bictegravir/entricitabina/tenofovir alafenamida 50/200/25 mg/dia e efavirenz 600 mg/dia + fumarato de tenofovir desoproxila 300 mg/dia + lamivudina 300 mg/dia não tiveram descontinuação, mas ambos foram avaliados em estudos únicos (KITYO *et al*., 2019; NAICKER *et al*., 2017) e o segundo esquema foi usado por apenas 29 mulheres (NAICKER *et al*., 2017). Darunavir/cobicistate 800/150 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia, em um estudo (RASHBAUM *et al*., 2019), n=41, e efavirenz 600 mg/dia + lamivudina/zidovudina 150/300 mg 12/12 horas, em um estudo (NAICKER *et al*., 2017), n=30, apresentaram, respectivamente, 121,30 (ICr 95% 0,21-67219,50) e 126,40 (ICr 95% 0,23-69389,00) descontinuações por 1000 pessoas-ano. Porém, ambos foram utilizados por poucas mulheres e o intervalo de credibilidade foi muito amplo.

A análise combinada de todos as TARV mostrou uma taxa de incidência média de descontinuação do tratamento de 20,78 eventos por 1000 pessoas-ano (ICr 95% 5,58-57,31; APÊNDICE G, Figura 5). No entanto, houve heterogeneidade estatística clinicamente relevante. O efeito verdadeiro em 95% das vezes, caso se estudasse um novo grupo de tratamento, poderia variar de 0,25 a 1270,00 descontinuações por 1000 pessoas-ano.

A descontinuação por eventos adversos relacionados a TARV foi reportada por metade dos estudos (HUHN *et al*., 2019; KITYO *et al*., 2019; LOCKMAN *et al*., 2012; NAICKER *et al*., 2017; RASHBAUM *et al*., 2019) e a taxa de incidência variou de zero a 121,30 eventos por 1000 pessoas-ano. Todos os tratamentos agregados tiveram uma média de descontinuação relacionada a TARV de 4,31 por 1000 pessoas-ano (ICr 95% 0,13-54,72; APÊNDICE G, Figura 6). Porém, a probabilidade de 95% desse resultado em novos estudos seria de zero a 5103,95.

5.4.4 Total de eventos adversos

O desfecho de qualquer evento adverso clínico e/ou laboratorial apresentou uma taxa de incidência média de 888,20 eventos por 1000 pessoas-ano (ICr 95% 759,90-1045,00) para todos os tratamentos combinados (APÊNDICE G, Figura 7). Nas análises para cada esquema ARV em separado, o resultado variou de 718,40 com bictegravir/entricitabina/tenofovir alafenamida 50/200/25 mg/dia a 972,10 com atazanavir 300 mg/dia + ritonavir 100 mg/dia + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia, mas os intervalos de credibilidade em geral foram muito amplos, conforme apresentado na Tabela 1. A ocorrência de qualquer evento adverso laboratorial foi avaliada por um único estudo (FIRNHABER *et al*., 2015), que contribuiu para essa revisão somente com esse desfecho. Nenhum artigo reportou a incidência de qualquer evento adverso clínico.

Os braços dos estudos agrupados mostraram uma taxa de incidência média de eventos adversos clínicos e/ou laboratoriais relacionados a TARV de 341,60 eventos por 1000 pessoas-ano (ICr 95% 133,60-862,70). Isoladamente, os esquemas ARV tiveram uma variação nesse desfecho de 91,31 a 594,80, mas também com intervalos de credibilidade muito amplos (Tabela 1). Os eventos adversos clínicos relacionados a TARV foram relatados apenas pelo estudo de Squires *et al.* (2016) e nenhum descreveu os laboratoriais separadamente.

5.4.5 Eventos adversos graves (graus 3 e/ou 4) e sérios

Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 foram avaliados em apenas 284 mulheres, que utilizaram quatro esquemas ARV diferentes contendo efavirenz ou darunavir/cobicistate associados com dois NRTI. A taxa de incidência para esse desfecho variou de 77,39 a 137,80 eventos por 1000 pessoas-ano, mas com amplos intervalos de credibilidade (Tabela 1). A análise agrupada dessas TARV mostrou 96,34 eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 por 1000 pessoas-ano (ICr 95% 55,04-158,90).

A taxa de incidência de eventos adversos clínicos graus 3 e/ou 4 foi analisada para quatro esquemas ARV distintos, com uma variação de 45,40 a 117,60 eventos por 1000 pessoas-ano, e a média do resultado agrupado para essas TARV foi de 59,93 (ICr 95% 33,74-104,60). Já os eventos adversos graves laboratoriais graus 3 e/ou 4 variaram de 71,04 a 703,70 em cinco esquemas diferentes, com uma análise agregada de 145,10 eventos por 1000 pessoas-ano (ICr 95% 57,71-359,90).

Eventos graves clínicos e/ou laboratoriais grau 3 e eventos adversos graves clínicos e/ou laboratoriais grau 4 foram avaliados por somente um estudo (ORRELL *et al*., 2017), com uma taxa de incidência média na análise agrupada dos dois braços de, respectivamente, 125,50 (ICr 95% 3,51-4295,00) e 25,05 (ICr 95% 0,50-1017,00). O mesmo ocorreu com os eventos adversos clínicos grau 4, avaliados pelo estudo de Lockman *et al*. (2012), com um resultado agregado dos dois esquemas ARV avaliados de 9,31 (ICr 95% 0,39-216,30).

Houve relato de resultado sobre a ocorrência de eventos adversos sérios clínicos e/ou laboratoriais para nove dos 11 esquemas ARV incluídos nessa revisão. A taxa de incidência média agrupada de todos os tratamentos foi de 49,34 eventos por 1000 pessoas-ano (ICr 95% 31,60-77,10). A probabilidade de 95% do valor verdadeiro desse resultado em novos estudos seria de 10,82 a 226,20. Ao observar as TARV separadamente, a taxa de incidência de eventos variou de 20,74 (ICr 95% 0,78-491,70) com lopinavir/ritonavir 400/100 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia (n=371) a 126,40 por 1000

pessoas-ano (ICr 95% 0,23-69389,00) com efavirenz 600 mg/dia + lamivudina/zidovudina 150/300 mg 12/12h (n=30).

Os demais eventos adversos graves e sérios descritos nos métodos não tiveram dados reportados em nenhum dos estudos incluídos. Para eventos dessa natureza descritos pelos estudos como relacionados a TARV, quatro desfechos foram contemplados: 1) eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4; 2) eventos adversos sérios clínicos e/ou laboratoriais; 3) eventos adversos sérios clínicos; 4) eventos adversos sérios laboratoriais.

Os eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 relacionados a TARV foram avaliados em dois estudos, com 225 mulheres, que utilizaram dois esquemas ARV contendo darunavir/cobicistate + entricitabina associado com tenofovir alafenamida ou fumarato de tenofovir desoproxila. A taxa de incidência média agrupada para esses tratamentos foi de 22,75 eventos por 1000 pessoas-ano (ICr 95% 2,56-272,90).

A taxa de incidência de eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV variou de nenhum evento com três esquemas de tratamento a 68,36 por 1000 pessoas-ano. No entanto, para os dois esquemas em que foi reportado algum evento, o intervalo de credibilidade foi bastante amplo, conforme Tabela 1.

Os eventos adversos sérios clínicos relacionados a TARV foram ausentes com três tratamentos, enquanto outros dois apresentaram 10,21 e 18,85 por 1000 pessoas-ano, também com amplo intervalo de credibilidade (Tabela 1). Três esquemas ARV (dolutegravir/ abacavir/ lamivudina 50/600/300 mg/dia; darunavir/ cobicistate/ entricitabina/ tenofovir alafenamida 800/150/200/10 mg/dia; bictegravir/ entricitabina/ tenofovir alafenamida 50/200/25 mg/dia) foram avaliados quanto aos eventos adversos sérios laboratoriais relacionados a TARV, com nenhum evento registrado.

5.4.6 Morte

A morte por todas as causas foi avaliada em 2388 mulheres para dez esquemas ARV diferentes. A taxa de incidência média agrupada para todos esses tratamentos foi de 4,47 eventos por 1000 pessoas-ano (ICr 95% 1,42-7,91; APÊNDICE G, Figura 8). O valor verdadeiro para esse desfecho teria probabilidade de 95% de se situar entre 0,45 e 20,09 em novos estudos. Quatro das dez TARV não tiveram nenhuma morte nos seus grupos de tratamento, conforme a Tabela 1.

Oito desses dez esquemas ARV não tiveram mortes por eventos adversos relacionados a TARV, sendo que a taxa de incidência média combinada foi de 0,2 eventos por 1000 pessoas-

ano (ICr 95% 0,00-1,60; APÊNDICE G, Figura 9). Os dois tratamentos com ocorrência de eventos foram nevirapina 200 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia (uma morte) e lopinavir/ritonavir 400/100 mg 12/12h + entricitabina/fumarato de tenofovir desoproxila 200/300 mg/dia (três mortes), ambos no estudo de Lockman *et al*. (2012). No outro estudo (LOCKMAN *et al*., 2010) em que esses dois esquemas foram avaliados, não houve mortes relacionadas a TARV. A taxa de incidência média foi, respectivamente, de 0,29 (ICr 95% 0,00-20,77) e 0,94 (ICr 95% 0,00-60,39).

Tabela 1 – Eventos adversos reportados pelos estudos (continua)

Osteoporose por eventos adversos				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	59	6,15	0,01 - 4037,00
Descontinuação por eventos adversos				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	18,05	0,03 - 9868,95
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	533	81,97	4,16 - 1611,00
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	2	307	61,58	2,14 - 1797,00
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	370	44,25	2,38 - 838,60
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	371	0,31	0,00 - 29,70
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	15,41	0,21 - 876,59
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	121,30	0,21 - 67219,50
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	0,00	0,00 - 0,20
Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia	1	29	0,00	0,00 - 0,48
Efavirenz 600 mg/dia + Lamivudina/Zidovudina 150/300 mg 12/12h	1	30	126,40	0,23 - 69389,00

Tabela 1 – Eventos adversos reportados pelos estudos (continuação)

Descontinuação por eventos adversos				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Todos os tratamentos	15	2388	20,78	5,58 - 57,31
Descontinuação por eventos adversos relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	249	44,89	0,09 - 24219,50
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	251	0,00	0,00 - 0,06
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	15,41	0,21 - 876,59
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	121,30	0,21 - 67219,50
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	0,00	0,00 - 0,20
Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia	1	29	0,00	0,00 - 0,48
Todos os tratamentos	7	988	4,31	0,13 - 54,72
Eventos adversos clínicos e/ou laboratoriais				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	247	972,10	1,82 - 511395,00
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	248	933,00	1,69 - 498690,00
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	922,90	56,88 - 15170,00
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	913,40	1,67 - 482400,00
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	718,40	1,35 - 375995,00
Todos os tratamentos	6	954	888,20	759,90 - 1045,00

Tabela 1 – Eventos adversos reportados pelos estudos (continuação)

Eventos adversos clínicos e/ou laboratoriais relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	247	594,80	1,10 - 318800,00
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	248	395,20	0,73 - 211000,00
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	357,80	8,25 - 15370,00
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	545,80	0,99 - 304395,00
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	91,31	0,17 - 49459,50
Todos os tratamentos	6	954	341,60	133,60 - 862,70
Eventos adversos clínicos relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	322,40	0,60 - 174800,00
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	286	570,60	1,07 - 315895,00
Todos os tratamentos	2	575	431,50	13,84 - 13630,00
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	80,75	3,16 - 2072,00
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	95,23	0,17 - 53989,50
Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia	1	29	77,39	0,14 - 42889,50
Efavirenz 600 mg/dia + Lamivudina/Zidovudina 150/300 mg 12/12h	1	30	137,80	0,25 - 74109,50
Todos os tratamentos	5	284	96,34	55,04 - 158,90

Tabela 1 – Eventos adversos reportados pelos estudos (continuação)

Eventos adversos graves clínicos graus 3 e/ou 4				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	93,37	0,17 - 50589,50
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	286	117,60	0,22 - 62379,00
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	370	45,83	2,46 - 876,20
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	371	45,40	1,90 - 1001,00
Todos os tratamentos	6	1316	59,93	33,74 - 104,60
Eventos adversos graves laboratoriais graus 3 e/ou 4				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	251,40	0,46 - 136000,00
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	286	703,70	1,32 - 364000,00
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	370	86,76	5,09 - 1528,00
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	371	71,04	4,07 - 1235,00
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	188,80	0,35 - 100900,00
Todos os tratamentos	7	1550	145,10	57,71 - 359,90
Eventos adversos graves clínicos e/ou laboratoriais grau 3				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	247	181,00	0,34 - 98849,50
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	248	83,97	0,16 - 45879,50
Todos os tratamentos	2	495	125,50	3,51 - 4295,00

Tabela 1 – Eventos adversos reportados pelos estudos (continuação)

Eventos adversos graves clínicos e/ou laboratoriais grau 4				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	247	42,49	0,08 - 23669,50
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	248	12,36	0,02 - 7240,75
Todos os tratamentos	2	495	25,05	0,50 - 1017,00
Eventos adversos graves clínicos grau 4				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	249	8,60	0,02 - 4567,85
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	251	9,79	0,02 - 5430,00
Todos os tratamentos	2	500	9,31	0,39 - 216,30
Eventos adversos sérios clínicos e/ou laboratoriais				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	247	96,95	0,18 - 51859,50
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	2	307	67,41	2,66 - 1763,95
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	370	30,05	1,33 - 637,10
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	371	20,74	0,78 - 491,70
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	40,91	1,16 - 1488,95
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	95,23	0,17 - 53989,50
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	30,64	0,06 - 17229,50
Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia	1	29	112,10	0,21 - 61089,00

Tabela 1 – Eventos adversos reportados pelos estudos (continuação)

Eventos adversos sérios clínicos e/ou laboratoriais				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Efavirenz 600 mg/dia + Lamivudina/Zidovudina 150/300 mg 12/12h	1	30	126,40	0,23 - 69389,00
Todos os tratamentos	13	1813	49,34	31,60 - 77,10
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	21,91	0,47 - 943,60
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	42,17	0,06 - 24359,50
Todos os tratamentos	3	225	27,75	2,56 - 272,90
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	247	12,70	0,02 - 7228,85
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	248	0,00	0,00 - 0,21
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	0,00	0,00 - 0,12
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	68,36	0,11 - 39559,00
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	0,00	0,00 - 0,20
Todos os tratamentos	6	954	1,09	0,01 - 21,47
Eventos adversos sérios clínicos relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	10,21	0,02 - 5968,00
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	286	18,85	0,03 - 10450,00
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	1	248	0,00	0,00 - 0,21

Tabela 1 – Eventos adversos reportados pelos estudos (continuação)

Eventos adversos sérios clínicos relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	1	140	0,00	0,00 - 0,35
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	0,00	0,00 - 0,20
Todos os tratamentos	5	1197	1,53	0,01 - 21,29
Morte por todas as causas				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	0,00	0,00 - 0,17
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	533	0,73	0,00 - 60,56
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	2	307	1,04	0,00 - 72,82
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	370	7,87	0,26 - 238,40
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	371	5,75	0,08 - 226,10
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	0,00	0,00 - 0,09
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	0,00	0,00 - 1,07
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	0,00	0,00 - 0,20
Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia	1	29	7,30	0,01 - 4814,00
Efavirenz 600 mg/dia + Lamivudina/Zidovudina 150/300 mg 12/12h	1	30	7,42	0,01 - 4967,95
Todos os tratamentos	15	2388	4,47	1,42 - 7,91

Tabela 1 – Eventos adversos reportados pelos estudos (conclusão)

Morte por eventos adversos relacionados a TARV				
TARV	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia	1	289	0,00	0,00 - 0,17
Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	533	0,00	0,00 - 0,03
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia	2	307	0,00	0,00 - 0,05
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	370	0,29	0,00 - 20,77
Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	2	371	0,94	0,00 - 60,39
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia	2	184	0,00	0,00 - 0,12
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia	1	41	0,00	0,00 - 1,07
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia	1	234	0,00	0,00 - 0,20
Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia	1	29	0,00	0,00 - 0,48
Efavirenz 600 mg/dia + Lamivudina/Zidovudina 150/300 mg 12/12h	1	30	0,00	0,00 - 0,49
Todos os tratamentos	15	2388	0,18	0,00 - 1,56

Fonte: Elaboração própria

5.5 Heterogeneidade e análises de subgrupo

Os amplos intervalos de credibilidade encontrados em nossa revisão apontam para grande heterogeneidade dos resultados apresentados e diminuem a validade de possíveis análises de subgrupo. Ademais, as diferenças clínicas existentes entre os estudos, como os diferentes esquemas ARV utilizados, o nível de CD4 inicial dos participantes e sua exposição prévia a TARV, além das diferentes análises dos dados (por protocolo ou intenção de tratar) e fontes de financiamento (somente pela indústria, apenas por órgãos governamentais ou ambos), fazem com que variações nas estimativas encontradas nas análises de subgrupo possam decorrer apenas de confundimento residual, sem qualquer implicação para a prática clínica. A maioria

de tais análises não demonstrou diferença entre os grupos e as poucas estimativas diferentes encontradas parecem refletir a ausência ou número muito baixo de eventos (como no caso de morte) e, principalmente, a heterogeneidade clínica, em especial os diferentes esquemas ARV avaliados nos estudos.

As análises de subgrupo para os resultados dos desfechos primários dessa revisão, relativas ao cegamento, análise por protocolo ou intenção de tratar, nível de CD4, exposição prévia a TARV e financiamento podem ser vistas no APÊNDICE H (Tabela 3). Os dados referentes ao nível de CD4 e ao financiamento não foram apresentados para o total de eventos adversos clínicos e/ou laboratoriais e para os eventos adversos clínicos e/ou laboratoriais relacionados a TARV, pois eles não tiveram subgrupos. Ambos os desfechos foram reportados apenas em estudos com participantes cujo nível médio inicial de CD4 era maior que 250 células/mm^3 e com financiamento exclusivo da indústria farmacêutica.

Não realizamos análise de subgrupo por esquema ARV, pois um mesmo esquema foi avaliado em no máximo dois braços dos estudos incluídos. Também não fizemos algumas das análises previstas no nosso protocolo, devido aos dados disponíveis. Os estudos tinham basicamente mulheres adultas, com pouquíssimas idosas, e não havia nenhuma criança ou adolescente, o que não permitiu uma análise por faixa etária. Também não foi possível avaliar de acordo com o nível de desenvolvimento dos locais dos estudos, uma vez que 80% deles eram multicêntricos e foram conduzidos em países com diferentes níveis de desenvolvimento, conforme definido pelo banco mundial. O tempo de seguimento foi utilizado para ajuste da taxa de incidência, não cabendo uma análise de subgrupo. Em geral, os estudos monitoraram os eventos adversos de forma mais ativa e todos utilizaram esquemas ARV com três ou mais medicamentos associados, não caracterizando a existência de diferentes subgrupos nesses aspectos. Não efetuamos análise de subgrupo segundo o risco de viés, pois 90% dos estudos tiveram alto risco, e também de acordo com o sigilo de alocação, uma vez que isso se relacionou diretamente ao cegamento, visto que 80% dos estudos eram abertos e os 20% que foram duplo-cegos não descreveram como se deu o sigilo.

5.6 Avaliação da certeza da evidência

O GRADE normalmente é utilizado para avaliar a qualidade da evidência em estudos que fazem análises comparativas entre diferentes intervenções. Nossa revisão tem caráter descritivo, ao estimar a taxa de incidência de eventos por 1000 pessoas-ano para cada

intervenção, usando como unidade de análise os braços dos estudos primários. De qualquer forma, optamos por elaborar o GRADE, utilizando sua ferramenta de avaliação da certeza de evidência para questões de prognóstico (APÊNDICE I, Tabela 4).

6 DISCUSSÃO

6.1 Principais achados

Apesar da ampla busca da literatura realizada, há poucos estudos que analisaram a ocorrência de eventos adversos especificamente em mulheres com HIV/Aids. A maioria dos estudos incluídos nessa revisão foram publicados entre 2015 e 2020.

Não foi possível estabelecer recomendações sobre algum esquema ARV preferencial para uso em mulheres com HIV/Aids, visando minimizar o risco de eventos adversos e melhorar a adesão ao tratamento.

6.2 Comparação com evidências sumárias prévias

Eventos adversos sobre a saúde óssea e reprodutiva de mulheres foram escassos ou não abordados. Apenas um estudo relatou a ocorrência de osteoporose e dois estudos avaliaram fraturas relacionadas a essa condição, mas sem nenhum evento. Uma revisão sistemática (BEDIMO; ROSENBLATT; MYERS, 2016), que avaliou a segurança óssea da TARV, não especificamente em mulheres, e incluiu 11 ensaios clínicos com o esquema efavirenz + entricitabina + fumarato de tenofovir desoproxila, não identificou fraturas ósseas relacionadas ao tratamento. O único estudo de nossa revisão que avaliou esse esquema ARV (FIRNHABER *et al*., 2015) não abordou desfechos sobre a saúde óssea. Outra revisão sistemática (CARVALHO *et al*., 2010) analisou osteopenia, osteoporose e fraturas por osteoporose em mulheres com HIV/Aids em uso de ARV. Eles identificaram somente estudos transversais com esses desfechos. Seus resultados demonstraram 40% de osteopenia no fêmur proximal (um estudo) e 22% no fêmur proximal e na coluna lombar (um estudo). Osteoporose foi descrita na coluna lombar em 42,8% (um estudo de mulheres na pós-menopausa), no fêmur proximal em 5% (um estudo) e em ambos os locais em 7,3% (um estudo). Houve apenas um caso de fratura vertebral em uma mulher na pós-menopausa. Apesar da preocupação do efeito da TARV sobre o risco de osteoporose e fraturas ósseas, especialmente em mulheres, esses desfechos ainda são pouco abordados na literatura, em especial em ensaios clínicos controlados e randomizados. Em nossa revisão, apenas um estudo relatou a ocorrência de osteoporose e dois estudos avaliaram fraturas relacionadas a essa condição, mas sem nenhum evento. No entanto, o tempo de seguimento em ambos foi de apenas 48 semanas, o que é insuficiente para avaliação adequada deste desfecho.

A descontinuação dos ARV por eventos adversos compromete o objetivo atual de tratar todas as pessoas com HIV/Aids com o intuito de reduzir a transmissão da doença. Isso traz a importância de se estar atento a ocorrência de tais eventos na prática clínica, para que se possa abordar adequadamente a adesão ao tratamento. Seu conhecimento também propicia a escolha de TARV com menor risco de efeitos adversos. Nessa revisão, a descontinuação variou bastante entre os diferentes esquemas ARV. O resultado encontrado para os dois esquemas com maior risco de descontinuação por eventos adversos deve ser considerado com cautela, pois o número de mulheres avaliados foi muito pequeno.

Em geral, as TARV demonstraram uma taxa de incidência média de descontinuação de 20,78 por 1000 pessoas-ano, mas cujo valor verdadeiro pode variar bastante em futuros estudos. Revisão sistemática (CARR; AMIN, 2009), que incluiu 64 ensaios clínicos e 15 coortes com ambos os sexos, encontrou que a causa mais comum de interrupção do tratamento foi a ocorrência de eventos adversos (9%). No entanto, os autores ressaltaram que somente metade dos estudos reportaram tais eventos. Uma metanálise (HERMES *et al*., 2012) buscou avaliar a segurança de esquemas contendo lopinavir/ritonavir em mulheres com HIV/Aids. A descontinuação por eventos adversos ocorreu em 6,8% das mulheres. Em nossa revisão, lopinavir/ritonavir foi avaliado em dois estudos (LOCKMAN *et al*., 2010, 2012), vinculados a um mesmo protocolo, associado a entricitabina/fumarato de tenofovir desoproxila, com resultado similar. A taxa de incidência média de descontinuação por eventos adversos com esse esquema foi de 0,31 por 1000 pessoas-ano, correspondendo a 6,2% das mulheres avaliadas para esse desfecho.

Mortes por eventos adversos relacionados a TARV ocorreram com apenas dois esquemas de tratamento, dentre dez avaliados para esse desfecho. Uma com nevirapina + entricitabina/fumarato de tenofovir desoproxila (0,27% das mulheres que receberam esse esquema) e três com lopinavir/ritonavir + entricitabina/fumarato de tenofovir desoproxila (0,81%). Esse último achado foi similar a descontinuação da TARV por morte na metanálise de Hermes *et al.* (2012), que avaliou esquemas contendo lopinavir/ritonavir em mulheres com HIV/Aids, em que cinco mulheres morreram (0,8%).

Outras revisões sistemáticas publicadas que identificamos sobre eventos adversos da TARV avaliaram eventos adversos específicos, diferentes dos abordados em nossa revisão, ou focaram na comparação de esquemas contendo ARV específicos, não sendo possível utilizar seus resultados para comparar com nossos achados.

6.3 Pontos fortes e limitações

De acordo com nosso conhecimento, nossa revisão foi a primeira que buscou reunir o conhecimento científico existente sobre os eventos adversos em mulheres com HIV/Aids de todas as TARV em uso na prática clínica atual. Anteriormente, as revisões publicadas sobre mulheres focaram em eventos adversos específicos, como na saúde óssea, ou na avaliação comparativa de no máximo dois esquemas contendo determinados ARV. Destacamos a busca ampla que realizamos na literatura, com um grande número de estudos triados na etapa de seleção, sem limitação de data de publicação ou idioma.

A quantidade de esquemas de ARV nos poucos estudos encontrados diluiu a quantidade de mulheres a ser analisada em cada esquema, refletindo nos amplos intervalos de credibilidade encontrados.

Pretendíamos avaliar a análise agrupada de todos os ARV segundo o risco de viés para desfechos como a descontinuação por eventos adversos, mas não o fizemos, uma vez que quase todos os estudos, com exceção de um, tinham alto risco. Avaliamos ainda se conseguiríamos elaborar uma metanálise em rede com os estudos que incluíam 100% de mulheres, mas não foi possível, visto que havia apenas cinco estudos com dois braços com esquemas ARV únicos, ou seja, sem que fossem utilizados múltiplos esquemas ARV em um mesmo braço, e que tais estudos praticamente não analisaram TARV em comum.

Como já citado anteriormente, uma limitação de nosso trabalho deriva do fato de haver poucos estudos que descreveram eventos adversos separadamente em mulheres. O mesmo esquema ARV foi utilizado em no máximo dois estudos. Isso se traduziu em análises com amplo intervalo de credibilidade, com resultados verdadeiros que poderiam variar ainda mais em novas pesquisas. A escassez de dados, associada ao alto risco de viés de quase todos os estudos, dificultou conclusões definitivas sobre os desfechos avaliados e praticamente impossibilitou que se apontasse a preferência por alguma das TARV. Pouco menos da metade dos fármacos ARV utilizados na prática clínica atual compunham os esquemas de tratamento avaliados. Também foram escassos os dados disponíveis sobre mulheres idosas e nenhum dos estudos incluíam crianças.

Optamos por selecionar apenas ensaios clínicos controlados randomizados, principalmente em virtude do outro objetivo previsto no nosso protocolo, que pretende avaliar a diferença entre os sexos na ocorrência de eventos adversos comparativamente entre as diferentes TARV, considerando o percentual de mulheres participantes em cada braço dos estudos. No entanto, para a descrição da frequência de eventos adversos especificamente em

mulheres, utilizamos dados de apenas um braço de alguns estudos, uma vez que o comparador tinha múltiplos esquemas ARV, não sendo possível isolar os eventos adversos para um esquema específico. Assim, resultados de estudos experimentais com um único braço, que relatassem eventos adversos em mulheres, poderiam ter sido incluídos nesse último objetivo. Futuras pesquisas podem ampliar a busca por esse tipo de estudo com o intuito de atualizar os achados de nossa revisão.

6.4 Implicações para a pesquisa

Nossa revisão demonstra a necessidade de mais pesquisas que avaliem os eventos adversos da TARV em mulheres, não só com os esquemas aqui avaliados, mas principalmente com aqueles que não apareceram em nenhum dos estudos. Da mesma forma, há necessidade de pesquisar os fármacos que sequer fizeram parte dos esquemas incluídos nessa revisão, que correspondem a pouco mais da metade dos ARV disponíveis para uso na prática clínica atual.

Os estudos devem comparar esquemas ARV isolados ao invés de permitir múltiplos esquemas ARV em algum dos braços do estudo, ou descrever os eventos adversos separadamente para cada um dos esquemas utilizados, de forma a possibilitar a avaliação de segurança para cada esquema específico. Como o conhecimento e o manejo dos efeitos adversos da TARV tem implicação direta na adesão ao tratamento, fundamental para que se mantenha as pessoas com a carga viral indetectável, sem risco de transmissão para terceiros, tais estudos devem conseguir avaliar a efetividade da terapia. Nesse sentido, é necessário considerar a realização de ensaios clínicos pragmáticos, que permitem incorporar as necessidades individuais dos participantes, avaliando os resultados em condições que se aproximam da prática clínica cotidiana (COUTINHO; HUF; BLOCH, 2003).

6.5 Implicações clínicas

A escassez de informações sobre eventos adversos da TARV especificamente em mulheres, aliado ao alto risco de viés da quase totalidade dos estudos existentes, grande parte deles com participação da indústria farmacêutica, não permite que se estabeleçam conclusões sobre esquemas preferenciais para uso em mulheres vivendo com HIV/Aids. Assim, o conhecimento científico disponível não permite que façamos recomendações para a elaboração de guias de prática clínica ou sobre abordagens para minimizar o risco de eventos adversos com intuito de melhorar a adesão ao tratamento ARV.

Os resultados de nossa revisão podem não se aplicar completamente ao contexto brasileiro. Somente um dos estudos (FIRNHABER *et al*., 2015) incluiu o Brasil entre os locais de realização da pesquisa. O Protocolo Clínico e Diretriz Terapêutica brasileiro para manejo da infecção pelo HIV em adultos recomenda como opção preferencial de tratamento o esquema com dolutegravir + lamivudina + fumarato de tenofovir desoproxila (BRASIL *et al*., 2018a). No entanto, tal esquema não foi avaliado em nenhum dos estudos selecionados em nosso trabalho. Ademais, fumarato de tenofovir desoproxila tem como um de seus efeitos adversos a possibilidade de redução da densidade mineral óssea, com consequente aumento do risco de fraturas patológicas (BRASIL *et al*., 2018a).

O protocolo do *National Institute of Health* norte-americano (NATIONAL INSTITUTE OF HEALTH, 2019) recomenda que se evite esse fármaco em quem tenha osteoporose. Porém, a maioria dos estudos não avaliou desfechos referentes à saúde óssea, em especial aqueles que importam para as pessoas, como osteoporose e fraturas relacionadas. Fumarato de tenofovir desoproxila foi avaliado quanto ao risco de fraturas por osteoporose em apenas um estudo, em um esquema com darunavir, cobicistate e entricitabina (RASHBAUM *et al*., 2019).

7 CONCLUSÃO

Atualmente, com o objetivo de controlar a infecção pelo HIV e reduzir sua transmissão, tem-se proposto o tratamento de todas as pessoas com o vírus. Para tanto, é essencial que se invista em estratégias que visem a adesão e o manejo adequado de efeitos adversos dos ARV. No entanto, apesar do grande número existente de ensaios clínicos controlados randomizados sobre a TARV para HIV/Aids e das possíveis diferenças sugeridas por alguns estudos na ocorrência de eventos adversos entre os sexos, pouco ainda tem sido produzido para avaliar tais diferenças em ensaios clínicos, ainda mais de alta qualidade.

Em nossa revisão, percebemos a escassez de informações disponíveis sobre a incidência de eventos adversos especificamente em mulheres em tratamento com ARV. Os poucos ensaios clínicos controlados randomizados existentes têm em sua quase totalidade alto risco de viés e a maioria recebeu financiamento da indústria farmacêutica, o que representa um potencial conflito de interesses. Quando observamos os resultados encontrados para os esquemas ARV incluídos nesses estudos, deparamo-nos com uma grande imprecisão, refletida em amplos intervalos de credibilidade e probabilidades de valores verdadeiros para os desfechos em futuros estudos que poderão ser muito diferentes dos apresentados em nosso trabalho.

Novos estudos são necessários, com desenho metodológico e qualidade científica adequados para avaliar os eventos adversos da TARV em mulheres, de maneira a propiciar informações para subsidiar uma abordagem centrada nas pessoas, capaz de manejar oportunamente os efeitos adversos e garantir ao máximo a adesão ao tratamento. Nesse sentido, ensaios clínicos pragmáticos podem contribuir na avaliação da efetividade das terapias atualmente disponíveis, ao gerar resultados que se aproximem mais da realidade enfrentada na prática clínica diária.

REFERÊNCIAS

BEDIMO, R.; ROSENBLATT, L.; MYERS, J. Systematic review of renal and bone safety of the antiretroviral regimen efavirenz, emtricitabine, and tenofovir disoproxil fumarate in patients with HIV infection. **HIV Clinical Trials**, v. 17, n. 6, p. 246–266, 1 nov. 2016.

BMJ GROUP. **British National Formulary for Children (BNF)**. London: [s.n.].

BMJ GROUP. **British National Formulary (BNF)**. London: [s.n.]. v. 80

BONOLO, P. DE F.; GOMES, R. R. DE F. M.; GUIMARÃES, M. D. C. Adesão à terapia anti-retroviral (HIV/aids): fatores associados e medidas da adesão. **Epidemiologia e Serviços de Saúde**, v. 16, n. 4, dez. 2007.

BRASIL et al. **Protocolo clínico e diretrizes terapêuticas para manejo da infecção pelo HIV em adultos**. Brasília: Ministério da Saúde, 2018a.

BRASIL et al. **Protocolo clínico e diretrizes terapêuticas para manejo da infecção pelo HIV em crianças e adolescentes**. Brasília: Ministério da Saúde, 2018b.

BRASIL; MINISTÉRIO DA SAÚDE; DEPARTAMENTO DE DOENÇAS DE CONDIÇÕES CRÔNICAS E INFECÇÕES SEXUALMENTE TRANSMISSÍVEIS. **Casos de Aids diminuem no Brasil**. Disponível em: <http://www.aids.gov.br/pt-br/noticias/casos-de-aids-diminuem-no-brasil>. Acesso em: 26 mar. 2022.

BRASIL; MINISTÉRIO DA SAÚDE; SECRETARIA DE VIGILÂNCIA EM SAÚDE. **Boletim epidemiológico: HIV/Aids 2021**. , dez. 2021.

CAMPBELL, T. B. et al. Efficacy and safety of three antiretroviral regimens for initial treatment of HIV-1: a randomized clinical trial in diverse multinational settings. **PLoS medicine**, v. 9, n. 8, p. e1001290, 2012.

CARR, A.; AMIN, J. Efficacy and tolerability of initial antiretroviral therapy: a systematic review. **AIDS**, v. 23, n. 3, p. 343–353, 28 jan. 2009.

CARVALHO, E. H. DE et al. Bone mineral density in HIV-infected women taking antiretroviral therapy: a systematic review. **Arquivos Brasileiros De Endocrinologia E Metabologia**, v. 54, n. 2, p. 133–142, mar. 2010.

CEZARINO, P. Y. A. et al. Are women living with HIV prone to osteoporosis in postmenopause? A systematic review. **Revista Da Associacao Medica Brasileira (1992)**, v. 64, n. 5, p. 469–473, maio 2018.

CLARK, R. A.; SQUIRES, K. E. Gender-specific considerations in the antiretroviral management of HIV-infected women. **Expert Review of Anti-Infective Therapy**, v. 3, n. 2, p. 213–227, abr. 2005.

COCHRANE. **Revised Cochrane risk-of-bias tool for randomized trials (Rob 2)**. , ago. 2019.

COUTINHO, E. DA S. F.; HUF, G.; BLOCH, K. V. Ensaios clínicos pragmáticos: uma opção na construção de evidências em saúde. **Cadernos de Saúde Pública**, v. 19, p. 1189–1193, ago. 2003.

COUTINHO, M. F. C.; O'DWYER, G.; FROSSARD, V. Tratamento antirretroviral: adesão e a influência da depressão em usuários com HIV/Aids atendidos na atenção primária. **Saúde em Debate**, v. 42, n. 116, p. 148–161, jan. 2018.

Covidence - Better systematic review management. Disponível em: <https://www.covidence.org/>. Acesso em: 24 jul. 2022.

CURNO, M. J. et al. A Systematic Review of the Inclusion (or Exclusion) of Women in HIV Research: From Clinical Studies of Antiretrovirals and Vaccines to Cure Strategies. **Journal of Acquired Immune Deficiency Syndromes (1999)**, v. 71, n. 2, p. 181–188, 1 fev. 2016.

EGGER, M. et al. Bias in meta-analysis detected by a simple, graphical test. **BMJ (Clinical research ed.)**, v. 315, n. 7109, p. 629–634, 13 set. 1997.

ERON, J. J. et al. A week-48 randomized phase-3 trial of darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naive HIV-1 patients. **AIDS**, v. 32, n. 11, p. 1431–1442, 17 jul. 2018.

EUROPEAN AIDS CLINICAL SOCIETY. **Guidelines**. , out. 2021. Disponível em: <https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf>

FIRNHABER, C. et al. Differences in antiretroviral safety and efficacy by sex in a multinational randomized clinical trial. **HIV Clinical Trials**, v. 16, n. 3, p. 89–99, maio 2015.

FLETCHER, C. V. Overview of antiretroviral agents used to treat HIV. Em: **UpToDate**. [s.l: s.n.].

GORDIS, L. **Epidemiology**. [s.l.] Elsevier Health Sciences, 2013.

GOUDIE, R. J. B. et al. MultiBUGS: A Parallel Implementation of the BUGS Modelling Framework for Faster Bayesian Inference. **Journal of Statistical Software**, v. 95, p. 7, 7 out. 2020.

HADDAWAY, N. R.; MCGUINNESS, L. A.; PRITCHARD, C. C. **PRISMA2020: R package and ShinyApp for producing PRISMA 2020 compliant flow diagrams**. Zenodo, , 8 jul. 2021. Disponível em: <https://zenodo.org/record/4287834>. Acesso em: 21 abr. 2022

HERMES, A. et al. Meta-analysis of the safety, tolerability, and efficacy of lopinavir/ritonavir-containing antiretroviral therapy in HIV-1-infected women. **HIV clinical trials**, v. 13, n. 6, p. 308–323, dez. 2012.

HIV.GOV; NATIONAL INSTITUTE OF HEALTH. **Drug Database**. , 2022.

HUHN, G. D. et al. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-experienced, virologically suppressed patients with HIV-1: subgroup analyses of the phase 3 EMERALD study. **AIDS Research and Therapy**, v. 16, n. 1, p. 23, dez. 2019.

IBRAHIM, F. et al. Bone mineral density, kidney function, weight gain and insulin resistance in women who switch from TDF/FTC/NNRTI to ABC/3TC/DTG. **HIV Medicine**, v. 22, n. 2, p. 83–91, 2020.

KING, E. M.; ALBERT, A. Y.; MURRAY, M. C. M. HIV and amenorrhea: a meta-analysis. **AIDS (London, England)**, v. 33, n. 3, p. 483–491, 1 mar. 2019.

KITYO, C. et al. Switching to Fixed-Dose Bictegravir, Emtricitabine, and Tenofovir Alafenamide (B/F/TAF) in Virologically Suppressed HIV-1 Infected Women: A Randomized, Open-Label,

Multicenter, Active-Controlled, Phase 3, Noninferiority Trial. **JAIDS Journal of Acquired Immune Deficiency Syndromes**, v. 82, n. 3, p. 321–328, 1 nov. 2019.

LIMA, B. V. S. **Efeitos adversos à terapia antirretroviral em pessoas infectadas pelo HIV: dificuldades na adesão ao tratamento e mudanças dos esquemas terapêuticos**. Dissertação (Mestrado em Biologia Aplicada à Saúde)—Recife: Universidade Federal de Pernambuco, 2019.

LOCKMAN, S. et al. Antiretroviral Therapies in Women after Single-Dose Nevirapine Exposure. **n engl j med**, p. 11, 2010.

LOCKMAN, S. et al. Nevirapine- versus lopinavir/ritonavir-based initial therapy for HIV-1 infection among women in Africa: a randomized trial. **PLoS medicine**, v. 9, n. 6, p. e1001236, 2012.

MASSAD, L. S. et al. Effects of HIV infection and its treatment on self-reported menstrual abnormalities in women. **Journal of Women's Health (2002)**, v. 15, n. 5, p. 591–598, jun. 2006.

MCGOWAN, J. et al. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. **Journal of Clinical Epidemiology**, v. 75, p. 40–46, jul. 2016.

NAICKER, N. et al. Efficacy and Safety of Tenofovir-Containing Antiretroviral Therapy in Women who Acquired HIV while Enrolled in Tenofovir Gel Prophylaxis Trials. **Antiviral Therapy**, v. 22, n. 4, p. 287–293, maio 2017.

NATIONAL INSTITUTE OF HEALTH. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV**. [s.l: s.n.].

NATIONAL INSTITUTE OF HEALTH; NATIONAL LIBRARY OF MEDICINE; NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION. **PubChem**. , 2022. Disponível em: <https://pubchem.ncbi.nlm.nih.gov/>

ORRELL, C. et al. Fixed-dose combination dolutegravir, abacavir, and lamivudine versus ritonavir-boosted atazanavir plus tenofovir disoproxil fumarate and emtricitabine in previously untreated women with HIV-1 infection (ARIA): week 48 results from a randomised, open-label, non-inferiority, phase 3b study. **The Lancet HIV**, v. 4, n. 12, p. e536–e546, dez. 2017.

PADOIN, S. M. DE M. et al. Adesão à terapia antirretroviral para HIV/Aids. **Cogitare Enfermagem**, v. 18, n. 3, p. 446–451, set. 2013.

PASCHOAL, E. P. et al. Adherence to antiretroviral therapy and its representations for people living with HIV/AIDS. **Escola Anna Nery - Revista de Enfermagem**, v. 18, n. 1, 2014.

RASHBAUM, B. et al. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naïve patients with HIV-1: subgroup analyses of the phase 3 AMBER study. **HIV Research & Clinical Practice**, v. 20, n. 1, p. 24–33, 2 jan. 2019.

SANTOS, S. L. F. et al. Fatores desfavorávies na adesão à terapia anti-retroviral e diagnóstico sorológico: revisão da literatura. **Revista Expressão Católica Saúde**, v. 3, n. 1, p. 42, 28 set. 2018.

SQUIRES, K. et al. Integrase inhibitor versus protease inhibitor based regimen for HIV-1 infected women (WAVES): a randomised, controlled, double-blind, phase 3 study. **The Lancet HIV**, v. 3, n. 9, p. e410–e420, set. 2016.

THOMPSON, J.; PALMER, T.; MORENO, S. Bayesian Analysis in Stata with WinBUGS. **The Stata Journal**, v. 6, n. 4, p. 530–549, 1 nov. 2006.

TSIBRIS, A. Antiretroviral therapy in adults and adolescents with HIV infection. Em: **Dynamed**. [s.l.] EBSCO, 2022.

UNAIDS. **Global HIV & AIDS statistics — Fact sheet**. Disponível em: <https://www.unaids.org/en/resources/fact-sheet>. Acesso em: 26 mar. 2022.

US DEPARTMENT OF HEALTH AND HUMAN SERVICES et al. **Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events**. [s.l: s.n.].

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; NATIONAL INSTITUTES OF HEALTH; NATIONAL CANCER INSTITUTE. **Common Terminology Criteria for Adverse Events (CTCAE)**. , nov. 2017.

U.S. FOOD & DRUG ADMINISTRATION; OFFICE OF THE COMMISSIONER. What is a Serious Adverse Event? **FDA**, 9 set. 2020.

VALIAVEETTIL, C. et al. High prevalence of abnormal menstruation among women living with HIV in Canada. **PloS One**, v. 14, n. 12, p. e0226992, 2019.

WISHART, D. S. et al. DrugBank 5.0: a major update to the DrugBank database for 2018. **Nucleic Acids Research**, v. 46, n. D1, p. D1074–D1082, 4 jan. 2018.

WORLD HEALTH ORGANIZATION. **Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach**. 2. ed. [s.l: s.n.].

WORLD HEALTH ORGANIZATION; WHO COLLABORATING CENTRE FOR DRUG STATISTICS METHODOLOGY. **ATC/DDD Index 2022**. , 2022.

APÊNDICE A – PROTOCOLO DO BMJ OPEN

Open access Protocol

BMJ Open

Sex differences and adverse events of antiretrovirals in people living with HIV/AIDS: a systematic review and meta-analysis protocol

Jardel Corrêa de Oliveira,[1,2] Maíra Ramos Alves,[1] Luis Phillipe Nagem Lopes,[3] Rodrigo Suguimoto Iwami,[4] Fabiane Raquel Motter ,[1] Cristiane de Cássia Bergamaschi,[1] Marcus Tolentino Silva ,[1] Alexander Itria,[5] Diogo Luis Scalco,[2] Donavan de Souza Lucio ,[2] Lauren Giustti Mazzei,[6] Rodrigo D'Agostini Derech,[7] Tiago Veiga Pereira,[8] Jorge Otávio Maia Barreto,[9] Luciane Cruz Lopes [1]

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For numbered affiliations see end of article.

Correspondence to
Professor Luciane Cruz Lopes; luslopesbr@gmail.com

ABSTRACT

Introduction Antiretroviral therapy (ART) for HIV/AIDS is associated with adverse events (AEs). However, little is known about the differences in the risk of AEs between women and men living with HIV/AIDS. This study aims to determine (1) whether there are sex differences in the risk of AEs in people with HIV/AIDS treated with ART and (2) the prevalence of AEs to the reproductive system and bone mineral density in women.

Methods and analysis This systematic review (SR) will include randomised trials evaluating ART in people living with HIV/AIDS with at least 12 weeks of duration follow-up. Searches will be conducted in Medline, Embase, Cochrane Library, Epistemonikos, Lilacs, trial registries and grey literature databases, without restriction on publication status, year of publication and language. The primary outcome will be the risk of ART discontinuation or drop-outs/withdrawals of ART due to AEs and the number of any treatment-emergent AE. The secondary outcomes are the incidence of serious clinic or laboratory (grade 3 and/or 4) treatment-emergent AEs, hospitalisation, death and AEs specific to the reproductive system and bone mineral density (osteoporosis, osteopenia and fractures) of women. Selection, data extraction and quality assessment will be performed by pairs of reviewers. Cochrane collaboration tools will be used to assess the risk of bias. If appropriate, a meta-analysis will be conducted to synthesise results. The overall quality of the evidence for each outcome will be determined by the Grades of Recommendation, Assessment, Development and Evaluation.

Ethics and dissemination The results of this SR will assist the formulation of public policies aimed at the management and monitoring of AEs of ART in people living with HIV/AIDS. A deliberative dialogue will be scheduled with the Department of Chronic Conditions and Sexually Transmitted Infections of Brazil's Ministry of Health to align the project with policymakers' interests.

PROSPERO registration number CRD42021251051.

Strengths and limitations of this study

- This systematic review, in addition to studying the differences between the sexes, will scrutinise the literature to estimate the prevalence of adverse events specific to women, about which the existing literature is quite conflicting.
- This study will use the key stakeholders (eg, policymakers, opinion leader healthcare professional, community representative of patients) through deliberative dialogue, to overcome barriers to implement the evidence summarised.
- Our systematic review may have limited generalisability due to the reduced availability of data on within-study sex-by-treatment interaction effects and the possibility of aggregation bias.
- The primary studies could bring limitations to this review considering the confusion between the report of adverse events and signs and symptoms of HIV/AIDS.

INTRODUCTION

The HIV remains a major global public health problem. In 2020, 37.6 million people were living with HIV.[1] About 16% of them were unaware of being infected by the virus.[2] Most of these people are in low-income and middle-income countries.[3]

Antiretroviral therapy (ART) has now been recommended for all patients, regardless of CD4 lymphocyte count, to decrease the transmissibility of the disease and to reduce long-term complications, such as HIV-related dementia.[4] Currently, around 27.4 million people in the world use ART.[2] Since therapy must be continued indefinitely, the focus of patient management should evolve towards the identification and management of early toxicities related to pharmacological treatment.[5] Viral suppression sustained throughout life must be accompanied by individualised management

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and adjustments in advance, to overcome toxicities and adverse events (AEs) in ART, both in the short and long term.[6]

In addition to HIV itself and possible AEs to ART, women need to live with hormonal changes and unique health problems.[7] Sex inequalities in response to the combination of antiretrovirals have been reported in several studies summarised in a meta-analysis.[8] ART was evaluated for at least 48 weeks, between the years 2000 and 2008, finding several significant differences related to sex, in addition to demonstrating that there was better effectiveness of ART in men than in women.

AEs to antiretrovirals have been reported with the use of all drugs and are the main reason for discontinuation, exchanges in therapy, and non-adherence to treatment.[9] Changes in the immune system, common in people with HIV, also affect female hormones, causing problems in the menstrual period, uterine fibroids, genital tract infections and early menopause.[10]

Ovarian function in women with HIV is reportedly shorter than in women uninfected by the virus, which leads to an increase in the burden of the disease as menopause impacts on the onset and progression of chronic diseases and bone mineral density (BMD).[11] Observational studies are controversial regarding the influence of ART on menstrual abnormalities. A retrospective cohort[12] was not associated with ART, while a cross-sectional study[13] showed increased abnormal menstruation in women using ART compared with treatment-naïve women (Odds Ratio (OR) 2.36, 95% CI 1.25 to 4.45). A systematic review (SR)[14] that combined six observational studies showed an increase in amenorrhoea in women with HIV, which may be associated with low BMD. The authors reinforce the need to assess the reproductive health and last menstrual period of women with the virus.

Studies suggest an increased bone mineral loss in women with HIV, but its relationship with the disease or the use of ART is uncertain. A SR[15] with one clinical trial and four cross-sectional studies showed a difference greater than 3% in BMD of the femoral neck in women using regimens containing protease inhibitors, but failed to conclude on the risk of fractures. Another review,[16] also based mainly on cross-sectional studies, points out that HIV infection reduces bone density in postmenopausal women, but that additional studies are needed to understand the mechanism of this effect and whether ART has an impact on BMD.

Brazil is considered a vanguard country in terms of healthcare policy for patients living with HIV/AIDS, especially regarding access to medication.[17] Discontinuation due to AEs, however, remains one of the central problems, even when access to the service is available.[18] Despite the general benefits of viral suppression and improved immune function due to ART far outweigh the risks associated with AEs, in general, it appears that women are more susceptible than men to develop toxicities associated with ART, and this can affect outcomes, care and treatment.[19]

Clinical studies on HIV rarely focus only on outcomes in women, with data on sex analysis often scarce and controversial.[20–22] It is worth mentioning that the long-term complications of ART can be underestimated since most clinical trials use highly specific inclusion criteria for recruiting patients and the duration of patient follow-up is relatively short.[8 23]

Understanding the occurrence of AEs associated with sex is important to assess the need to define public policies that can adapt ART to minimise the damage, improve adherence and guarantee the success of the therapy. Consequently, this could also help reduce disease transmission.[24]

In a preliminary search conducted on 16 May 2021, with the terms ('Anti-Retroviral Agents' OR 'Antiretroviral Agents' OR 'anti-HIV Agents') in the International Prospective Register of Systematic Reviews (Prospero), Open Science Framework, Cochrane Protocols; and with the title terms (Adverse AND Protocol) in the journals that publish SR protocols (eg, Systematic Reviews, BMJ Open, Plos One, Medicine) we identified 66 records of systematic review protocols, but none intended to study AEs related to sex.

This systematic review has two objectives. Objective 1 is to determine whether there are sex differences in the risk of AEs in people with HIV/AIDS treated with ART and objective 2 is to determine the prevalence of AEs to the reproductive system and BMD (osteoporosis, osteopenia and fractures) in women.

METHODS AND ANALYSIS

Study design and protocol

This SR study will be performed according to the recommendations of the Cochrane Handbook for Intervention Reviews.[25] This protocol is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols[26] (online supplemental material 1).

Patient and public involvement

We will conduct a deliberative dialogue (DD), involving relevant decision-makers, healthcare professionals, and users of the Brazilian public health system living with HIV/AIDS. We will present the results and get suggestions on implementation, monitoring, and management of AEs in women living with HIV/AIDS using the DD approach.

Eligibility criteria

The research question was structured using the Population, Intervention, Comparison and Outcomes structure.

Objective 1

Inclusion criteria

Type of studies

We will include only randomised controlled trials (RCTs) with at least 12 weeks of follow-up duration. For cross-over

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RCTs, we will include the first period of data only. Although observational studies may have larger samples and longer follow-up times than RCTs, providing information on rarer or longer-term AEs, non-randomised studies will be excluded due to the higher risk of bias (RoB) compared with RCTs. In an RCT, we have more monitored/controlled, standardised and reported diagnoses of AEs compared with observational studies.

Type of participants

Individuals of both sexes living with HIV/AIDS and receiving antiretroviral—regardless of age. Our study intends to analyse sex differences according to their biological definition, not the distinction between females and males by the choice of gender identity.[27]

Type of interventions

1. Any combinations of complexities and classes of ART regimens, specific ART drugs and timings of ART initiation.

Types of comparators

1. Oral placebo.
2. Any combinations of complexities and classes of ART regimens, specific ART drugs and timings of ART initiation.

Types of outcome measures

Primary outcomes

1. Risk of discontinuation or dropouts/withdrawals of ART due to AEs.
2. Risk of any AE.
3. Risk of treatment-related AEs.

Secondary outcomes

1. Risk of any serious clinic or laboratory AE (grade 3 and/or 4).
   We will extract the AEs as reported or defined by studies (serious, separate AEs grade 3, separate grade 4, grade 3, and 4). We adopted AEs grades 3 and 4 as defined by the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Paediatric Adverse Events.[28]
2. Risk of treatment-related serious clinic or laboratory AEs (grade 3 and/or 4).
   We will extract the AEs as reported or defined by studies (serious, separate AEs grade 3, separate grade 4, grade 3, and 4). We adopted AEs grades 3 and 4 as defined by the DAIDS Table for Grading the Severity of Adult and Paediatric Adverse Events.[28]
3. Risk of osteoporosis (osteopenia, osteoporosis or any osteoporosis fractures).
4. Risk of hospitalisation
5. Risk of death due to AEs.

Objective 2

Inclusion criteria

Type of studies

We will include only RCTs with at least 12 weeks of follow-up duration. For cross-over RCTs, we will include the first period of data only. Although observational studies may have larger samples and longer follow-up times than RCTs, providing information on rarer or longer-term AEs, non-randomised studies will be excluded due to the higher RoB compared with RCTs.

Type of participants

Women living with HIV/AIDS and receiving ART—regardless of age.

Type of interventions

1. Any combinations of complexities and classes of ART regimens, specific ART drugs, and timings of ART initiation.

Types of comparators

1. Any combinations of complexities and classes of ART regimens, specific ART drugs and timings of ART initiation.

Types of outcome measures

Prevalence of women with:

1. Delayed puberty
   It means the absence of breast development by age 12–13 years in girls.[29]
2. Amenorrhoea
   Amenorrhoea was defined as the absence of menses for more than 3 months.[14 30]
3. Other menstrual irregularities will be considered present whenever the participant reports any of the five variations from normal menstruation including changes in regularity, frequency, volume, duration and intermenstrual bleeding as defined by the International Federation of Gynecology and Obstetrics.
4. Early menopause
   Premature ovarian failure is considered when it occurs in women under the age of 40 years.[30]
5. Vasomotor symptoms of menopause (hot flushes)
   Presence of hot flushes.
   Frequency of hot flushes by severity.[31]
6. Osteopenia
   It is defined as BMD t-score −2.5 to −1 in women with 30 years or more and as BMD z-score −2 to −1 in those under 30 years.[28]
7. Osteoporosis
   It is defined as BMD t-score <−2.5 in women with 30 years or more and as BMD z-score < −2 in those under 30 years.[28]
8. Osteoporosis fractures
   Vertebral, non-vertebral, wrist, spine and hip fractures will be considered.

Objectives 1 and 2

Exclusion criteria

Studies evaluating ART regimens for HIV pre-exposure and post-exposure prophylaxis will be excluded. We will exclude studies focusing on pregnant, breastfeeding, or perinatal women; studies that examined the use of ART in the presence of co-infections, such as viral hepatitis B and C and tuberculosis; secondary or post hoc analysis; and open-label extensions. We will also exclude studies

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with antiretrovirals, or ART doses no longer used in clinical practice, and with ART in the study phase, not yet used.

Search methods for identification of trials

The search strategy will use Descritores em Ciências da Saúde/Medical Subject Headings (DeCS/MeSH) descriptors and synonyms, being adapted according to each database searched (online supplemental material 2). The searches will be conducted by an experienced librarian and will be reviewed by another professional librarian, according to the Peer Review of Electronic Search Strategies (Press).[32] No limitations will be imposed on the publication status, duration of follow-up, year of publication and language (we will be using a professional translation service).

Electronic searches

A structured search for eligible primary studies will be conducted in the main electronic databases: MEDLINE via PubMed; Embase via Elsevier; Cochrane Central Register of Controlled Trials (Central); Epistemonikos; and Latin American and Caribbean Health Sciences Literature (Lilacs).

Searching other resources

A manual search will be conducted in the references of the included trials. We will adapt a specific structured search strategy for the grey literature, including dissertations databases (ProQuest Dissertations and Theses Database), records of clinical trials (Global Index Medicus of WHO—WHO; Brazilian Registry of Clinical Trials—Rebec; ClinicalTrials.gov), summaries of selected international symposium/conferences on HIV, websites of government agencies and non-governmental organisations that conduct research or implement relevant programmes.

Data collection and analysis

Selection of studies

Trial selection and data extraction will be performed based on the Cochrane Handbook for Intervention Reviews.[25] More specifically, reviewers will work in pairs and independently to assess the eligibility of titles and abstracts. A similar process will be used to track full texts. Discrepancies between the assessments will be resolved by consensus or adjudication by a third reviewer. In case of duplicate publication, we will use the article with the most complete data. Secondary publications from the same trial will also be used as online supplemental information. We will perform detailed assessments of each eligible trial to minimise the possibility of overlapping trials (ie, trials that report data from the same participants). Subsequently, two team members will independently examine the references for each full-text article to identify additional relevant studies.

Data extraction and management

A prepiloted and standardised form will be used to extract data from the included studies. The reviewers will be calibrated by extracting at least three articles, in pairs and independently, and, afterward, they will carry out consensus. This process will take place until the standardisation of the extracted data. The overlap of two articles in all teams of reviewers will be adopted to assess the reliability between reviewers in extracting data in the different teams.

After this stage, two reviewers will extract the data independently, and any discrepancies will be identified and resolved (with a third author, when necessary). The data collected will be characteristics of studies (sponsorship, country, registered number, number of sites, duration of the study, timing of outcome measurement (in weeks or months); bibliometric information; information about patients (inclusion, exclusion criteria, age, ART exposure (naive vs experienced), CD4 level, numbers in each arm, drug regimen); and if the study reported AEs as specified in the section outcomes (number of participants who experienced an event) for dichotomous outcomes. We will also check the method of AE assessment: did the researchers actively monitor for AEs (low RoB), or did they simply provide spontaneous reporting of AEs that arose (high RoB)? For studies identified only in clinical trial registry websites, we will check the same data and check if they are ongoing.

When two or more papers are found for the same study, we will report it using only one ID and will extract the data of all the studies to provide the most complete report.

Assessment of methodological quality and RoB

The quality of individual studies will be assessed using Cochrane's RoB Tool version 2.0 for randomised trials on bias arising from the randomisation process, deviations from intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. The reviewers will independently assign 'definitely yes', 'probably yes', 'probably not', 'definitely not' or 'not informed' for each of the domains, classifying, according to the answers, as 'low RoB', 'some concern about the RoB' or 'high RoB'. Reviewers will resolve disagreements through discussion, and a third person will judge unresolved disagreements. Publication bias will be assessed using the funnel graph[33] for each outcome.

Statistical analysis

Objective 1

The statistical approach to summarise trial results will depend vastly on the type of available data. Differences between sexes in the risk of an event after treatment with antiretrovirals can be considered covariate-by-treatment interactions. Hence, we will attempt to employ statistical techniques that explicitly disentangle within-trial interactions effects from between-trial interaction effects, thereby minimising the risk of ecological bias.[34]

We anticipate that some trials may report information sufficient to reconstruct individual-participant data (IPD) (eg, the number of events by treatment group stratified by sex). In contrast, other trials may report information

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adequate to calculate only the OR of the event and the proportion of women in each arm (ie, aggregate data only). Thus, our primary analysis model will be based on an adaption of the model by Saramago *et al*.[35] Specifically, we will use a Bayesian IPD-AD pair-wise random-effects model that separates the within-trial interaction effects from between-trial interaction effects.

However, if only aggregate data is available (eg, OR estimates and proportion of female by treatment group), we will perform a 'daft' approach, combining across-trial interactions alone.[34] More specifically, we will conduct a Bayesian random-effects meta-regression to assess the association between the log-odds of the event and the proportion of women in the trial. We will graphically display these results using bubble plots and prediction lines with 95% credible intervals.

If only aggregate data is available, but it is possible to estimate the OR by sex separately, we will perform the 'deft' approach, combining within-trial interactions only. This approach eliminates the risk of ecological bias seen in the daft approach.[34] The log ratio of ORs will be used as a metric, and the summary estimate will be obtained by a Bayesian random-effects model.[36]

All primary analyses will employ uninformative priors. However, for the between-trial variances, we will use informative prior distributions in sensitivity analyses.[37] We will estimate the between-trial heterogeneity from the median between-trial variance, τ2, observed in the posterior distribution. A τ^2 of up to 0.04 was prespecified to denote low heterogeneity, 0.16 to denote moderate, and 0.36 to denote high statistical heterogeneity among trial estimates.[38]

Ninety-five per cent credible intervals (95% CrIs) will be calculated from the 2.5 and 97.5 percentiles of the posterior distributions. Bayesian models will be implemented in the BUGS language, and estimates will be obtained via Markov chain Monte Carlo methods (Gibbs sampling). Convergence will be checked graphically by running three chains and using the Gelman-Rubin statistic. An R statistic >1.1 will be considered evidence of non-convergence.[39] The burning-in period will have 100 000 simulations, and three different chains with 166 667 simulations each will be used (500 000 simulations in total). Starting values were manually selected to guarantee very different random draws for the three chains. Results were summarised using posterior medians with 95% CrIs. The autocorrelation and density of the estimates were checked graphically. Funnel plot asymmetry will be examined by contour-enhanced plots using frequentist estimates of log-OR on the horizontal axis and their corresponding SE estimates on the vertical axis. We will also investigate funnel plot asymmetry with Habord's test. For the latter, a p<0.10 will be considered statistically significant.

For all analyses, we will use Stata V.16 and MultiBUGS V.2.0 (Cambridge, UK).

Objective 2

We will meta-analyse proportions using a random-effects Bayesian model. Specifically, the model uses the binomial likelihood and the logit transformation of the proportions. The proportions are considered a random variable, and the mean of the logit proportions is assumed to follow a normal distribution.[40] We will use a non-informative prior for the mean of the logit-transformed study-specific proportions and the between-study variance. The burning-in period will have 50 000 simulations, and three different chains with 50 000 simulations each will be used (150 000 simulations in total). Starting values were manually selected to guarantee very different random draws for the three chains. Results were summarised using posterior medians with 95% CrIs. All model diagnostics will be performed as described above.

Subgroup analysis or sensitivity analysis

When appropriate, subgroup analysis will be employed. The subgroup that will be used includes age groups (<18 years vs 18–60 years vs >60 years); level of economic development of the study setting (low or lower-middle-income country vs middle or high-income country, as defined by the World Bank[41]); immunological status (CD4 <250 *vs* CD4 ≥250 cells/μL); time of follow-up (≤24 weeks vs 25 to 48 weeks *vs* ≥48 weeks); industry-independent funding (no vs yes); Intention-to-treat (ITT) analysis of AEs (no vs yes); attribution of AEs to drugs (no vs yes); combined vs single ART; RoB (high vs moderated and low; blinded vs open-label; adequate allocation concealment vs unclear allocation concealment).

Assessment of the certainty of the evidence and the strength of the recommendation

After the results are grouped, two reviewers will independently assess the overall certainty of the evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[42] The main results of the review will be presented in outcome tables (Summary of Findings (SoF)), as recommended by The Cochrane Collaboration.[43] The SoF table includes a general classification of the evidence related to each of the main outcomes, using the GRADE approach.[44] This table will be built with the aid of the GRADEpro software program.

The use of the GRADE allows evaluating the certainty of the evidence for each result considering the methodological quality, the objectivity of the evidence, the heterogeneity, the precision of the effect estimates and the risk of publication bias.[43] If the analysis of an outcome is not possible, for example, due to the lack of data, we will present the reasons for this in the SoF table as a footnote.

ETHICS AND DISSEMINATION

We plan on sharing our results through publication in scientific journals of high impact, peer-reviewed, and presenting it at national and international conferences.

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We hope that the results will serve to assist in the formulation of public policies aimed at guiding professionals on the management and monitoring of the AEs of ART in people living with HIV/AIDS. For this purpose, meetings are scheduled with the Department of Chronic Conditions and Sexually Transmitted Infections of Brazil's Ministry of Health during the project, seeking to align it with the interests of policy-makers.

We will also present the results and discuss the implementation, monitoring, and management of AEs in people living with HIV/AIDS in a DD with stakeholders, policymakers, and other researchers. Considering that the results of the DD can make adjustments in the recommendations of the SR, the stakeholders have to disclaim their potential conflicts of interest. For this reason, this protocol will be submitted for approval to the ethics committee before the conduction of the DD.

DISCUSSION

The results of this SR could highlight important findings to decision-making, considering the management of AEs in the different age ranges of women.

Our future results could impact public policies for people living with HIV/AIDS by offering evidence that can highlight challenges and areas of improvement, with a special view over the diversity of people and their contexts. However, there are potential limitations.

The primary studies could bring limitations to this review considering the confusion between the report of AEs and signs and symptoms of HIV/AIDS; some trials do not report the time of initiation of ART and do not separate the outcomes by sex. To overcome this limitation, we will extract the information of all trials that report the time of initiation of ART and if possible, we will meta-analyse this result.

Antiretroviral drugs also are usually given in combination, being difficult to ascertain which agent causes the AE, this could be another potential limitation of this SR.

This study did not include real-world studies that reported adverse drug reactions in patients receiving antiretrovirals because we consider that RCTs provide a more accurate diagnosis of AEs as they can be better monitored/controlled, standardised and reported compared with real-world studies.

Author affiliations
[1]Graduate Course in Pharmaceutical Sciences, University of Sorocaba, Sorocaba, São Paulo, Brazil
[2]Family Physician, Florianópolis Family Medicine Residency Program, Florianópolis, Santa Catarina, Brazil
[3]Pharmacy Undergraduate Course, Federal University of Rio de Janeiro, Rio de Janeiro, Rio de Janeiro, Brazil
[4]Nursing Undergraduate Course, University of Sorocaba, Sorocaba, São Paulo, Brazil
[5]Department of Economics, Federal University of São Carlos, Sorocaba, São Paulo, Brazil
[6]Department of Physiotherapy, University of Sorocaba, Sorocaba, São Paulo, Brazil
[7]Geriatrician, Municipal Health Department of the Florianópolis City Hall, Florianópolis, Santa Catarina, Brazil
[8]Department of Health Sciences, University of Leicester, Leicester, Leicestershire, UK
[9]Fiocruz Brasília, Oswaldo Cruz Foundation, Brasília, Federal District, Brazil

Twitter Fabiane Raquel Motter @Fabiane Mooter and Luciane Cruz Lopes @lulopesbr

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ORCID iDs
Fabiane Raquel Motter http://orcid.org/0000-0003-0796-1130
Marcus Tolentino Silva http://orcid.org/0000-0002-7186-9075
Donavan de Souza Lucio http://orcid.org/0000-0002-8434-9781
Luciane Cruz Lopes http://orcid.org/0000-0002-3684-3275

REFERENCES

1 HIV/AIDS fact sheet Geneva: World Health Organization, 2019. Available: https://www.who.int/news-room/fact-sheets/detail/hiv-aids
2 UNAIDS. Global HIV & AIDS statistics — 2020 fact sheet, 2020. Available: https://www.unaids.org/en/resources/fact-sheet
3 UNAIDS. Ending AIDS progress towards the 90-90-90 targets, 2017. Available: https://www.unaids.org/sites/default/files/media_asset/Global_AIDS_update_2017_en.pdf
4 Brazil. *Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Adultos*. Brasília: Ministério da Saúde, 2018.
5 World Health Organization. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach*. Geneva, 2016. http://www.who.int/hiv/pub/arv/arv-2016/en
6 Brazil. *Cuidado integral s pessoas que vivem com HIV pela Atenção Básica: manual para a equipe multiprofissional*. Brasília: Ministério da Saúde, 2017.
7 Scully EP. Sex differences in HIV infection. *Curr HIV/AIDS Rep* 2018;15:136–46.
8 Soon GG, Min M, Struble KA, *et al*. Meta-analysis of gender differences in efficacy outcomes for HIV-positive subjects in randomized controlled clinical trials of antiretroviral therapy (2000-2008). *AIDS Patient Care STDS* 2012;26:444–53.
9 Gesesew HA, Ward P, Hajito KW, *et al*. Discontinuation from antiretroviral therapy: a continuing challenge among adults in HIV care in Ethiopia: a systematic review and meta-analysis. *PLoS One* 2017;12:e0169651.

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10 Cejtin HE. Gynecologic issues in the HIV-infected woman. *Infect Dis Clin North Am* 2008;22:709–39.
11 Imai K, Sutton MY, Mdodo R, *et al*. HIV and menopause: a systematic review of the effects of HIV infection on age at menopause and the effects of menopause on response to antiretroviral therapy. *Obstet Gynecol Int* 2013;2013:1–11.
12 Massad LS, Evans CT, Minkoff H, *et al*. Effects of HIV infection and its treatment on self-reported menstrual abnormalities in women. *J Womens Health* 2006;15:591–8.
13 Valiaveettil C, Loutfy M, Kennedy VL, *et al*. High prevalence of abnormal menstruation among women living with HIV in Canada. *PLoS One* 2019;14:e0226992.
14 King EM, Albert AY, Murray MCM. HIV and amenorrhea: a meta-analysis. *AIDS* 2019;33:483–91.
15 Carvalho EHde, Gelenske T, Bandeira F, *et al*. Bone mineral density in HIV-infected women taking antiretroviral therapy: a systematic review. *Arq Bras Endocrinol Metabol* 2010;54:133–42.
16 Cezarino PYA, Simões RDS, Baracat EC, *et al*. Are women living with HIV prone to osteoporosis in postmenopause? A systematic review. *Rev Assoc Med Bras* 2018;64:469–73.
17 Brazil. "O Brasil tem um dos melhores programas de HIV/aids do mundo", diz Drauzio Varella, 2018. Available: http://www.aids.gov.br/pt-br/noticias/o-brasil-tem-um-dos-melhores-programas-de-hivaids-do-mundo-diz-drauzio-varella
18 Li H, Marley G, Ma W, *et al*. The role of ARV associated adverse drug reactions in influencing adherence among HIV-infected individuals: a systematic review and qualitative Meta-Synthesis. *AIDS Behav* 2017;21:341–51.
19 Geretti AM, Loutfy M, D'Arminio Monforte A, *et al*. Out of focus: tailoring the cascade of care to the needs of women living with HIV. *HIV Med* 2017;18 Suppl 2:3–17.
20 Loutfy MR, Sherr L, Sonnenberg-Schwan U, *et al*. Caring for women living with HIV: gaps in the evidence. *J Int AIDS Soc* 2013;16:18509.
21 Rosin C, Elzi L, Thurnheer C, *et al*. Gender inequalities in the response to combination antiretroviral therapy over time: the Swiss HIV cohort study. *HIV Med* 2015;16:319–25.
22 Loutfy MR, Walmsley SL, Klein MB, *et al*. Factors affecting antiretroviral pharmacokinetics in HIV-infected women with virologic suppression on combination antiretroviral therapy: a cross-sectional study. *BMC Infect Dis* 2013;13:256.
23 Curno MJ, Rossi S, Hodges-Mameletzis I, *et al*. A systematic review of the inclusion (or exclusion) of women in HIV research: from clinical studies of antiretrovirals and vaccines to cure strategies. *J Acquir Immune Defic Syndr* 2016;71:181–8.
24 Hewitt RG PN, Gugino L. *The role of gender in HIV progression*. . Spring, 2001: 14. 13–16.
25 Cochrane. Cochrane Handbook for systematic reviews of interventions. Available: https://training.cochrane.org/handbook
26 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
27 et alDoull M, Shea B, Puil L. Addressing Sex/Gender in systematic reviews: cochrane HIV/AIDS group Briefing note. version 2014-01, 2021. Available: http://equity.cochrane.org/sex-and-gender-analysis
28 U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Allergy and Infectious Diseases, AIDS Do. Table for grading the severity of adult and pediatric adverse events, corrected version 2.1, 2017. Available: https://rsc.niaid.nih.gov/sites/default/files/daidsgradingcorrectedv21.pdf
29 Crowley WF, Pitteloud N. Approach to the patient with delayed puberty UpToDate, 2020. Available: https://www.uptodate.com/contents/approach-to-the-patient-with-delayed-puberty
30 Munro MG, Critchley HOD, Fraser GS. *Abnormal uterine bleeding in reproductive-age patients: FIGO system 1 terminology and symptoms and system 2 PALM-COEIN etiology classification: UpToDate*, 2021.
31 Maclennan AH, Broadbent JL, Lester S, *et al*. Oral oestrogen and combined oestrogen/progestogen therapy versus placebo for hot flushes. *Cochrane Database Syst Rev* 2004;2004:Cd002978.
32 McGowan J, Sampson M, Salzwedel DM, *et al*. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol* 2016;75:40–6.
33 Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
34 Fisher DJ, Carpenter JR, Morris TP, *et al*. Meta-analytical methods to identify who benefits most from treatments: daft, deluded, or deft approach? *BMJ* 2017;356:j573.
35 Saramago P, Sutton AJ, Cooper NJ, *et al*. Mixed treatment comparisons using aggregate and individual participant level data. *Stat Med* 2012;31:3516–36.
36 Warn DE, Thompson SG, Spiegelhalter DJ. Bayesian random effects meta-analysis of trials with binary outcomes: methods for the absolute risk difference and relative risk scales. *Stat Med* 2002;21:1601–23.
37 Turner RM, Davey J, Clarke MJ, *et al*. Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane database of systematic reviews. *Int J Epidemiol* 2012;41:818–27.
38 da Costa BR, Juni P. Systematic reviews and meta-analyses of randomized trials: principles and pitfalls. *Eur Heart J* 2014;35:3336–45.
39 Kanters S, Karim ME, Thorlund K, *et al*. When does the use of individual patient data in network meta-analysis make a difference? A simulation study. *BMC Med Res Methodol* 2021;21:21.
40 Wong WL, Su X, Li X, *et al*. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *Lancet Glob Health* 2014;2:e106–16.
41 World Bank. Country and lending groups, 2021. Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519
42 Guyatt GH, Oxman AD, Schünemann HJ, *et al*. GRADE guidelines: a new series of articles in the Journal of clinical epidemiology. *J Clin Epidemiol* 2011;64:380–2.
43 Grade Handbook, 2013. Available: https://gdt.gradepro.org/app/handbook/handbook.html
44 Balshem H, Helfand M, Schünemann HJ, *et al*. Grade guidelines: 3. rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.

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APÊNDICE B – PROTOCOLO MODIFICADO NO PROSPERO

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PROSPERO
International prospective register of systematic reviews

Sex differences and adverse events of antiretrovirals in people living with HIV/AIDS: a systematic review and meta-analysis protocol

To enable PROSPERO to focus on COVID-19 submissions, this registration record has undergone basic automated checks for eligibility and is published exactly as submitted. PROSPERO has never provided peer review, and usual checking by the PROSPERO team does not endorse content. Therefore, automatically published records should be treated as any other PROSPERO registration. Further detail is provided here.

Review methods were amended after registration. Please see the revision notes and previous versions for detail.

Citation

Jardel Oliveira, Maíra Alves, Rodrigo Iwami, Fabiane Motter, Cristiane Bergamaschi, Marcus Silva, Alexander Itria, Diogo Scalco, Donavan Lúcio, Lauren Mazzei, Rodrigo Derech, Tiago Pereira, Jorge Barreto, Luciane Lopes. Sex differences and adverse events of antiretrovirals in people living with HIV/AIDS: a systematic review and meta-analysis protocol. PROSPERO 2021 CRD42021251051 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021251051

Review question [1 change]

Are there any sex differences in the risk of adverse events in people with HIV/AIDS treated with ART?

What is the prevalence of adverse events to the reproductive system and bone mineral density (osteoporosis, osteopenia, and fractures) in women?

Searches

A comprehensive search will be conducted using the following electronic databases: MEDLINE via PubMed, EMBASE via Elsevier, Cochrane Central Register of Controlled Trials (Central); Espitemonikos; Latin American and Caribbean Health Sciences Literature (LILACS); grey literature databases such as ProQuest Dissertations and Theses Database; and clinical trial registration portals such as Global Index Medicus of World Health Organization – WHO, Registro Brasileiro de Ensaios Clínicos – Rebec, and ClinicalTrials.gov. We will also scan the reference lists of studies meeting our inclusion criteria for further studies. In the process, we will approach prominent authors of studies meeting our inclusion criteria for further studies that they may know of. There will be no language restriction in studies considered relevant.

Types of study to be included [1 change]

We will include only randomized controlled trials (RCTs) with at least 12 weeks of follow-up duration. For cross-over RCTs, we will include the first period of data only. Although observational studies may have larger samples and longer follow-up times than RCTs, providing information on rarer or longer-term AE, non-randomized studies will be excluded due to the higher risk of bias compared to RCTs.

Condition or domain being studied [1 change]

The human immunodeficiency virus (HIV) is responsible for the progressive dysregulation of the cell-mediated immune system and could ultimately lead to the acquired immunodeficiency syndrome (AIDS). ART is established as one of the most effective interventions for the treatment of HIV/AIDS. However, research has shown that AE measures considering

sex are insufficient.

Participants/population [1 change]

Inclusion criteria:

Objective 1: Individuals of both sexes living with HIV/AIDS and receiving antiretroviral – regardless of age.

Objective 2: Women living with HIV/AIDS and receiving ART – regardless of age.

Exclusion criteria:

Coexisting diseases (e.g. hepatitis B and C; tuberculosis); pregnant; breastfeeding; or perinatal women.

Intervention(s), exposure(s) [1 change]

Inclusion criteria:

Any combinations of complexities and classes of ART regimens, specific ART drugs, and timings of ART initiation.

Exclusion criteria:

Studies assessing ART regimens for pre-exposure(PREP) and post-exposure (PEP) prophylaxis for HIV.

Comparator(s)/control [1 change]

Inclusion criteria:

Objective 1:

Oral Placebo.

Any combinations of complexities and classes of ART regimens, specific ART drugs, and timings of ART initiation.

Objective 2:

Any combinations of complexities and classes of ART regimens, specific ART drugs, and timings of ART initiation.

Exclusion criteria:

Studies assessing ART regimens for pre-exposure(PREP) and post-exposure (PEP) prophylaxis for HIV.

Context

In particular, we do not place any restrictions on the country, ethnicity, setting (rural/urban), place of delivery (home/hospital), treatment time, ART drugs and regimens, the timing of ART initiation, smoking/alcohol/drug use, stage of HIV disease, CD4 count or viral load, socio-economic status, educational attainment.

Main outcome(s) [1 change]

Objective 1:

1. Risk of discontinuation or dropouts/withdrawals of ART due to AE

2. Risk of any AE

3. Risk of treatment-emergent AE.

Objective 2:

Prevalence of women with:

1. Delayed puberty

Absence of breast development by age 12 to 13 years in girls.

2. Amenorrhea

Absence of menses for more than 3 months.

3. Other menstrual irregularities as defined by the International Federation of Gynecology and Obstetrics.

4. Early menopause

Premature ovarian failure is considered when it occurs in women under the age of 40 years.

5. Vasomotor symptoms of menopause

Presence or frequency of hot flushes by severity.

6. Osteopenia

It's defined as bone mineral density (BMD) t-score -2.5 to -1 in women with 30 years or more and as BMD z-score -2 to -1 in those under 30 years.

7. Osteoporosis

It's defined as BMD t-score < -2.5 in women with 30 years or more and as BMD z-score < -2 in those under 30 years.

8. Osteoporosis fractures

Vertebral, non-vertebral, wrist, spine, and hip fractures will be considered.

Measures of effect

Objective 1: Odds ratio.

Objective 2: Proportions.

Additional outcome(s) [1 change]

Objective 1:

1. Risk of any serious clinic or laboratory AE (grade 3 and/or 4)

We will extract the AE as reported or defined by studies (serious, separate AE grade 3, separate grade 4, grade 3, and 4). We adopted AE grades 3 and 4 as defined by the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events.

2. Risk of treatment-emergent serious clinic or laboratory AE (grade 3 and/or 4)

We will extract the AE as reported or defined by studies (serious, separate AE grade 3, separate grade 4, grade 3, and 4). We adopted AE grades 3 and 4 as defined by the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events.

3. Risk of osteoporosis (bone mineral density or fracture)

4. Risk of hospitalization

5. Risk of death due to AE.

Measures of effect

Odds Ratio.

Data extraction (selection and coding) [1 change]

A pre-piloted and standardized form will be used to extract data from the included studies. The reviewers will be calibrated by extracting at least three articles, in pairs and independently, and, afterward, they will carry out consensus. This process will take place until the standardization of the extracted data. The overlap of two articles in all teams of reviewers will be adopted to assess the reliability between reviewers in extracting data in the different teams.

After this stage, two reviewers will extract the data independently, and any discrepancies will be identified and resolved (with a third author, when necessary). The data collected will be characteristics of studies (sponsorship, country, registered number, number of sites, duration of the study, timing of outcome measurement (in weeks or months); bibliometric information; information about patients (inclusion, exclusion criteria, age, ART exposure (naive versus experienced), CD4 level, numbers in each arm, drug regimen); and if the study reported AE as specified in the section outcomes (number of participants who experienced an event) for dichotomous outcomes. We will also check the method of AE assessment: did the researchers actively monitor for AEs (low risk of bias), or did they simply provide spontaneous reporting of AEs that arose (high risk of bias)? For studies identified only in clinical trial registry websites, we will check the same data and check if they are ongoing.

When two or more papers are found for the same study, we will report it using only one ID and will extract the data of all the studies to provide the most complete report.

Risk of bias (quality) assessment [1 change]

The quality of individual studies will be assessed using Cochrane's Risk of Bias (RoB) Tool version 2.0 for randomized trials on bias arising from the randomization process, deviations from intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. The reviewers will independently assign "definitely yes", "probably yes", "probably not", "definitely not" or "not informed" for each of the domains, classifying, according to the answers, as “low risk of bias”, “some concern about the risk of bias” or “high risk of bias”. Reviewers will resolve disagreements through discussion, and a third person will judge unresolved disagreements. Publication bias will be assessed using the funnel graph for each outcome.

Strategy for data synthesis [1 change]

Objective 1:

Our primary analysis model will be based on an adaption of the model by Saramago et al., 2012. Specifically, we will use a Bayesian IPD-AD pair-wise random-effects model that separates the within-trial interaction effects from between-trial interaction effects.

Objective 2:

We will meta-analyze proportions using a random-effects Bayesian model. Specifically, the model uses the binomial likelihood and the logit transformation of the proportions. The proportions are considered a random variable, and the mean of the logit proportions is assumed to follow a normal distribution. We will use a non-informative prior for the mean of the logit-transformed study-specific proportions and the between-study variance.

However, the statistical approach to summarize trial results will depend vastly on the type of available data.

Analysis of subgroups or subsets [1 change]

When appropriate, subgroup analysis will be employed. The subgroup that will be used includes age groups (<18 years vs 18-60 years vs >60 years); level of economic development of the study setting (low or lower-middle-income country vs middle or high-income country, as defined by the World Bank); immunological status (CD4 <250 vs CD4 ≥250 cells/μl); time of follow-up (≤ 24 weeks vs 25 to 48 weeks vs ≥ 48 weeks); industry-independent funding (no vs yes); ITT analysis of AE (no vs yes); attribution of AEs to drugs (no vs yes); combined versus single antiretroviral therapy; risk of bias (high vs moderated and low; blinded vs open-label; adequate allocation concealment vs unclear allocation concealment).

Contact details for further information

Luciane Lopes

luslopesbr@gmail.com

Organisational affiliation of the review

University of Sorocaba - Uniso

https://uniso.br

Review team members and their organisational affiliations [1 change]

Jardel Oliveira. University of Sorocaba

Maíra Alves. University of Sorocaba

Rodrigo Iwami. University of Sorocaba

Dr Fabiane Motter. University of Sorocaba

Dr Cristiane Bergamaschi. University of Sorocaba

Dr Marcus Silva. University of Sorocaba

Dr Alexander Itria. Federal University of São Carlos

Diogo Scalco. Florianópolis Family Medicine Residency Program

Donavan Lúcio. Florianópolis Family Medicine Residency Program

Lauren Mazzei. University of Sorocaba

Rodrigo Derech. Florianópolis City Hall

Dr Tiago Pereira. University of Leicester

Dr Jorge Barreto. Oswaldo Cruz Foundation

Dr Luciane Lopes. University of Sorocaba

Type and method of review

Intervention, Meta-analysis, Network meta-analysis, Systematic review

Anticipated or actual start date

01 September 2021

Anticipated completion date

01 September 2022

Funding sources/sponsors

Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP

Grant number(s)

State the funder, grant or award number and the date of award

2018168938

Conflicts of interest

None known

Language

English

Country

Brazil

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Acquired Immunodeficiency Syndrome; Female; HIV Infections; Humans; Qualitative Research

Date of registration in PROSPERO

22 June 2021

Date of first submission

22 May 2021

Stage of review at time of this submission [1 change]

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Revision note

Our changes in the protocol were based on an understanding that there were two objectives in this SR, instead of the initial one, that would more deeply answer questions related to sex differences and the prevalence of specific AE related to women. Thus, the outcomes had to be adjusted to answer each question. We divided the outcomes into outcomes for objective 1 and outcomes for objective 2 and rewrote the measures of effect for each. We also adjusted the statistical section accordingly to the new arrangement of objectives.

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

22 June 2021

22 June 2021

27 September 2022

APÊNDICE C – BASES DE DADOS E ESTRATÉGIAS DE BUSCA

Quadro 5 – Bases de dados e estratégias de busca (continua)

Fonte	Estratégia de busca
Pubmed	(HIV infections [MeSH] OR HIV [MeSH] OR Acquired Immunodeficiency Syndrome [MeSH] OR HIV Seropositivity [MeSH] OR HIV OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR HIV/AIDS) AND (Anti-retroviral agents [Mesh] OR antiretroviral therapy, highly active [Mesh] OR Antiretroviral* OR ((anti) AND (retroviral*)) OR ARV OR ART OR "antiretroviral therapy" OR HAART OR ((highly) AND (active) AND (antiretroviral*) AND (therap*)) OR ((anti) AND (hiv)) OR ((anti) AND (acquired immunodeficiency)) OR ((anti) AND (acquired immuno-deficiency)) OR (anti AND (acquired immune-deficiency)) OR (anti AND (acquired immun*) AND (deficienc*)) OR Saquinavir [tiab] OR Lopinavir [tiab] OR Indinavir [tiab] OR Ritonavir [Tiab] OR Nelfinavir [tiab] OR Amprenavir [tiab] OR Fosamprenavir [tiab] OR Atazanavir [Tiab] OR Tipranavir [tiab] OR Darunavir [tiab] OR Cobicistat [Tiab] OR Emtricitabine [Tiab] OR Zidovudine [Tiab] OR Didanosine [tiab] OR Stavudine [tiab] OR Lamivudine [Tiab] OR Abacavir [Tiab] OR Nevirapine [tiab] OR Darunavir [Tiab] OR Etravirine [Tiab] OR Elvitegravir [Tiab] OR Alafenamide [Tiab] OR "Tenofovir disoproxil fumarate" [Tiab] OR "Tenofovir Alafenamide" [Tiab] OR Tenofovir [Tiab] OR Efavirenz [Tiab] OR Enfuvirtide [Tiab] OR Raltegravir [tiab] OR Maraviroc [tiab] OR Dolutegravir [tiab] OR Bictegravir [tiab]) AND (("abnormalities, drug-induced"[mesh] OR "drug hypersensitivity"[mesh] OR "drug monitoring"[mesh] OR "drug recalls"[mesh] OR "poisoning"[mesh] OR "safety-based drug withdrawals"[mesh] OR "substance-related disorders"[mesh] OR "Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "Long Term Adverse Effects"[Mesh] OR "product surveillance, postmarketing"[mesh] OR "adverse effects"[sh] OR "complications"[sh] OR "drug effects"[sh] OR "safe"[tw] OR "safety"[tw] OR "side effect*"[tw] OR "undesirable effect*"[tw] OR "treatment emergent"[tw] OR "tolerability"[tw] OR "toxicity"[tw] OR "adverse drug reaction*"[tw] OR "adrs"[tw] OR "adverse effect*"[tw] OR "adverse drug effect*"[tw] OR "adverse reaction*"[tw] OR "adverse event*"[tw] OR "adverse drug event*"[tw] OR "adverse outcome*"[tw] OR "complication*"[tw] OR "harm"[tw] OR "harmful"[tw] OR "harms"[tw] OR "risk"[tw] OR (adverse[tw] AND (effect[tw] OR effects[tw] OR reaction[tw] OR reactions[tw] OR event[tw] OR events[tw] OR outcome[tw] OR outcomes[tw])))) AND ((((((randomized controlled trial [pt]) OR controlled clinical trial [pt]) OR randomized [tiab]) OR placebo [tiab]) OR clinical trials as topic [mesh: noexp] OR randomly [tiab]) OR trial [tiab]) NOT (animals [MeSH] NOT humans [MeSH])

Quadro 5 – Bases de dados e estratégias de busca (continuação)

Fonte	Estratégia de busca
Embase	**No.** **Query** **Results** **610,204** **#1** '**human immunodeficiency virus infection**'/exp OR '**acquired immune deficiency syndrome**'/exp OR '**human immunodeficiency virus 1**'/exp OR '**human immunodeficiency virus 1 infection**'/exp OR '**human immunodeficiency virus 2**'/exp OR '**human immunodeficiency virus 2 infection**'/exp OR '**hiv aids**'/exp OR **hiv** OR **hiv-1** OR **hiv-2** OR **hiv1** OR **hiv2** OR (**hiv** AND **infect***) OR (**human** AND **immunodeficiency** AND **virus**) OR (**human** AND **immune** AND **deficiency** AND **virus**) OR (**human** AND **immuno-deficiency** AND **virus**) OR (**human** AND **immune-deficiency** AND **virus**) OR (**human** AND **immun*** AND **deficiency** AND **virus**) OR (**acquired** AND **immunodeficiency** AND **syndromes**) OR (**acquired** AND **immune** AND **deficiency** AND **syndrome**) OR (**acquired** AND **immuno-deficiency** AND **syndrome**) OR (**acquired** AND **immune-deficiency** AND **syndrome**) OR (**acquired** AND **immun*** AND **deficiency** AND **syndrome**) **522,768** **#2** '**antiretrovirus agent**'/exp OR '**highly active antiretroviral therapy**'/exp OR **antiretroviral*** OR (**anti** AND **retroviral***) OR **arv** OR **art** OR '**antiretroviral therapy**' OR **haart** OR (**highly** AND **active** AND **antiretroviral*** AND **therap***) OR (**anti** AND **hiv**) OR (**anti** AND **acquired** AND **immunodeficiency**) OR (**anti** AND **acquired** AND **immuno-deficiency**) OR (**anti** AND **acquired** AND **immune-deficiency**) OR (**anti** AND **acquired** AND **immun*** AND **deficienc***) OR **saquinavir**:ab,ti OR **lopinavir**:ab,ti OR **indinavir**:ab,ti OR **ritonavir**:ab,ti OR **nelfinavir**:ab,ti OR **amprenavir**:ab,ti OR **fosamprenavir**:ab,ti OR **atazanavir**:ab,ti OR **tipranavir**:ab,ti OR **cobicistat**:ab,ti OR **emtricitabine**:ab,ti OR **zidovudine**:ab,ti OR **didanosine**:ab,ti OR **stavudine**:ab,ti OR **lamivudine**:ab,ti OR **abacavir**:ab,ti OR **nevirapine**:ab,ti OR **darunavir**:ab,ti OR **etravirine**:ab,ti OR **elvitegravir**:ab,ti OR **alafenamide**:ab,ti OR '**tenofovir disoproxil fumarate**':ab,ti OR '**tenofovir alafenamide**':ab,ti OR **tenofovir**:ab,ti OR **efavirenz**:ab,ti OR **enfuvirtide**:ab,ti OR **raltegravir**:ab,ti OR **maraviroc**:ab,ti OR **dolutegravir**:ab,ti OR **bictegravir**:ab,ti **10,788,807** **#3** '**adverse drug reaction**'/exp OR '**drug hypersensitivity**'/exp OR '**drug monitoring**'/exp OR '**drug recall**'/exp OR '**drug intoxication**'/exp OR '**side effect**'/exp OR '**postmarketing surveillance**'/exp OR '**drug safety**'/exp OR '**drug surveillance program**'/exp OR '**drug toxicity**'/exp OR '**adverse event**'/exp OR '**complication**'/exp OR '**drug effect**'/exp OR **safe** OR **safety** OR '**side effect***' OR '**undesirable effect***' OR '**treatment emergent**' OR '**tolerability**' OR '**toxicity**' OR '**adverse drug reaction***' OR '**adrs**' OR '**adverse effect***' OR '**adverse drug effect***' OR '**adverse reaction***' OR '**adverse event***' OR '**adverse drug event***' OR '**adverse outcome***' OR '**complication***' OR '**harm**' OR '**harmful**' OR '**harms**' OR '**risk**' OR (**adverse** AND (**effect** OR **effects** OR **reaction** OR **reactions** OR **event** OR **events** OR **outcome** OR **out comes**)) **1,832,252** **#4** '**randomized controlled trial**':it OR '**controlled clinical trial**':it OR **randomized**:ab,ti OR **placebo**:ab,ti OR ('**clinical trial**'/de AND **topic**) OR **randomly**:ab,ti OR **trial**:ab,ti

Quadro 5 – Bases de dados e estratégias de busca (continuação)

Fonte	Estratégia de busca
Embase	**5,615,547** **#5** '**animal**'/exp NOT '**human**'/exp **11,308** **#6** #**1** AND #**2** AND #**3** AND #**4** NOT #**5**
Cochrane Central	Search Name: Cochrane RADAR Last Saved: 25/05/2021 20:49:52 Comment: ID Search #1 MeSH descriptor: [HIV Infections] explode all trees #2 MeSH descriptor: [HIV] explode all trees #3 MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees #4 MeSH descriptor: [HIV Seropositivity] explode all trees #5 (HIV OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR AIDS):ti,ab,kw #6 #1 OR #2 OR #3 OR #4 OR #5 #7 MeSH descriptor: [Anti-Retroviral Agents] explode all trees #8 MeSH descriptor: [Antiretroviral Therapy, Highly Active] explode all trees #9 (Antiretroviral* OR ((anti) AND (retroviral*)) OR ARV OR ART OR "antiretroviral therapy" OR HAART OR ((highly) AND (active) AND (antiretroviral*) AND (therap*)) OR ((anti) AND (hiv)) OR ((anti) AND (acquired immunodeficiency)) OR ((anti) AND (acquired immuno-deficiency)) OR (anti AND (acquired immune-deficiency)) OR (anti AND (acquired immun*) AND (deficienc*))):ti,ab,kw #10 (Saquinavir OR Lopinavir OR Indinavir OR Ritonavir OR Nelfinavir OR Amprenavir OR Fosamprenavir OR Atazanavir OR Tipranavir OR Darunavir OR Cobicistat OR Emtricitabine OR Zidovudine OR Didanosine OR Stavudine OR Lamivudine OR Abacavir OR Nevirapine OR Darunavir OR Etravirine OR Elvitegravir OR Alafenamide OR "Tenofovir disoproxil fumarate" OR "Tenofovir Alafenamide" OR Tenofovir OR Efavirenz OR Enfuvirtide OR Raltegravir OR Maraviroc OR Dolutegravir OR Bictegravir):ti,ab #11 #7 OR #8 OR #9 OR #10 #12 MeSH descriptor: [Abnormalities, Drug-Induced] explode all trees #13 MeSH descriptor: [Drug Hypersensitivity] explode all trees #14 MeSH descriptor: [Drug Monitoring] explode all trees #15 MeSH descriptor: [Drug Recalls] explode all trees #16 MeSH descriptor: [Poisoning] explode all trees #17 MeSH descriptor: [Safety-Based Drug Withdrawals] explode all trees #18 MeSH descriptor: [Substance-Related Disorders] explode all trees #19 MeSH descriptor: [Drug-Related Side Effects and Adverse Reactions] explode all trees #20 MeSH descriptor: [Long Term Adverse Effects] explode all trees #21 MeSH descriptor: [Product Surveillance, Postmarketing] explode all trees #22 MeSH descriptor: [] explode all trees and with qualifier(s): [adverse effects - AE] #23 MeSH descriptor: [] explode all trees and with qualifier(s): [complications - CO] #24 MeSH descriptor: [] explode all trees and with qualifier(s): [drug effects - DE]

Quadro 5 – Bases de dados e estratégias de busca (continuação)

Fonte	Estratégia de busca
Cochrane Central	#25 ("safe" OR "safety" OR "side effect*" OR "undesirable effect*" OR "treatment emergent" OR "tolerability" OR "toxicity" OR "adverse drug reaction*" OR "adrs" OR "adverse effect*" OR "adverse drug effect*" OR "adverse reaction*" OR "adverse event*" OR "adverse drug event*" OR "adverse outcome*" OR "complication*" OR "harm" OR "harmful" OR "harms" OR "risk" OR (adverse AND (effect OR effects OR reaction OR reactions OR event OR events OR outcome OR outcomes))) #26 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 #27 #22 OR #23 OR #24 #28 #25 OR #26 OR #27 #29 #6 AND #11 AND #28
BVS	((mh:(HIV infections)) OR (mh:(HIV)) OR (mh:(Acquired Immunodeficiency Syndrome)) OR (mh:(HIV Seropositivity)) OR ((HIV OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR AIDS))) AND ((mh:(Anti-Retroviral Agents)) OR (mh:(Antiretroviral Therapy, Highly Active)) OR ((Antiretroviral* OR ((anti) AND (retroviral*)) OR ARV OR ART OR "antiretroviral therapy" OR HAART OR ((highly) AND (active) AND (antiretroviral*) AND (therap*)) OR ((anti) AND (hiv)) OR ((anti) AND (acquired immunodeficiency)) OR ((anti) AND (acquired immuno-deficiency)) OR (anti AND (acquired immune-deficiency)) OR (anti AND (acquired immun*) AND (deficienc*)))) OR (ti:((Saquinavir OR Lopinavir OR Indinavir OR Ritonavir OR Nelfinavir OR Amprenavir OR Fosamprenavir OR Atazanavir OR Tipranavir OR Darunavir OR Cobicistat OR Emtricitabine OR Zidovudine OR Didanosine OR Stavudine OR Lamivudine OR Abacavir OR Nevirapine OR Darunavir OR Etravirine OR Elvitegravir OR Alafenamide OR "Tenofovir disoproxil fumarate" OR "Tenofovir Alafenamide" OR Tenofovir OR Efavirenz OR Enfuvirtide OR Raltegravir OR Maraviroc OR Dolutegravir OR Bictegravir))) OR (ab:((Saquinavir OR Lopinavir OR Indinavir OR Ritonavir OR Nelfinavir OR Amprenavir OR Fosamprenavir OR Atazanavir OR Tipranavir OR Darunavir OR Cobicistat OR Emtricitabine OR Zidovudine OR Didanosine OR Stavudine OR Lamivudine OR Abacavir OR Nevirapine OR Darunavir OR Etravirine OR Elvitegravir OR Alafenamide OR "Tenofovir disoproxil fumarate" OR "Tenofovir Alafenamide" OR Tenofovir OR Efavirenz OR Enfuvirtide OR Raltegravir OR Maraviroc OR Dolutegravir OR Bictegravir)))) AND ((mh:(Abnormalities, Drug-Induced)) OR (mh:(Drug Hypersensitivity)) OR (mh:(Drug Monitoring)) OR (mh:(Drug Recalls)) OR (mh:(Poisoning)) OR (mh:(Safety-Based Drug Withdrawals)) OR (mh:(Substance-Related Disorders)) OR (mh:(Drug-Related Side Effects and Adverse Reactions)) OR (mh:(Long Term Adverse Effects)) OR (mh:(Product Surveillance, Postmarketing)) OR ("adverse effect" OR "adverse effects" OR "drug effects" OR safe OR safety OR "side effect" OR "side effects" OR "undesirable effect" OR "undesirable effects" OR "treatment emergent" OR tolerability OR toxicity OR "adverse drug reaction" OR "adverse drug reactions" OR adrs OR "adverse drug effect" OR "adverse drug effects" OR "adverse reaction" OR "adverse reactions" OR "adverse event" OR "adverse events" OR "adverse drug event" OR "adverse drug events" OR "adverse outcome" OR "adverse outcomes" OR complication OR complications OR harm OR harmful OR harms OR risk OR ((adverse) AND (effect OR effects OR reaction OR reactions OR event OR events OR outcome OR outcomes)))) AND ((mh:(clinical trials)) OR (randomized controlled trial) OR (controlled clinical trial) OR randomized OR placebo OR randomly OR trial)

Quadro 5 – Bases de dados e estratégias de busca (continuação)

Fonte	Estratégia de busca
Epistemonikos	((HIV infections) OR HIV OR (Acquired Immunodeficiency Syndrome) OR (HIV Seropositivity) OR (hiv-1) OR (hiv-2) OR hiv1 OR hiv2 OR (hiv infect*) OR (human immunodeficiency virus) OR (human immune deficiency virus) OR (human immuno-deficiency virus) OR (human immune-deficiency virus) OR ((human immun*) AND (deficiency virus)) OR (acquired immunodeficiency syndromes) OR (acquired immune deficiency syndrome) OR (acquired immuno-deficiency syndrome) OR (acquired immune-deficiency syndrome) OR ((acquired immun*) AND (deficiency syndrome)) OR AIDS) AND ((Anti-retroviral agents) OR (antiretroviral therapy, highly active) OR Antiretroviral* OR ((anti) AND (retroviral*)) OR ARV OR ART OR "antiretroviral therapy" OR HAART OR ((highly) AND (active) AND (antiretroviral*) AND (therap*)) OR ((anti) AND (hiv)) OR ((anti) AND (acquired immunodeficiency)) OR ((anti) AND (acquired immuno-deficiency)) OR (anti AND (acquired immune-deficiency)) OR (anti AND (acquired immun*) AND (deficienc*)) OR Saquinavir OR Lopinavir OR Indinavir OR Ritonavir OR Nelfinavir OR Amprenavir OR Fosamprenavir OR Atazanavir OR Tipranavir OR Darunavir OR Cobicistat OR Emtricitabine OR Zidovudine OR Didanosine OR Stavudine OR Lamivudine OR Abacavir OR Nevirapine OR Darunavir OR Etravirine OR Elvitegravir OR Alafenamide OR "Tenofovir disoproxil fumarate" OR "Tenofovir Alafenamide" OR Tenofovir OR Efavirenz OR Enfuvirtide OR Raltegravir OR Maraviroc OR Dolutegravir OR Bictegravir) AND ("abnormalities, drug-induced" OR "drug hypersensitivity" OR "drug monitoring" OR "drug recalls" OR "poisoning" OR "safety-based drug withdrawals" OR "substance-related disorders" OR "Drug-Related Side Effects and Adverse Reactions" OR "Long Term Adverse Effects" OR "product surveillance, postmarketing" OR "adverse effects" OR "complications" OR "drug effects" OR "safe" OR "safety" OR "side effect*" OR "undesirable effect*" OR "treatment emergent" OR "tolerability" OR "toxicity" OR "adverse drug reaction*" OR "adrs" OR "adverse effect*" OR "adverse drug effect*" OR "adverse reaction*" OR "adverse event*" OR "adverse drug event*" OR "adverse outcome*" OR "complication*" OR "harm" OR "harmful" OR "harms" OR "risk" OR (adverse AND (effect OR effects OR reaction OR reactions OR event OR events OR outcome OR outcomes))) AND ((randomized controlled trial) OR (controlled clinical trial) OR randomized OR placebo OR randomly OR trial)

Quadro 5 – Bases de dados e estratégias de busca (conclusão)

Fonte	Estratégia de busca
Global Index Medicus	((mh:(HIV infections)) OR (mh:(HIV)) OR (mh:(Acquired Immunodeficiency Syndrome)) OR (mh:(HIV Seropositivity)) OR ((HIV OR hiv-1 OR hiv-2 OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR AIDS))) AND ((mh:(Anti-Retroviral Agents)) OR (mh:(Antiretroviral Therapy, Highly Active)) OR ((Antiretroviral* OR ((anti) AND (retroviral*)) OR ARV OR ART OR "antiretroviral therapy" OR HAART OR ((highly) AND (active) AND (antiretroviral*) AND (therap*)) OR ((anti) AND (hiv)) OR ((anti) AND (acquired immunodeficiency)) OR ((anti) AND (acquired immuno-deficiency)) OR (anti AND (acquired immune-deficiency)) OR (anti AND (acquired immun*) AND (deficienc*)))) OR (ti:((Saquinavir OR Lopinavir OR Indinavir OR Ritonavir OR Nelfinavir OR Amprenavir OR Fosamprenavir OR Atazanavir OR Tipranavir OR Darunavir OR Cobicistat OR Emtricitabine OR Zidovudine OR Didanosine OR Stavudine OR Lamivudine OR Abacavir OR Nevirapine OR Darunavir OR Etravirine OR Elvitegravir OR Alafenamide OR "Tenofovir disoproxil fumarate" OR "Tenofovir Alafenamide" OR Tenofovir OR Efavirenz OR Enfuvirtide OR Raltegravir OR Maraviroc OR Dolutegravir OR Bictegravir))) OR (ab:((Saquinavir OR Lopinavir OR Indinavir OR Ritonavir OR Nelfinavir OR Amprenavir OR Fosamprenavir OR Atazanavir OR Tipranavir OR Darunavir OR Cobicistat OR Emtricitabine OR Zidovudine OR Didanosine OR Stavudine OR Lamivudine OR Abacavir OR Nevirapine OR Darunavir OR Etravirine OR Elvitegravir OR Alafenamide OR "Tenofovir disoproxil fumarate" OR "Tenofovir Alafenamide" OR Tenofovir OR Efavirenz OR Enfuvirtide OR Raltegravir OR Maraviroc OR Dolutegravir OR Bictegravir)))) AND ((mh:(Abnormalities, Drug-Induced)) OR (mh:(Drug Hypersensitivity)) OR (mh:(Drug Monitoring)) OR (mh:(Drug Recalls)) OR (mh:(Poisoning)) OR (mh:(Safety-Based Drug Withdrawals)) OR (mh:(Substance-Related Disorders)) OR (mh:(Drug-Related Side Effects and Adverse Reactions)) OR (mh:(Long Term Adverse Effects)) OR (mh:(Product Surveillance, Postmarketing)) OR ("adverse effect" OR "adverse effects" OR "drug effects" OR safe OR safety OR "side effect" OR "side effects" OR "undesirable effect" OR "undesirable effects" OR "treatment emergent" OR tolerability OR toxicity OR "adverse drug reaction" OR "adverse drug reactions" OR adrs OR "adverse drug effect" OR "adverse drug effects" OR "adverse reaction" OR "adverse reactions" OR "adverse event" OR "adverse events" OR "adverse drug event" OR "adverse drug events" OR "adverse outcome" OR "adverse outcomes" OR complication OR complications OR harm OR harmful OR harms OR risk OR ((adverse) AND (effect OR effects OR reaction OR reactions OR event OR events OR outcome OR outcomes)))) AND ((mh:(clinical trials)) OR (randomized controlled trial) OR (controlled clinical trial) OR randomized OR placebo OR randomly OR trial)

APÊNDICE D – ESTUDOS EXCLUÍDOS

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continua)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Walker	1988	Anemia and erythropoiesis in patients with the acquired immunodeficiency syndrome (AIDS) and Kaposi sarcoma treated with zidovudine
2	Richman	1988	Results of continued monitoring of participants in the placebo-controlled trial of zidovudine for serious human immunodeficiency virus infection
3	Gelmon	1989	Nature, time course and dose dependence of zidovudine-related side effects: results from the Multicenter Canadian Azidothymidine Trial
4	Lindley	1989	AIDS: AZT for children in extended US trial
5	Hooker	1990	Antiretroviral therapy and the use of zidovudine for HIV infection
6	Levitt	1990	Psychogenic panic after zidovudine therapy: The therapeutic benefit of an N of 1 trial
7	Skowron	1990	Phase II trial of alternating and intermittent regimens of zidovudine (ZDV) and 2',3'-dideoxycytidine (ddC) in ARC and AIDS
8	NR	1990	Zidovudine for symptomless HIV infection
9	McKinney	1991	A multicenter trial of oral zidovudine in children with advanced human immunodeficiency virus disease. The Protocol 043 Study Group
10	Butler	1991	Drug trial benefited HIV children
11	Darbyshire	1992	Didanosine for zidovudine-intolerant patients with HIV disease
12	Seidlin	1992	Pancreatitis and pancreatic dysfunction in patients taking dideoxyinosine
13	Collier	1993	Combination therapy with zidovudine and didanosine compared with zidovudine alone in HIV-1 infection
14	Williams	1993	Pharmacokinetics of 2-fluorodideoxycytidine (2FddC) in patients infected with human immunodeficiency virus
15	Dayan	1993	A comparison of the toxicity and efficacy of two doses of dideoxycytidine (ddC) in patients with AIDS or AIDS related complex (ARC)
16	NR	1993	ddI trial results reported
17	Lüthy	1994	[Antiretroviral therapy. Current status and perspectives]
18	NR	1994	L-697,661 trial results
19	Choo	1995	Combination superior to zidovudine in Delta trial
20	Montaner	1995	The safety profile of stavudine (d4T) in advanced HIV infection-experience from the Canadian expanded access program (EAP)
21	Pollard	1995	Safety of Didanosine plus Stavudine Combination Therapy in HIV-infected Subjects in a Pilot Randomized Double-blinded Trial
22	Soo	1995	Inter-Company Collaboration Combination Trials. Clinical Trial Subcommittee of the Inter-Company Collaboration for AIDS Drug Development
23	Mulder	1995	[Clinical effectiveness of zidovudine]
24	NR	1995	Anti-HIV therapy lowers risk of AIDS, death in patients with intermediate-stage HIV disease
25	Blum	1996	Low-dose zalcitabine-related toxic neuropathy: frequency, natural history, and risk factors
26	Wachsman	1996	Pharmacokinetics, safety and bioavailability of HPMPC (cidofovir) in human immunodeficiency virus-infected subjects
27	James	1996	Ritonavir (Abbott protease inhibitor) proves survival benefit in late-stage AIDS

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
28	Jablonowski	1996	[Antiretroviral therapy in HIV infection]
29	Randall	1996	CPCRA 007: preliminary results of combination antiretroviral study
30	NR	1996	Mortality reduced by ritonavir
31	NR	1996	Ritonavir increases lymphocyte subsets
32	NR	1996	Saquinavir for treatment of patients with HIV
33	d'Arminio Monforte	1997	Italian multicentre study of didanosine compassionate use in advanced HIV infection. Italian BMS-906 Study Group
34	Villalba	1997	Safety and efficacy of two different triple drug combinations in which either lamivudine or didanosine were administered with stavudine plus indinavir
35	NR	1997	Final CESARE trial results show continued clinical and survival benefit
36	NR	1997	d4T and ddI shown to be safe and effective
37	NR	1997	Anti-HIV effects of nelfinavir reported after ten months of combination therapy
38	NR	1997	Clinical trial results of GEM91 show activity against advance HIV
39	Breckenridge	1997	Antiretroviral drug trials
40	NR	1997	More new drugs for HIV and associated infections
41	Cato	1998	Pharmacokinetic interaction between ritonavir and didanosine when administered concurrently to HIV-infected patients
42	Bradbeer	1998	Ritonavir reduced AIDS complications and risk for death in HIV-1 infection
43	Mayers	1998	A double-blind, placebo-controlled study to assess the safety, tolerability and antiretroviral activity of efavirenz (EFV, Sustiva, DMP 266) in combination with open-label zidovudine and lamivudine in HIV-1 infected patients. Presented at: XIII Internatio
44	Ruxrungtham	1998	HIV-NAT 002: a randomized, open-label study to explore the antiretroviral efficacy and tolerability of immediate vs deferred switching from ddI/d4t to AZT in a Thai HIV-1 infected population pretreated with ddI/d4t
45	Gürtler	1998	[AIDS triple therapy. The gap between viral load and side effects]
46	Reijers	1998	[Amsterdam duration of antiretroviral medication (ADAM)--study: induction-suppression treatment in HIV-I infection, preliminary results]
47	Hudson	1999	HIVNET nevirapine trials
48	Kline	1999	Combination therapy with stavudine (d4T) plus didanosine (ddI) in children with human immunodeficiency virus infection. The Pediatric AIDS Clinical Trials Group 327 Team
49	NR	1999	T-20: 5-drug combination trial for heavily treated NNRTI-naive patients now recruiting
50	NR	1999	Amprenavir: a new HIV protease inhibitor
51	NR	1999	Zidovudine + lamivudine
52	Gazzard	2000	Relative potencies of protease inhibitors
53	Cherry	2000	Deaths bring South African HIV drug trials to a premature halt
54	Cotton	2000	Antiretroviral therapy in children - Increased benefit from increased complexity
55	Gulick	2000	3-year suppression of HIV viremia with indinavir, zidovudine, and lamivudine
56	NR	2000	Lopinavir/ritonavir. (Kaletra)
57	NR	2000	Anti-HIV agents. Efavirenz versus indinavir: who really wins?
58	van der Valk	2001	Increased risk of lipodystrophy when nucleoside analogue reverse transcriptase inhibitors are included with protease inhibitors in the treatment of HIV-1 infection

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
59	Katzenstein	2001	Virologic and CD4 cell response to zidovudine or zidovudine and lamivudine following didanosine treatment of human immunodeficiency virus infection
60	Foudraine	2001	Durable HIV-1 suppression with indinavir after failing lamivudine-containing double nucleoside therapy: a randomized controlled trial
61	Kunches	2001	Tolerability of enteric-coated didanosine capsules compared with didanosine tablets in adults with HIV infection
62	Moreno	2001	Long-term outcomes of protease inhibitor-based therapy in antiretroviral treatment-naive HIV-infected injection drug users on methadone maintenance programmes
63	Wensing	2001	Replacing ritonavir by nelfinavir or nelfinavir/saquinavir as part of highly active antiretroviral therapy leads to an improvement of triglyceride levels
64	Huff	2001	Tenacious tenofovir struts its stuff in a virtual ICAAC
65	Dat	2001	Outcomes of a trial of HIV-1 immunogen in patients with HIV infection [1] mutiple letters
66	NR	2001	[HIV management requires strategic planning. Optimal sequencing of protease inhibitors]
67	NR	2001	[On the path to "e-HAART"? Glimpse at salvage therapy]
68	NR	2001	[Progress in HIV therapy. Effective and simple therapy with efavirenz]
69	NR	2001	[Positive change from protease inhibitor to non-nucleoside reverse transcriptase inhibitor efavirenz. Improved virus control thanks to protease inhibitor switch]
70	NR	2001	[Results of the AIDS-In-Europe Study. Non-nucleoside reverse transcriptase inhibitor does not equal non-nucleoside reverse transcriptase inhibitor]
71	Giles	2001	T-20 phase III studies underway
72	NR	2001	Switching to nevirapine--results after one year
73	PENTA	2002	Comparison of dual nucleoside-analogue reverse-transcriptase inhibitor regimens with and without nelfinavir in children with HIV-1 who have not previously been treated: the PENTA 5 randomised trial
74	Yogev	2002	Stavudine, nevirapine and ritonavir in stable antiretroviral therapy-experienced children with human immunodeficiency virus infection
75	Cheer	2002	Stavudine once daily
76	Chêne	2002	Role of long-term nucleoside-analogue therapy in lipodystrophy and metabolic disorders in human immunodeficiency virus-infected patients
77	Voigt	2002	First-line ritonavir/indinavir 100/800 mg twice daily plus nucleoside reverse transcriptase inhibitors in a German multicentre study: 48-week results
78	Gaytan	2002	Evaluation of the efficacy of two antiretroviral triple-drug therapy with indinavir or saquinavir in HIV-infected patients without previous treatment
79	Greub	2002	Intermittent and sustained low-level HIV viral rebound in patients receiving potent antiretroviral therapy
80	Valer	2002	Impact of HIV genotyping and drug levels on the response to salvage therapy with saquinavir/ritonavir
81	NR	2002	NEAT trial releases results
82	James	2002	Lipoatrophy and antiretroviral drug changes
83	NR	2002	Atazanavir demonstrates antiviral efficacy and a favorable lipid profile at 48 weeks
84	NR	2002	[New protease inhibitor atazanavir. Simple administration--less resistance]

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
85	NR	2002	[Simple, safe and effective. New protease inhibitor means progress]
86	Cao	2002	[A clinical trial using zidovudine and lamivudine plus indinavir triple therapy in Chinese individuals with human immunodeficiency virus infection]
87	Hirsch	2003	Long-term efficacy, safety, and tolerability of indinavir-based therapy in protease inhibitor-naive adults with advanced HIV infection
88	Coplan	2003	Incidence of myocardial infarction in randomized clinical trials of protease inhibitor-based antiretroviral therapy: an analysis of four different protease inhibitors
89	Greenberg	2003	Long-term efficacy and safety of twice-daily saquinavir soft gelatin capsules (SGC), with or without nelfinavir, and three times daily saquinavir-SGC, in triple combination therapy for HIV infection: 100-week follow-up
90	Hammer	2003	A randomized trial of nelfinavir and abacavir in combination with efavirenz and adefovir dipivoxil in HIV-1-infected persons with virological failure receiving indinavir
91	Tashima	2003	Lipid changes in patients initiating efavirenz- and indinavir-based antiretroviral regimens
92	Murphy	2003	Reviving protease inhibitors: new data and more options
93	Amin	2003	Combined analysis of two-year follow-up from two open-label randomized trials comparing efficacy of three nucleoside reverse transcriptase inhibitor backbones for previously untreated HIV-1 infection: OzCombo 1 and 2
94	Moyle	2003	Double "d" drug danger
95	Katlama	2003	Comparison of metabolic abnormalities 48 weeks after switching from highly active antiretroviral therapy containing a non-nucleoside reverse transcriptase inhibitor to Trizivir versus continued highly active antiretroviral therapy
96	Moyle	2003	Abacavir plus lamivudine: a thymidine analogue-sparing NRTI backbone
97	Bartlett	2003	Early intensification with abacavir in subjects at high risk for incomplete viral suppression
98	Zheng	2003	A short-term trial of didonosine, stavudine, and nevirapine combination t herapy for human immunodeficiency virus infection
99	Bartlett	2003	Atazanavir: clinical use
100	Moyle	2003	Protease inhibitor-sparing regimens: new evidence strengthens position
101	NR	2003	[Enduringly effective and tolerable initial therapy of HIV. Even after 5 years no resistance]
102	NR	2003	[Results of a large randomized study: after switch to LPV/r quality of life improved]
103	Pfeiffer	2003	One major HIV drug combo fails in trial, others succeed
104	Wang	2004	Pharmacokinetics and Safety of Single Oral Doses of Emtricitabine in Human Immunodeficiency Virus-Infected Children
105	Hudson	2004	HIVNET 012 and Petra
106	Hicks	2004	Long-term safety and durable antiretroviral activity of lopinavir/ritonavir in treatment-naive patients: 4 year follow-up study
107	Badía	2004	Health-related quality of life in HIV patients switching to twice-daily indinavir/ritonavir regimen or continuing with three-times-daily indinavir-based therapy
108	MacArthur	2004	Efficacy and safety of abacavir plus lamivudine versus didanosine plus stavudine when combined with a protease inhibitor, a nonnucleoside reverse transcriptase inhibitor, or both in HIV-1 positive antiretroviral-naive persons

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
109	Ruane	2004	Safety/Tolerability and Efficacy of Abacavir-Containing Combination Therapy in HIV-1-Infected Adults in a Clinical Practice Setting: Results of ZORRO
110	Wood	2004	Long-term efficacy and safety of atazanavir with stavudine and lamivudine in patients previously treated with nelfinavir or atazanavir
111	Arranz-Caso	2004	Treatment of HIV-infected patients with a combination of efavirenz, nevirapine and nucleoside reverse transcriptase inhibitors
112	Cahn	2004	Atazanavir--a once-daily HIV protease inhibitor that does not cause dyslipidemia in newly treated patients: results from two randomized clinical trials
113	Voigt	2004	Safety, efficacy and development of resistance under the new protease inhibitor lopinavir/ritonavir: 48-week results
114	Henry	2004	C-Reactive protein levels over time and cardiovascular risk in HIV-infected individuals suppressed on an indinavir-based regimen: AIDS Clinical Trials Group 5056s
115	Huff	2004	Boosted Reyataz: 48-week results
116	Baylor	2004	Hepatotoxicity associated with nevirapine use
117	Raffi	2004	[Clinical efficacy and tolerance of enfuvirtide (Fuzeon), new antiretroviral inhibitors of intracellular penetration of human immunodeficiency virus (HIV) type 1]
118	NR	2004	[Long-term tolerance. Favorable lipid profile--favorable effect on development of lipodystrophy?]
119	NR	2004	[3 years' data of tenofovir. Confirmed as a valuable building block]
120	NR	2004	[Atazanavir protects lipid metabolism. New PI with favorable metabolic profile]
121	NR	2004	[Approval of a new nucleoside. Component of complete once daily regimen]
122	NR	2004	[CROI--presentation of new study results. In a comparison of NNRTI nevirapine is equally effective]
123	NR	2004	Tenofovir: For first-line antiretroviral therapy: Wait and see
124	NR	2004	Anti-HIV agents. Once-daily lopinavir/ritonavir (Kaletra)
125	NR	2004	Complications & side effects. Clinical trial compares three face fillers
126	Dubé	2005	Glucose metabolism, lipid, and body fat changes in antiretroviral-naive subjects randomized to nelfinavir or efavirenz plus dual nucleosides
127	Fisac	2005	Metabolic benefits 24 months after replacing a protease inhibitor with abacavir, efavirenz or nevirapine
128	Johnson	2005	Atazanavir plus ritonavir or saquinavir, and lopinavir/ritonavir in patients experiencing multiple virological failures
129	Thompson	2005	Short-term safety and pharmacodynamics of amdoxovir in HIV-infected patients
130	Clifford	2005	Impact of efavirenz on neuropsychological performance and symptoms in HIV-infected individuals
131	Kappelhoff	2005	Are adverse events of nevirapine and efavirenz related to plasma concentrations?
132	Mootsikapun	2005	Efficacy and safety of indinavir/ritonavir 400/100 mg twice daily plus two nucleoside analogues in treatment-naive HIV-1-infected patients with CD4+ T-cell counts <200 cells/mm3: 96-week outcomes
133	Maggiolo	2005	Quadruple-drug induction HAART in advanced HIV infection
134	Trottier	2005	Safety of enfuvirtide in combination with an optimized background of antiretrovirals in treatment-experienced HIV-1-infected adults over 48 weeks
135	NR	2005	Tipranavir favored in RESIST-2

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
136	Moyle	2005	The impact of abacavir on lipids and lipodystrophy
137	Zhou	2005	A one-year clinical trial using didanosine, stavudine and nevirapine for highly active antiretroviral therapy
138	NR	2005	Investigational protease inhibitor meets trial goal
139	Hicks	2006	Durable efficacy of tipranavir-ritonavir in combination with an optimised background regimen of antiretroviral drugs for treatment-experienced HIV-1-infected patients at 48 weeks in the Randomized Evaluation of Strategic Intervention in multi-drug reSistant patients with Tipranavir (RESIST) studies: an analysis of combined data from two randomised open-label trials
140	Mulligan	2006	Mixed patterns of changes in central and peripheral fat following initiation of antiretroviral therapy in a randomized trial
141	Gandhi	2006	Effect of baseline- and treatment-related factors on immunologic recovery after initiation of antiretroviral therapy in HIV-1-positive subjects: Results from ACTG 384
142	Bellon	2006	Antiretroviral activity and safety of lopinavir/ritonavir in protease inhibitor-experienced HIV-infected children with severe-moderate immunodeficiency
143	Castillo	2006	Long-term safety and tolerability of the lamivudine/abacavir combination as components of highly active antiretroviral therapy
144	Maggiolo	2006	The Trivacan study
145	Llibre	2006	Sustained improvement of dyslipidaemia in HAART-treated patients replacing stavudine with tenofovir
146	Dwyer	2006	Enfuvirtide in HIV-1-infected individuals changing therapy to a nucleoside reverse transcriptase inhibitor sparing regimen: the ALLIANCE Study
147	NR	2006	Better lipid profile for Invirase
148	Dzwonek	2006	Body fat changes and lipodystrophy in HIV-infected children: impact of highly active antiretroviral therapy
149	Zhou	2006	Highly active antiretroviral treatment containing efavirenz or nevirapine and related toxicity in the TREAT Asia HIV Observational Database
150	Tebas	2007	Switching to a protease inhibitor-containing, nucleoside-sparing regimen (lopinavir/ritonavir plus efavirenz) increases limb fat but raises serum lipid levels: results of a prospective randomized trial (AIDS clinical trial group 5125s)
151	Boffito	2007	Pharmacokinetics and antiretroviral response to darunavir/ritonavir and etravirine combination in patients with high-level viral resistance
152	Reynes	2007	TORO: ninety-six-week virologic and immunologic response and safety evaluation of enfuvirtide with an optimized background of antiretrovirals
153	Cassetti	2007	The safety and efficacy of tenofovir DF in combination with lamivudine and efavirenz through 6 years in antiretroviral-naïve HIV-1-infected patients
154	Madruga	2007	The safety and efficacy of switching stavudine to tenofovir df in combination with lamivudine and efavirenz in hiv-1-infected patients: three-year follow-up after switching therapy
155	Martínez	2007	Three-year follow-up of protease inhibitor-based regimen simplification in HIV-infected patients
156	Raguin	2007	Salvage therapy with amprenavir, lopinavir and ritonavir is durably potent in HIV-infected patients in virological failure: 1-year results
157	NR	2007	Trial of tipranavir versus darunavir in treatment-experienced patients enrolling

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
158	NR	2007	Tipranavir demonstrates potent and durable treatment response in HIV-positive women
159	NR	2007	48-week data on raltegravir in naive patients
160	NR	2007	Maraviroc reduces viral load in naive patients at 48 weeks
161	Vispo	2007	SPRING: a new trial to evaluate tipranavir in heterogeneous treatment-experienced HIV populations
162	Truchis	2007	Long-term control of viral residual replication under maintenance therapy with Trizivir after a quadruple induction regimen in HIV-1-infected adults (suburbs trial) [1]
163	Bernard	2007	48-week study results show DRV's staying power
164	Ndegwa	2007	Maraviroc (Celsentri) for multidrug-resistant human immunodeficiency virus (HIV)-1
165	Winckler	2007	[A clinical study with an HIV integrase inhibitor]
166	NR	2007	Side effects and complications. Tesamorelin--results from Phase III
167	NR	2007	Complications and side effects. Bone changes after starting HAART
168	Peters	2008	Antiretroviral therapy improves renal function among HIV-infected Ugandans
169	Gulick	2008	Maraviroc for previously treated patients with R5 HIV-1 infection
170	Ananworanich	2008	Changes in metabolic toxicity after switching from stavudine/didanosine to tenofovir/lamivudine--a Staccato trial substudy
171	Cutrell	2008	Abacavir and the potential risk of myocardial infarction
172	Soriano	2008	Efficacy and safety of replacing lopinavir with atazanavir in HIV-infected patients with undetectable plasma viraemia: final results of the SLOAT trial
173	Steigbigel	2008	Raltegravir with optimized background therapy for resistant HIV-1 infection
174	Stein	2008	Lipoprotein Changes in HIV-Infected Antiretroviral-Naïve Individuals after Starting Antiretroviral Therapy: ACTG Study A5152s Stein: Lipoprotein Changes on Antiretroviral Therapy
175	Kottilil	2008	AIDS Clinical Trials Group (ACTG) A5095 study team. Three- vs four-drug antiretroviral regimens for the initial treatment of HIV-1 infection: A randomized controlled trial
176	Landovitz	2008	Phase II study of vicriviroc versus efavirenz (both with zidovudine/lamivudine) in treatment-naive subjects with HIV-1 infection
177	Lapadula	2008	Risk of early virological failure of once-daily tenofovir-emtricitabine plus twice-daily nevirapine in antiretroviral therapy-naive HIV-infected patients
178	Gallant	2008	The 3-year renal safety of a tenofovir disoproxil fumarate vs. a thymidine analogue-containing regimen in antiretroviral-naive patients
179	Curran	2008	[Darunavir as first-line therapy. The TITAN study]
180	Estrada	2008	[Darunavir in treatment-naïve patients. The ARTEMIS study]
181	Palacios	2008	[Adverse effects of atazanavir]
182	Elion	2008	Once-daily abacavir/lamivudine and ritonavir-boosted atazanavir for the treatment of HIV-1 infection in antiretroviral-naive patients: a 48-week pilot study
183	Murphy	2008	Seven-year efficacy of a lopinavir/ritonavir-based regimen in antiretroviral-naïve HIV-1-infected patients
184	NR	2008	Abacavir and didanosine increase the risk of heart attack
185	NR	2008	Ninety-six week data released on TMC278
186	NR	2008	Raltegravir phase III study data released
187	NR	2008	96-week CASTLE data show similar efficacy results

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
188	Portilla	2008	[Efficacy of atazanavir in rescue therapy]
189	Marcellin	2008	Depressive symptoms and exposure to efavirenz in West African HIV-infected adults
190	De Meyer	2008	Influence of baseline protease inhibitor resistance on the efficacy of darunavir/ritonavir or lopinavir/ritonavir in the TITAN trial
191	NR	2008	[Metabolic changes in PI-based HAART. Change to atazanavir: continued effectiveness with improved lipid profile]
192	NR	2008	[Also consider cardiovascular risk. Every HIV patient "his" HAART]
193	NR	2008	Anti-HIV agents. The Castle study: lopinavir vs. atazanavir
194	NR	2008	Anti-HIV agents. Receptor blocker (SCH 532706) enters clinical trials
195	Fujiwara	2009	Potent antiviral activity and well-characterized exposure-activity relationship of S/GSK1349572, a next generation integrase inhibitor (INI)
196	Girard	2009	A randomized trial of two-drug versus three-drug tenofovir-containing maintenance regimens in virologically controlled HIV-1 patients
197	Girard	2009	Etravirine (ETR) demonstrates a favourable safety and tolerability profile: Pooled 96-week results from the Phase III DUET trials
198	Carlevari	2009	The 48-week efficacy and safety of switching to fixed-dose efavirenz/emtricitabine/ tenofovir df in HIV-1-infected patients receiving HAART
199	Carlevari	2009	Patient reported outcomes after simplification to a single tablet regimen of efavirenz (EFV)/emtricitabine (FTC)/tenofovir DF (TDF)
200	Carlevari	2009	Simplification of therapy (ART) with efavirenz/ emtricitabine/tenofovir df single tablet regimen vs. continued art in suppressed, HIV-infected patients
201	Church	2009	Maraviroc for previously treated patients with R5 HIV-1 infection
202	Stellbrink	2009	Comparison of renal and bone toxicities, and CV serum risk markers, in the ASSERT study: 48-week results from a prospective randomised trial
203	Pitrak	2009	Head-to-head comparison of two first-line regimens and an NRTI-sparing regimen for initial therapy of HIV-1 infection: what should we start?
204	Katlama	2009	Efficacy and safety of etravirine in treatment-experienced, HIV-1 patients: pooled 48 week analysis of two randomized, controlled trials
205	Walmsley	2009	Multidrug-experienced HIV-1-infected women demonstrated similar virological and immunological responses to tipranavir/ritonavir compared with men
206	Arastéh	2009	Efficacy and safety of darunavir/ritonavir in treatment-experienced HIV type-1 patients in the POWER 1, 2 and 3 trials at week 96
207	Palter	2009	Etravirine in highly treatment-experienced patients
208	Cocohoba	2009	The SWITCHMRK studies: substitution of lopinavir/ritonavir with raltegravir in HIV-positive individuals
209	Markowitz	2009	Sustained antiretroviral effect of raltegravir after 96 weeks of combination therapy in treatment-naive patients with HIV-1 infection
210	Arastéh	2009	Efficacy and safety of darunavir/ritonavir in treatment-experienced HIV type-1 patients in the POWER 1, 2 and 3 trials at week 96
211	Boesecke	2009	Immune reconstitution diseases in HIV-infected, antiretroviral therapy-naive patients recruited into the ALTAIR study
212	Cahn	2009	Efficacy and safety of lopinavir/ritonavir monotherapy vs. standard of care consisting of a protease inhibitor and two NRTIs in adults with HIV-1

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
213	Cohen	2009	The ARTEMIS trial: once-daily darunavir/ritonavir in the management of treatment-naive, HIV-infected patients
214	Fatkenheuer	2009	ARTEMIS 96-week comparison of liver tolerability of once-daily darunavir/ritonavir (DRV/r) versus lopinavir/ ritonavir (LPV/r) in treatment-naive patients
215	Flamm	2009	Comparison of gastrointestinal adverse events (GI AES) of darunavir/ritonavir (DRV/R) and lopinavir/ritonavir (LPV/R) at week 96 in ARTEMIS
216	Gaultier	2009	Simplified antiretroviral therapy in special populations: clinical outcomes at week 48 of lopinavir/ritonavir (LPV/R) tablet dosed once daily (QD) or twice daily (BID), administered with (greater-than or equal to)2 nucleoside reverse transcriptase inhibi
217	Johnson	2009	Gender and race-based efficacy and safety analyses in ARV-naive patients treated with boosted protease inhibitors (PIs): results from the CASTLE study
218	Johnson	2009	CASTLE study: 96-week efficacy & safety of ATV/r versus LPV/r in antiretroviral-naive HIV-1-infected patients
219	Johnson	2009	Gender-based differences in antiretroviral-naive patients treated with ritonavir-boosted protease inhibitors: 96-week results from the CASTLE study
220	Cohen	2009	Efficacy and safety of etravirine (TMC125) in treatment-experienced HIV-1-infected patients: 48-week results of a phase IIb trial
221	NR	2009	96-Week MERIT ES analysis shows efficacy of Celsentri=Selzentry
222	NR	2009	Raltegravir as effective as efavirenz in 144-week data
223	NR	2009	Long-term data on vicriviroc released
224	McNiff	2009	CCR5 antagonists in the treatment of HIV-infected persons: is their cancer risk increased, decreased, or unchanged
225	Gupta	2009	Can the SMART study data be used to assess risk factors for renal disease?
226	Harris	2009	A randomized, open-label study of a nucleoside analogue reverse transcriptase inhibitor-sparing regimen in antiretroviral-naive HIV-infected patients
227	Warpakowski	2009	[One year with Atripla. Changeover to complete HIV therapy in a single tablet has proven successful]
228	Eron	2010	Switch to a raltegravir-based regimen versus continuation of a lopinavir-ritonavir-based regimen in stable HIV-infected patients with suppressed viraemia (SWITCHMRK 1 and 2): two multicentre, double-blind, randomised controlled trials
229	Gatell	2010	Long-term efficacy and safety of the HIV integrase inhibitor raltegravir in patients with limited treatment options in a Phase II study
230	Ghosn	2010	Long-term (96-week) follow-up of antiretroviral-naïve HIV-infected patients treated with first-line lopinavir/ritonavir monotherapy in the MONARK trial
231	Hardy	2010	Two-year safety and virologic efficacy of maraviroc in treatment-experienced patients with CCR5-tropic HIV-1 infection: 96-week combined analysis of MOTIVATE 1 and 2
232	Hizue	2010	Pharmacological profile and clinical findings of Maraviroc (Celsentri® Tablets)
233	Hull	2010	Etravirine in combination with darunavir/ritonavir and optimized background regimen results in suppression of HIV replication in treatment-experienced patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
234	Cooper	2010	Switching to Atripla (EFV/FTC/TDF) from Kivexa (ABC/3TC) plus EFV leads to improved perceptions of treatment: Results from the ROCKET 1 study
235	Coovadia	2010	Reuse of nevirapine in exposed HIV-infected children after protease inhibitor-based viral suppression: a randomized controlled trial
236	Currier	2010	Sex-based outcomes of darunavir-ritonavir therapy: a single-group trial
237	Schouten	2010	Substitution of nevirapine because of efavirenz toxicity in AIDS clinical trials group A5095
238	Steigbigel	2010	Long-term efficacy and safety of Raltegravir combined with optimized background therapy in treatment-experienced patients with drug-resistant HIV infection: week 96 results of the BENCHMRK 1 and 2 Phase III trials
239	Tungsiripat	2010	A pilot study to determine the impact on dyslipidemia of adding tenofovir to stable background antiretroviral therapy: ACTG 5206
240	Lampe	2010	Changes in lipids and lipoprotein particle concentrations after interruption of antiretroviral therapy
241	Manosuthi	2010	Renal impairment after switching from stavudine/lamivudine to tenofovir/lamivudine in NNRTI-based antiretroviral regimens
242	Landman	2010	Efficacy and safety of unboosted atazanavir in combination with lamivudine and didanosine in naive HIV type 1 patients in Senegal
243	Katlama	2010	Efficacy and safety of etravirine at week 96 in treatment-experienced HIV type-1-infected patients in the DUET-1 and DUET-2 trials
244	Zaccarelli	2010	Is there any potential for first-line etravirine use? Analysis from a large data set of antiretroviral therapy-naive HIV-infected patients undergoing resistance test
245	Peter	2010	DART and laboratory monitoring of HIV treatment
246	Rockstroh	2010	Once-daily S/GSK1349572 combination therapy in antiretroviral-naïve adults: Rapid and potent 24- week antiviral responses in SPRING-1 (ING112276)
247	DeJesus	2010	Nevirapine (NVP) vs ritonavir-boosted atazanavir (ATV/r) combined with tenofovir/emtricitabine (TDF/FTC) in first-line therapy: NEWART 48-week data
248	Izzo	2010	A magnifying glass onto renal function and serum lipid evolutions after tenofovir (TDF) and emtricitabine (FTC) in combination with atazanavir/ritonavir (ATV/r) versus efavirenz (EFV) as first-line HAART (the INCA trial)
249	Kumar	2010	SUPPORT: 48-week results of fosamprenavir/ ritonavir vs efavirenz with abacavir/lamivudine in under-represented, antiretroviral-naive patients
250	Martinez	2010	Long-term outcomes of switching to fixed-dose abacavir/lamivudine (ABC/3TC) or tenofovir/ emtricitabine (TDF/FTC): 3-year results of the BICOMBO study
251	Nozza	2010	Efficacy and safety of an NRTI-sparing regimen in antiretroviral-naive HIV-infected patients: once-daily maraviroc plus lopinavir/ritonavir
252	Stellbrink	2010	The SENSE trial: etravirine shows lower prevalence and severity of neuropsychiatric adverse events compared to efavirenz in treatment-naive patients
253	Winston	2010	Neuropsychiatric adverse events and CSF penetration effectiveness (CSF) score in the MONET trial of darunavir/ritonavir (DRV/r), with or without nucleoside analogues (NRTIs)
254	Overton	2010	Metabolic: week 48 comparison of metabolic parameters and biomarkers in subjects receiving darunavir/ritonavir or atazanavir/ritonavir

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
255	NR	2010	Tenofovir/emtricitabine combination results in lower bone-mineral density
256	Arribas	2010	Effects of once-daily versus twice-daily darunavir/ritonavir on lipid parameters at week 48 in treatment-experienced, HIV-1-infected patients with no darunavir resistance-associated mutations (RAMs) in the ODIN study
257	Garvey	2010	Changes in cerebral function parameters in HIV-1 infected subjects undergoing a treatment simplification to darunavir/ritonavir:A randomized, prospective study
258	Gathe	2010	Comparison of 48 week efficacy, pharmacokinetics and safety of 400 mg QD nevirapine (NVP) extended release (Viramune XR) versus 200 mg BID nevirapine immediate release (Viramune IR) formulations in combination with emtricitabine/tenofovir in antiretrovira
259	Moyle	2010	Comparison of bone and renal toxicities in the ASSERT study: Final 96 week results from a prospective randomized safety trial
260	Orkin	2010	Changes in patient-reported outcomes during the sense trial: First-line treatment with nrtis plus etravirine or efavirenz
261	DeJesus	2010	Improvement in fasting lipids but minimal recovery of limb fat were seen 96 weeks after switching from lamivudine/zidovudine (CBV) plus efavirenz (EFV) to fixed-dose efavirenz/emtricitabine/tenofovir df (ATR) in hiv-infected patients
262	Young	2010	A pilot study of abacavir/lamivudine and raltegravir in antiretroviral-naïve HIV-1-infected patients: 48-week results of the SHIELD trial
263	Simpkin	2010	Boosted protease inhibitor (PI/r) monotherapy is effective in clinical practice
264	Cahn	2010	Efficacy and safety of lopinavir/ritonavir (LPV/R) monotherapy vs. standard of care in HIV-infected patients on their first protease inhibitor-based regimen: 48 week-follow up
265	Wilkin	2010	TMC278 shows favorable tolerability and non-inferior efficacy compared to efavirenz over 192 weeks in HIV-1-infected treatment-naïve patients
266	Kumar	2010	Fosamprenavir/ritonavir (FPV/r) vs. Efavirenz (EFV) with abacavir/lamivudine (ABC/3TC) in underrepresented, antiretroviral (ARV) naïve, HIV-infected subjects (SUPPORT): 24Week efficacy, safety, and tolerability
267	NR	2010	First-line raltegravir. No evidence of comparative effectiveness
268	Dolgin	2011	Trial in youngest group points to HIV treatment overhaul
269	Ebeling	2011	Lowerfatmass and lowerbone formation predict greater bone loss with tenofovir in HIV-infected adults
270	Gallien	2011	Four year follow-up of simplification therapy with once-daily emtricitabine, didanosine and efavirenz in HIV-infected patients (ALIZE ANRS 099 trial)
271	Herath	2011	The 10-year safety and efficacy of a tenofovir disoproxil fumarate (TDF)-containing, once-daily highly active antiretroviral therapy (HAART)
272	Castagna	2011	Changes in patient-reported outcomes during the sense trial: First-line treatment with 2 Nrtis plus etravirine or efavirenz
273	Cooper	2011	The effects of enfuvirtide therapy on body composition and metabolic parameters over 48 weeks in the TORO body imaging substudy
274	Currier	2011	Effects of darunavir/ritonavir-based therapy on metabolic and anthropometric parameters in women and men over 48 weeks

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
275	Scourfield	2011	Absence of skin hypersensitivity in subjects switching to etravirine with undetectable plasma HIV RNA: A randomized prospective study
276	Tenorio	2011	The monoclonal CCR5 antibody PRO-140: the promise of once-weekly HIV therapy
277	Uglietti	2011	The sense trial: Etravirine shows lower prevalence and severity of neuropsychiatric adverse events compared to efavirenz in treatment-naïve patients
278	Lazzarin	2011	Artemis: 192-Week efficacy and safety of once daily darunavir/ritonavir (DRV/r) versus lopinavir/R (LPV/r) in treatment-naïve HIV-1-infected adults
279	MacArthur	2011	Clinical trial report: TMC278 (Rilpivirine) versus efavirenz as initial therapy in treatment-Naïve, HIV-1-infected patients
280	Dlamini	2011	Lactic acidosis and symptomatic hyperlactataemia in a randomized trial of first-line therapy in HIV-infected adults in South Africa
281	Battegay	2011	Bioavailability of extended-release nevirapine 400 and 300 mg in HIV-1: a multicenter, open-label study
282	Fourie	2011	Effect of baseline characteristics on the efficacy and safety of once-daily darunavir/ ritonavir in HIV-1-infected, treatment-naïve ARTEMIS patients at week 96
283	Young	2011	96-week results of a pilot study of Abacavir/Lamivudine and raltegravir in antiretroviral-Naïve HIV-1-infected patients: The SHIELD trial
284	Nelson	2011	Pooled week-48 safety and efficacy results from ECHO and THRIVE Phase III trials comparing TMC278 vs EFV in treatment-naïve HIV-1-infected patients receiving FTC/TDF
285	Nozza	2011	Efficacy and safety of once daily maraviroc plus lopinavir/ritonavir in antiretroviral naïve HIVinfected patients
286	Ribaudo	2011	No risk of myocardial infarction associated with initial antiretroviral treatment containing abacavir: short and long-term results from ACTG A5001/ALLRT
287	Ripamonti	2011	No correlation between risk of neuropsychiatric adverse events and csf penetration effectiveness (CPE) score in the monet trial of darunavir/ritonavir (DRV/R), with or without nucleoside analogues (NRTIS)
288	Lake	2011	Raltegravir as replacement for PI- or NNRTIbased ART in HIV-infected women with lipohypertrophy: the Women, Integrase, and Fat Accumulation Trial
289	Squires	2011	Efficacy/Tolerability of unboosted atazanavir versus Atazanavir/Ritonavir, each in combination with Abacavir/Lamivudine, after initial suppression with Abacavir/Lamivudine+Atazanavir/Ritonavir in HIV-1-infected patients: 144-week results of aries
290	NR	2011	Initial results reported on raltegravir once-daily dosing
291	Fatkenheuer	2011	The SENSE trial week 48 results: Etravirine shows lower prevalence of lipid abnormalities, compared to efavirenz in treatment-naive patients
292	Haskelberg	2011	Lower fat mass and lower bone formation predict greater bone loss with tenofovir in HIV-infected adults
293	Moyle	2011	Changes in bone mineral density after 96 weeks of treatment with tenofovir DF/emtricitabine plus atazanavir/ritonavir or lopinavir/ritonavir in HIV-1 infected treatment naive subjects: The CASTLE body composition sub-study
294	Soriano	2011	Resistance data in the ARTEN trial [2]

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
295	Winston	2011	Three-year evaluation of neuropsychiatric adverse events in the MONET trial of darunavir/ ritonavir (DRV/r), with or without nucleoside analogues (NRTIs)
296	Elion	2011	The single-tablet regimen of elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF; Quad) maintains a high rate of virologic suppression, and cobicistat (COBI) is an effective pharmacoenhancer through 48 weeks
297	Mills	2011	Neurologic and psychiatric safety profile of TMC278 compared with efavirenz (EFV) in treatment-naive HIV-1-infected patients: Pooled analysis from the randomized double-blind phase III ECHO and THRIVE trials at 48 weeks
298	Walmsley	2011	Pooled week 48 safety and efficacy results from ECHO and thrive phase III trials comparing TMC278 vs EFV in treatment-naïve HIV-1-infected patients receiving FTC/TDF
299	NR	2011	Rilpivirine (Edurant)--a new drug for HIV infection
300	Warpakowski	2011	[Long-term therapy strategy with raltegravir. Appropriate in all illness phases]
301	Warpakowski	2011	[Persistence in focus. Atazanavir proves itself anew in long-term therapy]
302	Alvarez	2011	Changes in patient-reported outcomes during the SENSE Trial: first-line treatment with 2 NRTIs plus etravirine or efavirenz for 48 weeks
303	Hodder	2012	Efficacy and Safety Outcomes Among Treatment-Experienced Women and Men Treated with Etravirine in Gender, Race and Clinical Experience
304	DeJesus	2012	Efficacy, safety and pharmacokinetic results of an ongoing international phase 3 study comparing elvitegravir/ cobicistat/emtricitabine/tenofovir DF (Quad) with ritonavirboosted atazanavir plus emtricitabine/tenofovir DF in treatment naive HIV-1 infected
305	Eron Jr	2012	Dolutegravir treatment response by baseline viral load and NRTI backbone in treatment-naïve HIV-infected individuals
306	Fisher	2012	SPIRIT: switching to emtricitabine/rilpivirine/tenofovir DF single-tablet regimen from boosted protease inhibitor maintains HIV suppression at week 48
307	Gallant	2012	Cobicistat versus ritonavir as pharmacoenhancers in combination with atazanavir plus tenofovir disoproxil fumarate/emtricitabine: phase 3 randomized, double blind, active-controlled trial, week 48 results
308	Girard	2012	Pooled week 96 results of the phase III DUET-1 and DUET-2 trials of etravirine: further analysis of adverse events and laboratory abnormalities of special interest
309	Henry	2012	SWIFT: switching from lamivudine/abacavir to emtricitabine/tenofovir improved lipids while maintaining virologic suppression in older HIV subjects
310	Hodder	2012	Effect of gender and race on the week 48 findings in treatment-naïve, HIV-1-infected patients enrolled in the randomized, phase III trials ECHO and THRIVE
311	Arasteh	2012	TRANxITION 144-week results: switching virologically stable HIV patients from immediate-release nevirapine (NVP IR) to extended-release NVP (XR)
312	Blanco	2012	Intensification with maraviroc in HIV-infected individuals (with or without liver cirrhosis) with a discordant CD4 response to cART

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
313	Bonora	2012	Short-term additional enfuvirtide therapy is associated with a greater immunological recovery in HIV very late presenters: a controlled pilot study
314	Brinson	2012	VERxVE 144 week results: nevirapine extended-release (NVP XR) QD versus NVP immediate-release (IR) BID with FTC/TDF in treatment-naive HIV-1 patients
315	Cohen	2012	A randomized pilot study of tenofovir/emtricitabine (TDF/ FTC) + boosted atazanavir (ATV/r) vs. raltegravir (RAL BID) + ATV/r vs. RAL BID + ATV BID
316	Cohen	2012	STAR Study: single tablet regimen emtricitabine/rilpivirine/ tenofovir DF is non-inferior to efavirenz/emtricitabine/ tenofovir DF in ART-naive adults
317	Cure	2012	Mixed-treatment comparison of the efficacy and safety of antiretroviral drugs indicated for treatment-experienced hiv patients
318	Sanford	2012	Rilpivirine
319	Sax	2012	Elvitegravir/cobicistat/emtricitabine/tenofovir DF (Quad) has non-inferior efficacy and favorable safety compared to efavirenz/emtricitabine/tenofovir DF in treatment naive HIV-1 infected subjects
320	Zala	2012	Safety and efficacy of GSK2248761, a next-generation nonnucleoside reverse transcriptase inhibitor, in treatment-naive HIV-1-infected subjects
321	Zolopa	2012	Elvitegravir/cobicistat/emtricitabine/tenofovir DF (QUAD) has durable efficacy and differentiated safety compared to efavirenz/emtricitabine/tenofovir DF at week 96 in treatment-naive HIV-1-infected patients
322	Martinez	2012	Metabolic effects of atazanavir/ritonavir vs darunavir/ ritonavir in combination with tenofovir/emtricitabine in antiretroviral-naive patients (ATADAR Study)
323	Wilkin	2012	Long-term efficacy, safety, and tolerability of rilpivirine (RPV, TMC278) in HIV type 1-infected antiretroviral-naive patients: week 192 results from a phase IIb randomized trial
324	Cahn	2012	Rilpivirine in the treatment of HIV infection: Evidence from the ECHO and THRIVE studies
325	Cohen	2012	Efficacy and safety of rilpivirine (TMC278) versus efavirenz at 48 weeks in treatment-naive HIV-1-infected patients: pooled results from the phase 3 double-blind randomized ECHO and THRIVE Trials
326	Caseiro	2012	Vicriviroc plus optimized background therapy for treatment-experienced subjects with CCR5 HIV-1 infection: final results of two randomized phase III trials
327	Nozza	2012	Maraviroc 150 mg QD plus lopinavir/ritonavir, a NRTIsparing regimen for HIV-infected naïve patients: 48-weeks final results
328	Orkin	2012	Incidence of rash in the 96-week analysis of the pooled Phase III randomised double-blind ECHO and THRIVE trials
329	Pasquau	2012	A clinical trial to compare the quality of life of HIV+ patients who start monotherapy with LPV/r versus continuing triple therapy with a boosted PI
330	Raffi	2012	Once-daily dolutegravir (DTG; S/GSK1349572) is non-inferior to raltegravir (RAL) in antiretroviral-naive adults: 48 week results from SPRING-2 (ING113086)
331	Rockstroh	2012	Elvitegravir/cobicistat/emtricitabine/tenofovir DF (QUAD) has durable efficacy and differentiated safety compared to atazanavir boosted by ritonavir plus emtricitabine/tenofovir DF at week 96 in treatment-naive HIV-1-infected patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
332	Anderson	2012	Week 96 outcomes of patients with less treatment experience versus more treatment experience receiving etravirine in the DUET trials
333	Bonjoch	2012	Switching the NNRTI or the PI/r to maraviroc in aviraemic subjects infected with R5 HIV by V3- loop population sequencing: 48-week, prospective, randomized, controlled, pilot study
334	De Jesus	2012	Week 48 results of an ongoing global phase 3 study comparing elvitegravir/cobicistat/emtricitabine/tenofovir DF (Quad) with ritonavir-boosted atazanavir plus emtricitabine/tenofovir DF in treatment naive HIV-1 infected subjects showing efficacy, safety
335	Elion	2012	Efficacy and safety results from a randomized, double blind, active controlled trial of elvitegravir (once-daily) versus raltegravir (twice-daily) in treatment-experienced HIV-positive patients: long term 96-week data
336	Li	2012	Efficacy and safety of an antiretroviral regimen containing six months of stavudine followed by long-term zidovudine for firstline HIV therapy in resource-limited settings: an open-label, randomized, multicenter trial in China
337	Logue	2012	SWIFT study: switching from lamivudine/abacavir (3TC/ABC) to emtricitabine/tenofovir DF (FTC/TDF) improved fasting lipid parameters while maintaining virologic suppression
338	Hodder	2012	Sustained efficacy and safety observed in women for rilpivirine (RPV) versus efavirenz (EFV) plus emtricitabine/tenofovir DF (FTC/TDF) and with few gender differences in treatment-naive, HIV- 1 infected adults-pooled 96-week ECHO and THRIVE analysis
339	Moyle	2012	Associations between visceral adipose tissue and hypertriglyceridaemic waist circumference phenotype in a randomized prospective comparison between atazanavir/ritonavir and lopinavir/ritonavir each in combination with tenofovir DF/emtricitabine in antiret
340	Pommer	2012	[A single tablet against HIV: new combination preparation improves therapy]
341	Palella	2012	SPIRIT study: Switching to emtricitabine/rilpivirine/ tenofovir df (FTC/RPV/TDF) single-tablet regimen (STR) from a ritonavir-boosted protease inhibitor and two nucleoside reverse transcriptase inhibitors (NRTIS) maintains HIV suppression and improves ser
342	Ryan	2013	Outcomes in Older Versus Younger Patients Over 96 Weeks in HIV-1-Infected Patients Treated with Rilpivirine or Efavirenz in ECHO and THRIVE
343	Eron	2013	Efficacy and safety of raltegravir for treatment of HIV for 5 years in the BENCHMRK studies: final results of two randomised, placebo-controlled trials
344	Fisher	2013	Efficacy and Safety of elvitegravir/cobicistat/emtricitabine/ tenofovir DF from an integrated analysis of Phase 2 and 3 clinical trials
345	Cohen	2013	Week 96 efficacy and safety of rilpivirine in treatment-naive, HIV-1 patients in two Phase III randomized trials
346	Molina	2013	Rilpivirine vs. efavirenz in HIV-1 patients with baseline viral load 100,000 copies/ml or less: week 48 phase III analysis
347	Nelson	2013	Rilpivirine versus efavirenz in HIV-1-infected subjects receiving emtricitabine/tenofovir DF: pooled 96-week data from ECHO and THRIVE Studies
348	Iwata	2013	Pharmacological properties of rilpivirine (Edurant Tablet), a new drug for the treatment of HIV, and results of its clinical studies
349	Arribas	2013	Predictors of long-term HIV RNA suppression on darunavir/ritonavir monotherapy in the MONET trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
350	Babiker	2013	Considerations in the rationale, design and methods of the Strategic Timing of AntiRetroviral Treatment (START) study
351	Martínez	2013	Abacavir/Lamivudine Versus Tenofovir/Emtricitabine in Virologically Suppressed Patients Switching from Ritonavir-Boosted Protease Inhibitors to Raltegravir
352	Mills	2013	Neurological and psychiatric tolerability of rilpivirine (TMC278) vs. efavirenz in treatment-naïve, HIV-1-infected patients at 48 weeks
353	Ouattara	2013	Early upper digestive tract side effects of zidovudine with tenofovir plus emtricitabine in West African adults with high CD4 counts
354	Eron	2013	Safety and efficacy of dolutegravir in treatment-experienced subjects with raltegravir-resistant HIV type 1 infection: 24-week results of the VIKING Study
355	Brown	2013	Changes in bone turnover markers and association with decreased total bone mineral density (tBMD) in treatment-naive subjects taking lopinavir/ritonavir combined with raltegravir or tenofovir/emtricitabine
356	Brunetta	2013	SPIRIT: switching to rilpivirine /emtricitabine / tenofovir DF single-tablet regimen from boosted protease inhibitor maintains HIV-1 virologic suppression through week 48 in HIV-1 infected subjects
357	Chang	2013	Elvitegravir /cobicistat /emtricitabine /tenofovir DF has durable efficacy and differentiated safety compared to atazanavir boosted by ritonavir plus emtricitabine /tenofovir DF at week 96 in treatment-naive HIV-1-infected patients
358	Cohen	2013	STAR: rilpivirine/Emtricitabine/TenofovirDF is non-inferior to Efavirenz/Emtricitabine/TenofovirDF in naive adult Latino, black & white subpopulations
359	Cohen	2013	STaR study: single-tablet regimen rilpivirine/ emtricitabine/tenofovir DF maintains noninferiority to efavirenz/emtricitabine/tenofovir DF and has minimal impact on fasting lipids in ART-naive adults through week 96
360	Orkin	2013	Week 96 efficacy and safety data: elvitegravir/cobicistat/ emtricitabine/tenofovir DF (Quad) compared to atazanavir boosted by ritonavir plus emtricitabine/tenofovir DF in treatment-naive HIV-1-infected patients
361	Pallela	2013	Efficacy of switching to rilpivirine/emtricitabine/tenofovir DF from boosted PI in HIV-1 virologically suppressed patients with or without the K103N
362	Trottier	2013	Star study: single-tablet regimen rilpivirine/ emtricitabine /tenofovir DF is non-inferior to efavirenz/emtricitabine /tenofovir DF in ART-naive HIV-1 infected adults
363	Dubé	2013	Effects of antiretroviral therapy initiation on soluble CD163 and asymmetric dimethyl arginine levels and their relationships with endothelial function: Results from a 24-week prospective randomized trial
364	Overton	2013	Immune activation analysis over 48 weeks in INROADS, a study of the nucleoside/tide-sparing regimen of once-daily etravirine and darunavir/ ritonavir
365	Fabbiani	2014	Simplification to atazanavir/ritonavir+lamivudine in virologically suppressed HIV-infected patients: 24-weeks interim analysis from ATLAS-M trial
366	Gatell	2014	Forty-eight-week efficacy and safety and early CNS tolerability of doravirine (MK-1439), a novel NNRTI, with TDF/FTC in ART-naive HIV-positive patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
367	Clumeck	2014	A randomized, double-blind comparison of single-tablet regimen elvitegravir/cobicistat/emtricitabine/tenofovir DF vs ritonavir-boosted atazanavir plus emtricitabine/tenofovir DF for initial treatment of HIV-1 infection: analysis of week 144 results
368	Stein	2014	Prospective randomized clinical trial of the effects of three modern antiretroviral therapies on carotid intima-media thickness in HIV-infected individuals (aids clinical trials group study A5260S)
369	Yazdanpanah	2014	48 week bone marker changes with Dolutegravir (DTG) plus Abacavir/ Lamivudine (ABC/3TC) vs. Tenofovir/Emtricitabine/Efavirenz (EFV/TDF/ FTC): the SINGLE trial
370	Kiwuwa-Muyingo	2014	Prevalence, incidence and predictors of peripheral neuropathy in African adults with HIV infection within the DART trial
371	Margolis	2014	Unexpected finding of delayed-onset seizures in HIV-positive, treatment-experienced subjects in the Phase IIb evaluation of fosdevirine (GSK2248761)
372	Allavena	2014	Switching from tenofovir/emtricitabine and nevirapine to a tenofovir/emtricitabine/rilpivirine single-tablet regimen in virologically suppressed, HIV-1-infected subjects
373	Antinori	2014	The PROTEA trial: darunavir/ritonavir with or without nucleoside analogues, for patients with HIV-1 RNA below 50 copies/mL
374	Behrens	2014	Rilpivirine versus efavirenz with emtricitabine/tenofovir disoproxil fumarate in treatment-naïve HIV-1-infected patients with HIV-1 RNA ≤100,000 copies/mL: week 96 pooled ECHO/THRIVE subanalysis
375	Carey	2014	Efavirenz 400 mg daily remains non-inferior to 600 mg: 96 week data from the double-blind, placebo-controlled ENCORE1 study
376	Clarke	2014	Analysis of neurocognitive function and CNS endpoints in the PROTEA trial: darunavir/ritonavir with or without nucleoside analogues
377	Spagnuolo	2014	Atazanavir/ritonavir monotherapy as maintenance strategy in HIV-1 treated subjects with viral suppression: 96-week analysis results of the MODAT study
378	Tebas	2014	Lipid levels and changes in body fat distribution in treatment-naive, HIV-1-Infected adults treated with rilpivirine or Efavirenz for 96 weeks in the ECHO and THRIVE trials
379	Wilkins	2014	STaR study: single-tablet regimen (STR) of Rilpivirine/Emtricitabine/Tenofovir DF demonstrates significant difference to Efavirenz/Emtricitabine/Tenofovir DF in subjects with a baseline HIV-1 RNA < 100,000 copies/mL through week 96
380	Molina	2014	Week 96 analysis of rilpivirine or efavirenz in HIV-1-infected patients with baseline viral load ≤ 100 000 copies/mL in the pooled ECHO and THRIVE phase 3, randomized, double-blind trials
381	Molina	2014	Once-daily dolutegravir is superior to once-daily darunavir/ritonavir in treatment-naïve HIV-1-positive individuals: 96 week results from FLAMINGO
382	Mollan	2014	Association between efavirenz as initial therapy for HIV-1 infection and increased risk for suicidal ideation or attempted or completed suicide: an analysis of trial data
383	Mondi	2014	Efficacy and safety of treatment simplification to atazanavir/ritonavir1lamivudine in HIV-infected patients with virological suppression: 144 week follow-up of the AtLaS pilot study
384	Mwafongo	2014	Renal events among women treated with tenofovir/emtricitabine in combination with either lopinavir/ritonavir or nevirapine

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
385	Orkin	2014	Week 144 efficacy and safety data: Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir DF (Stribild) demonstrates durable efficacy and differentiated safety compared to Atazanavir boosted by Ritonavir plus Emtricitabine/Tenofovir DF at week 144 in treatment-naïve HIV-1-infected patients
386	Paton	2014	The protease inhibitor versus ongoing triple-therapy (PIVOT) trial
387	Pinnetti	2014	Randomized trial of DRV/r or LPV/r QD monotherapy vs maintaining a PI/r-based antiretroviral regimen in persons with suppressed HIV replication
388	Reeves	2014	Renal safety profile of STB in virologically suppressed subjects from two randomized phase 3b switch trials
389	Rokx	2014	The efficacy, pharmacokinetics, safety and cardiovascular risks of switching nevirapine to rilpivirine in HIV-1 patients: the RPV switch study
390	Brown	2014	Bone Density Changes After Antiretroviral Initiation With Protease Inhibitors or Raltegravir
391	Cheret	2014	Paradoxical Impact of Maraviroc/Raltegravir Added To HAART in Acute HIV Infection: ANRS 147 Trial
392	Koulla-Shiro	2014	Randomized Comparison of Three Second Line ART Regimens in Africa: the 2 Lady/ANRS/EDCTP Study
393	Landovitz	2014	Efficacy and Tolerability of Atazanavir, Raltegravir, or Darunavir With FTC/Tenofovir: ACTG 5257
394	Margolis	2014	744 and Rilpivirine as Two-Drug Oral Maintenance Therapy: lAI116482 (LATTE) Week 48 Results
395	Murphy	2014	Elvite gravir/Cobicistat/Emtricitabine/Tenofovir DF (STB) has durable efficacy and differentiated safety compared to atazanavir boosted by ritonavir plus emtricitabine/Tenofovir DF at week 144 in treatment-naive HIV-1 infected patients
396	Musiime	2014	The Effect of Long-Term Zidovudine On Hematological Parameters in the ARROW Randomized Trial
397	Nathan	2014	Long-term efficacy and safety of elvitegravir/cobicistat/emtricitabine/tenofovir DF versus atazanavir plus ritonavir plus emtricitabine/tenofovir
398	O'Halloran	2014	Effect of Switch From Abacavir To Tenofovir DF On Platelet Function Markers: a SWIFT Trial Substudy
399	Paton	2014	Randomised Controlled Trial of a PI Monotherapy Switch Strategy for Long-Term HIV Management
400	Raffi	2014	First-Line RAL + DRV/r Is Non-Inferior To TDF/FTC + DRV/r: the NEAT001/ANRS143 Randomised Trial
401	Romo	2014	Renal and Metabolic Safety of Initial HIV-1 Therapy in Resource-Limited Settings
402	Saeedi	2014	Outcomes of Unboosting Atazanavir (ATZ) in Regimens with a Tenofovir (TDF) backbone
403	Taejaroenkul	2014	Randomized Comparison of Anthropometric Outcomes On EFV-Based Antiretroviral Therapies
404	Trevillyan	2014	Antiretroviral Therapy Is Associated With Significant Changes in Plasma Lipidome
405	Trevor	2014	Elvitegravir/cobicistat/emtricitabine/tenofovir DF demonstrates durable efficacy and safety versus efavirenz/emtricitabine/tenofovir DF at Week 144
406	Trottier	2014	Star study : single tablet regimen Rilpivirine/Emtricitabine/Tenofovir DF maintains non-inferiority to Efavirenz/Emtricitabine/Tenofovir DF in ART-naive adults through week 96

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
407	Walmsley	2014	Dolutegravir Regimen Statistically Superior To Tenofovir/Emtricitabine/Efavirenz: 96-Wk Data
408	Wohl	2014	A Randomized, Double-Blind Comparison of Single-Tablet Regimen Elvitegravir/Cobicistat/Emtricitabine/Tenofovir DF Versus Single-Tablet Regimen Efavirenz/Emtricitabine/Tenofovir DF for Initial Treatment of HIV-1 Infection: analysis of Week 144 Results
409	Lataillade	2014	HIV-1 attachment inhibitor prodrug BMS-663068 in antiretroviral-experienced subjects: Primary week 24 analysis of emergent drug resistance
410	Fisher	2014	Safety and efficacy of lopinavir/ritonavir-containing antiretroviral therapy in patients aged <50 versus >50 years from randomized trials
411	NR	2014	[Initial HIV therapy. ACTG 5257: convincing results for raltegravir compared with protease inhibitors]
412	NR	2014	[As simple and as compatible as possible. HIV patients profit from single tablet regimen]
413	Trevor	2014	STaR: Single tablet regimen RPV/FTC/TDF is safe and well tolerated compared to EVF/FTC/TDF in ART-naïve Latinos at week 96
414	Boyd	2015	Body composition outcomes at 96 weeks in the second-line RCT DXA substudy
415	Anabwani	2015	Nevirapine extended-release formulation tablets in HIV-1-infected children: long-term follow-up
416	Azvolinsky	2015	First-in-class HIV drug enters phase 3 trials
417	Sax	2015	Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials
418	Wanga	2015	Genomewide association study of tenofovir pharmacokinetics and creatinine clearance in AIDS Clinical Trials Group protocol A5202
419	Nachman	2015	Pharmacokinetics and 48-Week Safety and Efficacy of Raltegravir for Oral Suspension in Human Immunodeficiency Virus Type-1-Infected Children 4 Weeks to 2 Years of Age
420	Pozniak	2015	Switch to STRIBILD from NNRTI plus FTC/TDF regimens maintains HIV suppression and is well-tolerated: week 96 results of STRATEGY-NNRTI (Study 121)
421	Cournil	2015	Metabolic changes and second-line ART in Africa (2LADY/ANRS 12169 trial)
422	DeJesus	2015	Renal and bone safety of tenofovir alafenamide versus tenofovir disoproxil fumarate
423	DeJesus	2015	Tenofovir alafenamide in a single-tablet regimen in initial HIV-1 therapy
424	Gatell	2015	Efficacy and safety of doravirine 100 mg QD vs. efavirenz 600 mg QD with TDF/FTC in ART-naive HIV-infected patients: week 24 results
425	Hamzah	2015	Favourable effect on vitamin D and bone after switching from Atripla to darunavir/ritonavir: a randomised controlled clinical trial
426	Kroidl	2015	24-weeks virologic efficacy of fozivudine in ART-naive patients from Africa
427	Naidoo	2015	Randomized controlled trial on ART outcomes in tenofovir gel trial seroconvertors
428	Saez-Llorens	2015	Efficacy and safety of long-term tenofovir DF (TDF) therapy in HIV-infected children
429	Thompson	2015	Attachment inhibitor prodrug BMS-663068 in ARV-experienced subjects: week 48 analysis

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
430	Custodio	2015	Tenofovir (TFV) alafenamide (TAF) dose in the first pibased single tablet regimen (STR) darunavir/cobicistat/emtricitabine/TAF (DRV/COBI/FTC/TAF; D/C/F/TAF)
431	Klassen	2016	Associations between vitamin D metabolites, antiretroviral therapy and bone mineral density in people with HIV
432	Gagliardini	2016	Simplification to atazanavir/ritonavir+lamivudine versus maintaining atazanavir/ritonavir+2NRTIs in virologically suppressed HIV-infected patients: 96-week data of the ATLAS-M trial
433	Granados-Reyes	2016	HIV-1 attachment inhibitor prodrug BMS-663068 in antiretroviral-experienced subjects: week 96 subgroup analysis
434	Hagins	2016	fficacy of Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) Fixed-Dose Combination (FDC) Compared With Ritonavir-Boosted Atazanavir (ATV/r) Plus Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) in Treatment-Naive Women With Human Immunodeficiency Virus (HIV)-1 Infection (ARIA Study): Analyses by Race Subgroups
435	Giaquinto	2016	Pharmacokinetics, safety and efficacy of maraviroc in pediatric patients with R5 HIV
436	Perez-Valero	2016	Neurocognitive safety after 96-wks on ATV/r+3TC: results of the randomized salt trial
437	Huhn	2016	Strategic simplification: the efficacy and safety of switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) plus darunavir (DRV) in treatment-experienced HIV-1 infected adults (NCT01968551)
438	Arenas-Pinto	2016	Increased risk of suicidal behaviour with use of efavirenz: Results from the START trial
439	Bracchi	2016	Multicentre open-label pilot study of switching from efavirenz to dolutegravir for central nervous system (CNS) toxicity
440	Choi	2016	Efficacy and Safety of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate in Asian Subjects with Human Immunodeficiency Virus 1 Infection: A Sub-Analysis of Phase 3 Clinical Trials
441	Ciaffi	2016	Dual therapy with a boosted protease inhibitor plus lamivudine is an effective maintenance strategy in patients on second-line antiretroviral therapy in Africa: the ANRS 12286/MOBIDIP trial
442	Clarke	2016	A randomized, double-blind comparison of tenofovir alafenamide (TAF) vs tenofovir disoproxil fumarate (TDF), each coformulated with elvitegravir, cobicistat and emtricitabine (E/C/F) for initial HIV-1 treatment: week 96 results
443	Daar	2016	Efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate in human immunodeficiency virus (HIV)-infected, virologically suppressed older adults: subgroup analysis of a randomized, double-blind switch study
444	Waters	2016	Renal safety of tenofovir alafenamide in patients at high risk of kidney disease
445	Johnson	2016	Efficacy of dolutegravir/abacavir/lamivudine (DTG/ABC/ 3TC) fixed-dose combination (FDC) compared with ritonavir-boosted atazanavir (ATV/r) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in treatment-naïve women with HIV-1 infection (ARIA study): subgroup analyses
446	Keegan	2016	Tryptophan metabolism and its relationship with central nervous system toxicity in subjects switching from efavirenz to dolutegravir

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
447	Kityo	2016	12-week raltegravir-intensified quadruple therapy versus triple first-line ART reduces viral load more rapidly but does not reduce mortality in severely immunosuppressed African HIV-infected adults and older children: the REALITY trial
448	Kravchenko	2016	Safety and antiviral effect of Elpida (VM-1500), a novel NNRTI (+Truvada) in treatment-naïve HIV-1-infected patients at 24- to 48-week therapy
449	Lee	2016	Post-prandial lipid effects of raltegravir versus darunavir/ritonavir in HIV-1-infected adults commencing combination ART
450	Llibre	2016	An Indirect Comparison of Efficacy and Safety of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate and Abacavir/Lamivudine + Dolutegravir in Initial Therapy
451	Munderi	2016	SALIF trial: switching suppressed first-line patients to tenofovir/emtricitabine/rilpivirine (TDF/FTC/RPV) is non-inferior to TDF/FTC/efavirenz (TDF/FTC/EFV) and could be an alternative treatment option in LMICs
452	Oka	2016	Efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate in treatment-naïve Asian adults
453	Orkin	2016	Switching tenofovir disoproxil fumarate to tenofovir alafenamide in virologically suppressed adults
454	Orkin	2016	Switching from rilpivirine/emtricitabine/tenofovir disoproxil fumarate (RPV/FTC/TDF) to rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF): safety and efficacy through 48 weeks
455	Orrell	2016	Superior efficacy of dolutegravir/abacavir/lamivudine (DTG/ ABC/3TC) fixed dose combination (FDC) compared with ritonavir (RTV) boosted atazanavir (ATV) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in treatment naïve women with HIV-1 infection (ARIA Study)
456	Paton	2016	The Protease Inhibitor Monotherapy Versus Ongoing Triple Therapy (PIVOT) trial: a randomised controlled trial of a protease inhibitor monotherapy strategy for long-term management of human immunodeficiency virus infection
457	Prakash	2016	Safety and efficacy of dolutegravir and maraviroc plus background regimen in HIV-1 treatment-experienced participants
458	Pulido	2016	Non-inferiority of dual-therapy (DT) with darunavir/ ritonavir (DRV/r) plus 3TC versus triple-therapy (TT) with DRV/r plus TDF/FTC or ABC/3TC for maintenance of viral suppression: 48-week results of the DUAL-GESIDA 8014 trial
459	Quercia	2016	Psychiatric adverse events from the DTG ART-naive phase 3 clinical trials
460	Raffi	2016	Long-term (96-week) efficacy and safety after switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) in HIV-infected, virologically suppressed adults
461	Ciccarelli	2016	Cns safety of simplification to ATV/r+3TC in virologically suppressed HIV+ patients
462	D'Avino	2016	Bone-mineral density after switching to ATV/R+3TC: a substudy of the AtLaS-M trial
463	DeJesus	2016	Attachment inhibitor prodrug BMS-663068 in arv-experienced subjects: week 96 analysis
464	Gallant	2016	Switching tenofovir DF to tenofovir alafenamide in virologically suppressed adults
465	Gatell	2016	Doravirine 100mg QD vs efavirenz +TDF/FTC in ART-naive HIV+ patients: week 48 results

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
466	Koenig	2016	Improved safety and efficacy of TAF versus TDF singletablet regimen in HIV-1 treatment-naïve women through week 48
467	La Rosa	2016	ACTG 5273 randomized trial of second-line art supports who guidance
468	Margolis	2016	Cabotegravir+rilpivirine as long-acting maintenance therapy: latte-2 week 32 results
469	Ribaudo	2016	Gender and racial disparities in initial antiretroviral treatment outcome: ACTG A5257
470	Rijnders	2016	Longer-term renal safety of tenofovir alafenamide vs tenofovir disoproxil fumarate
471	Scherrer	2016	Early evidence of antiviral activity and safety of ABX464 in HIV treatment-naïve patients
472	Villanueva	2016	Influence of age on outcomes in HIV-positive adults initiating tenofovir alafenamide fumarate (TAF) versus tenofovir disoproxil fumarate (TDF) with elvitegravir, cobicistat and emtricitabine (E/C/F/TAF vs. E/C/F/TDF)
473	Shah	2016	Effectiveness and safety of combination of antiretroviral therapy in HIV-1 infected patients in western India
474	NR	2016	Genvoya--a new 4-drug combination for HIV
475	Flamm	2017	Efficacy and safety of tenofovir alafenamide vs. tenofovir disoproxil fumarate in HIV-infected, virologically suppressed black and non-blacks adults through week 96: subgroup analysis of a randomized switch study
476	Arribas	2017	A Randomized, Double-Blind Comparison of Tenofovir Alafenamide (TAF) vs. Tenofovir Disoproxil fumarate (TDF), Each Coformulated with Elvitegravir, Cobicistat, and Emtricitabine (E/C/F) for Initial HIV-1 Treatment: week 144 Results
477	Clarke	2017	Significant efficacy and long term safety difference with TAF-based STR in naive adults
478	Lombardi	2017	Evolution of blood-associated HIV-1 DNA levels after 48 weeks of switching to atazanavir/ritonavir+lamivudine dual therapy versus continuing triple therapy in the randomized AtLaS-M trial
479	Nakamoto	2017	[Pharmacological properties and clinical findings of new drugs for the treatment of HIV-1, FTC/TAF 200/10 and 200/25 mg (Descovy(®) Combination Tablet LT and HT)]
480	Okoli	2017	Safety and efficacy of dolutegravir in treatment naive patients, 50 years and over: subgroup analysis of 48-week results from SPRING-2, SINGLE, FLAMINGO and ARIA
481	Orkin	2017	Switching from efavirenz/emtricitabine/tenofovir (EFV/FTC/ TDF) or rilpivirine/emtricitabine/tenofovir disoproxil fumarate (RPV/FTC/TDF) to rilpivirine/emtricitabine/ tenofovir alafenamide (RPV/FTC/TAF): safety and efficacy through 48 weeks
482	Payne	2017	Does efavirenz replacement improve neurological function in treated HIV infection?
483	Murphy	2017	Elsulfavirine as compared to efavirenz in combination with TDF/FTC: 48-week study
484	Bracchi	2017	A randomized comparison of integrase inhibitors with TDF/FTC on renal markers
485	Hodder	2017	Efficacy and safety of switching to EVG/COBI/ FTC/TAF in virologically suppressed women
486	Hodder	2017	Efficacy & safety of switching to EVG/COBI/FTC/TAF in virologically suppressed women
487	Lombardi	2017	Cellular HIV-1 DNA levels after 96 weeks of switch to ATV/R +3TC in the AtLas-M trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
488	Molina	2017	Doravirine is non-inferior to darunavir/r in phase 3 treatment-naïve trial at week 48
489	Sax	2017	Randomized trial of bictegravir or dolutegravir with FTC/TAF for initial HIV therapy
490	Ward	2017	Week 96 efficacy and safety of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF) in older, hivinfected treatment-naïve adults
491	Eron	2018	Efficacy and Safety of Switching From Boosted-Protease Inhibitors (bPI) Plus Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF) Regimens to the Once Daily (QD), Single-Tablet Regimen (STR) of Darunavir/Cobicistat/Emtricitabine/ Tenofovir Alafenamide (D/C/F/TAF) in Virologically Suppressed, HIV-1-Infected Adults: Week 96 Results of the Phase 3, Randomized, Non-Inferiority EMERALD Trial
492	Funderburg	2018	Virally suppressed plh switching from abacavir to tenofovir alafenamide did not have changes in immune activation or inflammation
493	Hagins	2018	Switching to coformulated rilpivirine (RPV), emtricitabine (FTC) and tenofovir alafenamide from either RPV, FTC and tenofovir disoproxil fumarate (TDF) or efavirenz, FTC and TDF: 96-week results from two randomized clinical trials
494	Hodder	2018	Brief Report: Efficacy and Safety of Switching to Coformulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide (E/C/F/TAF) in Virologically Suppressed Women
495	Grinsztejn	2018	Results of ACTG A5288: a strategy study in RLS for 3rd-line ART candidates
496	Kozal	2018	Week-24 safety of fostemsavir in heavily treatment-experienced participants with HIV-1 (Study 205888, formerly AI438-047)
497	Puerto	2018	Symtuza® (DRV/c/FTC/TAF) in the management of previously treated patients
498	Aboud	2018	Superior efficacy of dolutegravir (DTG) plus two nucleoside reverse transcriptase inhibitors (NRTIs) compared with lopi-navir/ritonavir (LPV/RTV) plus two NRTIs in second-line treatment: interim data from the DAWNING study
499	Bhagwat	2018	Changes in Waist Circumference in HIV-Infected Individuals Initiating a Raltegravir or Protease Inhibitor Regimen: Effects of Sex and Race
500	Braun	2018	Simplification to dolutegravir monotherapy is non-inferior compared to continuation of combination antiretroviral therapy in patients who initiated combination antiretroviral therapy during primary HIV infection: a randomized, controlled, non-inferiority
501	Cahn	2018	Non-inferior efficacy of dolutegravir (DTG) plus lamivudine (3TC) versus DTG plus tenofovir/emtricitabine (TDF/FTC) fixed-dose combination in antiretroviral treatment-naive adults with HIV-1 infection-48-week results from the GEMINI studies
502	Cournil	2018	Dolutegravir-versus an efavirenz 400 mg-based regimen for the initial treatment of HIV-infected patients in Cameroon: 48-week efficacy results of the NAMSAL ANRS 12313 trial
503	Daar	2018	Phase 3, randomised, controlled trial of switching to fixed-dose bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) from boosted protease inhibitor-based regimens in virologically suppressed adults: week 48 results
504	Spinner	2018	Darunavir/cobicistat/emtricitabine/tenofovir alafenamide in HIV-1 treatment naïve patients: Week 48 results in subgroups based on baseline viral load, CD4+ count, and WHO clinical staging

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
505	Strehlau	2018	Substituting Abacavir for Stavudine in Children Who Are Virally Suppressed Without Lipodystrophy: Randomized Clinical Trial in Johannesburg, South Africa
506	Taiwo	2018	Dolutegravir Plus Lamivudine Maintains Human Immunodeficiency Virus-1 Suppression Through Week 48 in a Pilot Randomized Trial
507	Trevillyan	2018	Changes in plasma lipidome following initiation of antiretroviral therapy
508	Llibre	2018	Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies
509	Maggiolo	2018	Effect of age on efficacy and safety of elvitegravir, cobicistat, emtricitabine and tenofovir alafenamide (E/C/F/TAF) in virologically-suppressed, HIV-1-infected participants aged ≥65 years: Pooled analysis of two Phase III trials
510	Maggiolo	2018	Phase IIIb, randomized, open-label study to evaluate switching from a tenofovir disoproxil fumarate (TDF)-containing regimen to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) in virologically suppressed, HIV-1 infected participant
511	Molina	2018	Switch to bictegravir/F/TA from DTG and ABC/3TC
512	Murray	2018	Improvements in patient-reported outcomes of dolutegravir (DTG)-based second-line treatment compared to lopinavir/ ritonavir (LPV/r)-based treatment: results from the DAWNING study
513	Nicolè	2018	Darunavir/ritonavir 600/100 mg once daily: it's time for larger non-inferiority randomized trials
514	Orkin	2018	Efficacy and safety of the once-daily, darunavir/cobicistat/ emtricitabine/tenofovir alafenamide (D/C/F/TAF) singletablet regimen (STR) in ART-naive, HIV-1-infected adults: AMBER Week 96 results
515	Orkin	2018	Doravirine/lamivudine/tenofovir DF continues to be noninferior to efavirenz/emtricitabine/tenofovir DF in treatment-naïve adults with HIV-1 infection: Week 96 results of the DRIVE-AHEAD trial
516	Petchkum	2018	Efficacy of rilpivirine-based regimens as switch therapy from nevirapine-based regimens in HIV-infected patients with complete virological suppression: a randomised controlled trial
517	Podzamczer	2018	B/F/TAF versus ABC/DTG/3TC or DTG + F/TAF in treatment-naive adults with high baseline viral load or low baseline CD4 count in two Phase III randomized, controlled clinical trials: week 96 results
518	Lapadula	2018	No change in neurocognitive function after switching from efavirenz to rilpivirine
519	van der Heijden	2018	A switch to a raltegravir containing regimen does not lower platelet reactivity in HIV-infected individuals
520	Eron	2018	Analysis of HIV patients switching to D/C/F/TAF by prior ARV treatment experience
521	Figueroa	2018	DRV/R/3TC FDC for HIV-1 treatment-naïve patients: week 48 results of the ANDES study
522	Fox	2018	Phase 3, randomised, controlled trial of switching to fixed-dose bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) from boosted protease inhibitor-based regimens in virologically suppressed adults: sub-analysis of week-48 lipid results
523	Gibb	2018	Impact of raltegravir intensification of first-line ART on iris in the reality trial
524	Huhn	2018	HIV treatment experienced patients switched to D/C/F/TAF: age, gender, race analyses

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
525	Kityo	2018	Switching to bictegravir/emtracitabine/tenofovir alafenimide (B/F/TAF) in women
526	Kityo	2018	Switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in women
527	Kozal	2018	Phase 3 study of fostemsavir in heavily treatment experienced HIV-1 infected subjects: day 8 and week 24 primary efficacy and safety results (Study 205888, formerly AI438-047)
528	Mallon	2018	Platelet function upon switching to tenofovir alafenamide (TAF) verses continuing abacavir (ABC): a randomised substudy OVERRIDE
529	Mills	2018	Switching to RPV/FTC/TAF from RPV/FTC/TDF or EFV/FTC/TDF: week 96 results
530	Orkin	2018	Similar efficacy & safety by subgroup in drive-ahead: dOR/3TC/TDF versus EFV/FTC/TDF
531	Rashbaum	2018	Age, gender, and race analyses of D/C/F/TAF in HIV-1 treatment naïve patients
532	Ustianowski	2018	Switch to bictegravir/emtricitabine/tenofovir alafenamide from dolutegravir and abacavir/lamivudine OVERRIDE
533	Linares	2018	Favourable phenotype of LDL particles in subjects with high cardiovascular risk switching from a ritonavir-boosted protease inhibitor to dolutegravir. Results of the NEAT 022 study
534	Gallant	2018	Week-48 results of AMBER: phase 3, randomised, double-blind trial in antiretroviral treatment (ART)-naïve HIV-1-infected adults to evaluate the efficacy and safety of the once-daily, single-tablet regimen (STR) of darunavir/ cobicistat/emtricitabine/tenof
535	Orkin	2018	Week 48 results of EMERALD: a Phase 3, randomised, non-inferiority study evaluating the efficacy and safety of switching from boosted-protease inhibitors (bPI) plus emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) regimens to the once daily (QD), s
536	Hamzah	2019	Safety of tenofovir alafenamide (TAF) in patients with a history of proximal renal tubulopathy on tenofovir disoproxil fumarate (TDF)
537	Aboud	2019	Efficacy and safety of dolutegravir-rilpivirine for maintenance of virological suppression in adults with HIV-1: 100-week data from the randomised, open-label, phase 3 SWORD-1 and SWORD-2 studies
538	Ait-Khaled	2019	Switching to DTG/3TC fixed dose combination (FDC) is noninferior to continuing a TAF-based regimen (TBR) through 48 weeks: subgroup analyses from the TANGO study
539	Braun	2019	Sustained viral suppression with dolutegravir monotherapy during 9,899 patient weeks of follow-up in individuals starting combination antiretroviral therapy during primary HIV infection (EARLY SIMPLIFIED): a randomized, controlled, multi-site, non-inferiority trial
540	Cahn	2019	Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials
541	Rossetti	2019	The Effect of Switching to Maraviroc + Darunavir/Ritonavir Dual Therapy in Virologically Suppressed Patients on the Progression of Liver Fibrosis: Findings From a Randomized Study
542	Stellbrink	2019	Safety and efficacy of switching from tenofovir disoproxil fumarate to tenofovir alafenamide in people with HIV aged 50 years and older
543	Van Wyk	2019	Durable efficacy of two-drug regimen (2DR) of dolutegravir (DTG) plus lamivudine (3TC) in antiretroviral treatment-naïve adults with HIV-1 infection at 96 weeks: Subgroup analyses in the gemini studies

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
544	Van Wyk	2019	Durable suppression and low rate of virological failures 3 years after switch to DTG+RPV two-drug regimen: SWORD 1 and 2 studies
545	Walmsley	2019	Biologic sex is not the only difference between men and women: data from the Doravirine phase 2/3 clinical trials
546	Kaewpoowat	2019	Neurocognitive function change after switching from efavirenz to rilpivirine in HIV-infected adults: a randomized control trial
547	Llibre	2019	SWORD 1&2: maintenance or improvement in renal function in PLWH through 148 weeks after switch to the dolutegravir + rilpivirine 2-drug regimen
548	Maggiolo	2019	Switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in adults aged>65 or older: Week 48 results from a phase 3b, open-label trial
549	Margolis	2019	Long-acting cabotegravir + rilpivirine as maintenance therapy: ATLAS week-48 results
550	Molina	2019	Islatravir efficacy and safety for selected demographic and baseline subgroups from a Phase 2 trial in treatment naÃ¯ve adults with HIV-1 infection
551	Molina	2019	MK-8591 at doses of 0.25 to 2.25 mg QD, in combination with doravirine establishes and maintains viral suppression through 48 weeks in treatment-naïve adults with HIV-1 infection
552	Murray	2019	Patient views on long acting HIV treatment: cabotegravir + rilpivirine as maintenance therapy (ATLAS 48 week results)
553	Okoro	2019	Evaluation of the different adverse drug reactions (ADR's) and their grade among HIV patient's newly started/substituted on combined tenofovir/lamivudine/dolutegravir (TDF/3TC/DTG) in the two major hospitals in Onitsha metropolis, Anambra state, Nigeria
554	Orkin	2019	Long-term efficacy and safety of bictegravir/emtricitabine/ tenofovir alafenamide (B/F/TAF) in ART-naïve adults
555	Orkin	2019	Long-active cabotegravir + rilpivirine for HIV maintenance: FLAIR week-48 results
556	Pacheco	2019	Safety and efficacy of triple therapy with Dolutegravir plus 2 NRTIs, in treatment-naïve HIV-2 infected patients-48 weeks results from a phase II study
557	Perez Valero	2019	Reversibility of dolutegravir/lamivudine/abacavir neuropsychiatric toxicity after 24 weeks of switching to elvitegravir/cobicistat/emtricitabine/tenofovir-alafenamide (EVG/c/FTC/TAF). The DREAM Clinical Trial
558	Porteiro	2019	Efficacy of dolutegravir (DTG) plus lamivudine (3TC) versus DTG plus tenofovir/emtricitabine (TDF/FTC) in antiretroviral treatment-naive adults with HIV-1 infection: 48-week subgroup results from the GEMINI studies in Latin American participants
559	Quercia	2019	Outcomes for women in phase 3 trials of long-acting cabotegravir+rilpivirine: pooled ATLAS and FLAIR week 48 results
560	Mora-Peris	2019	Cerebral function parameters in people living with HIV switching integrase inhibitor
561	Songumpai	2019	Virologic response of switching tenofovir disoproxil fumarate (TDF)-based regimen to abacavir (ABC)-Based Regimen vs. Lopinavir/ Ritonavir(LPV/r) Plus Lamivudine(3TC) in HIV-infected patients with tdfinduced nephrotoxicity at 24 Weeks: a prospective, ope
562	Thompson	2019	Long-term safety & efficacy of fostemsavir in treatmentexperienced HIV participants

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

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Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
563	Assoumou	2019	Impact of the reproductive/hormonal status on weight, fat and insulin resistance in HIV-infected women switching from a PI regimen to dual raltegravir-etravirine therapy: Results from the ANRS163-ETRAL trial at 48 and 96 weeks
564	NR	2019	Dolutegravir/lamivudine (Dovato)--a two-drug complete regimen for HIV-1 infection
565	Eron	2019	Week 96 efficacy and safety results of the phase 3, randomized EMERALD trial to evaluate switching from boosted-protease inhibitors plus emtricitabine/tenofovir disoproxil fumarate regimens to the once daily, single-tablet regimen of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in treatment-experienced, virologically-suppressed adults living with HIV-1
566	D'Amico	2020	Safety and efficacy of cabotegravir + rilpivirine long-acting with and without oral lead-in: FLAIR Week 124 results
567	DeJesus	2020	Islatravir safety analysis through week 48 from a phase 2 trial in treatment naïve adults with HIV-1 infection
568	Dunn	2020	Gastrointestinal (GI) adverse events with darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) through Week 96: An EMERALD post-hoc analysis
569	Hagins	2020	Week 48 outcomes from the braave 2020 study: A randomized switch to B/F/TAF in african american adults with hiv
570	Krishnaratne	2020	Stigma and Judgment Toward People Living with HIV and Key Population Groups Among Three Cadres of Health Workers in South Africa and Zambia: analysis of Data from the HPTN 071 (PopART) Trial
571	Avihingsanon	2020	Third-line antiretroviral therapy including raltegravir, darunavir/ritonavir and/or etravirine is well tolerated and achieves durable virologic suppression over 144 + weeks in resource-limited settings ACTG: A5288 strategy trial
572	Benn	2020	Outcomes for women receiving long-acting cabotegravir + rilpivirine monthly and every two months: ATLAS-2M study Week 48 results
573	Brar	2020	Long-term follow-up after a switch to bictegravir, emtracitabine, tenofovir alafenamide from dolutegravir, abacavir, lamivudine
574	Bushen	2020	Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in treatment-naïve (AMBER) and virologically suppressed (EMERALD) patients with neurologic and/or psychiatric comorbidities: week 96 subgroup analysis
575	Cahn	2020	Durable efficacy of dolutegravir (DTG) plus lamivudine (3TC) in antiretroviral treatment-na€ive adults with HIV-1 infection: 3-year results from the GEMINI studies
576	Cahn	2020	Durable Efficacy of Dolutegravir Plus Lamivudine in Antiretroviral Treatment-Naive Adults With HIV-1 Infection: 96-Week Results From the GEMINI-1 and GEMINI-2 Randomized Clinical Trials
577	Chounta	2020	Comparability of 48-week efficacy and safety of cabotegravir + rilpivirine long-acting every 8 weeks to standard of care in suppressed HIV-1-infected patients
578	Smith	2020	Safety, Efficacy, and Durability of Long-Acting CAB and RPV as Maintenance Therapy for HIV-1 Infection: LATTE-2 Week 256 Results
579	Thompson	2020	Once-daily Doravirine for Initial Treatment of Adults Living With Human Immunodeficiency Virus-1: An Integrated Safety Analysis

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Estudos excluídos por não serem um ensaio clínico controlado randomizado ou realizarem a análise conjunta de dois ou mais ensaios clínicos			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
580	Venter	2020	The ADVANCE trial: phase 3, randomised comparison of TAF/FTC+DTG, TDF/FTC+DTG or TDF/FTC/EFV for first-line treatment of HIV-1 infection
581	Kozal	2020	Fostemsavir in Adults with Multidrug-Resistant HIV-1 Infection
582	Molina	2020	Islatravir in combination with doravirine maintains HIV-1 viral suppression through 96 weeks
583	Orkin	2020	Fixed-dose combination bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir-containing regimens for initial treatment of HIV-1 infection: week 144 results from two randomised, double-blind, multicentre, phase 3, non-inferiority trials
584	Post	2020	Renal safety through 96 weeks from a phase II trial (P011) of islatravir and doravirine in treatment-naive adults with HIV-1
585	Rockstroh	2020	Long-term follow-up after a switch to bictegravir, emtricitabine, tenofovir alafenamide, from a boosted protease inhibitor-based regimen
586	Rojas	2020	Switching to dolutegravir plus lamivudine (DTG + 3TC) is non-inferior to and as safe as continuing standard triple antiretroviral therapy (TAR)
587	Daar	2020	Dose-response relationship of subcutaneous long-acting HIV capsid inhibitor gs-6207
588	Ibrahim	2020	Bone mineral density improves in women who switch from TDF/ FTC/NNRTI to ABC/3TC/DTG
589	Assoumou	2020	Fat gain differs by sex and hormonal status in persons living with suppressed HIV switched to raltegravir/etravirine
590	Hagins	2020	Randomized switch to B/F/TAF in african american adults with HIV
591	Samarawickrama	2020	Increase in bone mineral density and weight in women who switch from TDF/FTC/NNRTI to ABC/3TC/DTG
592	Orkin	2020	Week 96 results of a phase 3 trial of darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naive HIV-1 patients
593	Huhn	2021	Week 96 subgroup analyses of the phase 3, randomized AMBER and EMERALD trials evaluating the efficacy and safety of the once daily darunavir/ cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) single-tablet regimen in antiretroviral treatment (ART)-naïve and -experienced, virologically-suppressed adults living with HIV-1
594	Gianotti	2021	Residual viremia in HIV-infected patients who continue a 2-drug or switch to a 3-drug integrase strand transfer inhibitor-based regimen
595	Erlandson	2021	Weight Change Following Antiretroviral Therapy Switch in People with Viral Suppression: Pooled Data from Randomized Clinical Trials
Estudos excluídos por não incluírem pessoas com HIV/Aids			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Raskino	1999	Neurologic, neurocognitive, and brain growth outcomes in human immunodeficiency virus-infected children receiving different nucleoside antiretroviral regimens. Pediatric AIDS Clinical Trials Group 152 Study Team
2	Buss	2001	Saquinavir and ritonavir pharmacokinetics following combined ritonavir and saquinavir (soft gelatin capsules) administration
3	Scelsa	2005	A pilot, double-blind, placebo-controlled trial of indinavir in patients with ALS
4	Ruel	2014	Virologic and immunologic outcomes of HIV-infected Ugandan children randomized to lopinavir/ritonavir or nonnucleoside reverse transcriptase inhibitor therapy

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não incluírem pessoas com HIV/Aids			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
5	Abhyankar	2017	Pharmacokinetics of fixed-dose combination of tenofovir disoproxil fumarate, lamivudine, and efavirenz: results of a randomized, crossover, bioequivalence study
Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Luthy	1988	Zidovudine for the treatment of thrombocytopenia associated with human immunodeficiency virus (HIV). A prospective study
2	Meng	1990	AIDS Clinical Trials Group: phase I/II study of combination 2',3'-dideoxycytidine and zidovudine in patients with acquired immunodeficiency syndrome (AIDS) and advanced AIDS-related complex
3	Hamilton	1992	A controlled trial of early versus late treatment with zidovudine in symptomatic human immunodeficiency virus infection. Results of the Veterans Affairs Cooperative Study
4	Kahn	1992	A controlled trial comparing continued zidovudine with didanosine in human immunodeficiency virus infection. The NIAID AIDS Clinical Trials Group
5	Abrams	1994	Treatment options in zidovudine intolerance or failure
6	Abrams	1994	A comparative trial of didanosine or zalcitabine after treatment with zidovudine in patients with human immunodeficiency virus infection
7	Spruance	1994	Didanosine compared with continuation of zidovudine in HIV-infected patients with signs of clinical deterioration while receiving zidovudine: A randomized, double-blind clinical trial
8	Spruance	1994	Didanosine compared with continuation of zidovudine in HIV-infected patients with signs of clinical deterioration while receiving zidovudine: A randomized, double-blind clinical trial
9	Been-Tiktak	1995	Safety, tolerance, and pharmacokinetics of atevirdine mesylate (U-87201E) in asymptomatic human immunodeficiency virus-infected patients
10	Haubrich	1995	A randomized trial of the activity and safety of Ro 24-7429 (Tat antagonist) versus nucleoside for human immunodeficiency virus infection. The AIDS Clinical Trials Group 213 Team
11	Ragni	1995	Randomized study of didanosine monotherapy and combination therapy with zidovudine in hemophilic and nonhemophilic subjects with asymptomatic human immunodeficiency virus-1 infection. AIDS Clinical Trial Groups
12	Jablonowski	1995	A dose comparison study of didanosine in patients with very advanced HIV infection who are intolerant to or clinically deteriorate on zidovudinne
13	Hammer	1996	A trial comparing nucleoside monotherapy with combination therapy in HIV-infected adults with CD4 cell counts from 200 to 500 per cubic millimeter. AIDS Clinical Trials Group Study 175 Study Team
14	Been-Tiktak	1996	Safety, tolerance, and efficacy of atevirdine in asymptomatic human immunodeficiency virus-infected individuals
15	Collier	1996	Treatment of human immunodeficiency virus infection with saquinavir, zidovudine, and zalcitabine. AIDS Clinical Trials Group
16	Saravolatz	1996	Zidovudine alone or in combination with didanosine or zalcitabine in HIV-infected patients with the acquired immunodeficiency syndrome or fewer than 200 CD4 cells per cubic millimeter. Investigators for the Terry Beirn Community Programs for Clinical Research on AIDS
17	Gatell	1996	Switching from zidovudine to didanosine in patients with symptomatic HIV infection and disease progression. ddI Iberian Study Group

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
18	Vella	1996	A randomized trial (ISS 901) of switching to didanosine versus continued zidovudine after the diagnosis of AIDS
19	Darbyshire	1996	The Alpha trial: European/Australian randomized double-blind trial of two doses of didanosine in zidovudine-intolerant patients with symptomatic HIV disease
20	Deeks	1997	The safety and efficacy of adefovir dipivoxil, a novel anti-human immunodeficiency virus (HIV) therapy, in HIV-infected adults: a randomized, double-blind, placebo-controlled trial
21	Floridia	1997	A randomized trial (ISS 902) of didanosine versus zidovudine in previously untreated patients with mildly symptomatic human immunodeficiency virus infection
22	Gerstoft	1997	Alternating treatment with didanosine and zidovudine versus either drug alone for the treatment of advanced HIV infection. The Alter Study. Nordic HIV Therapy Group
23	Cooper	1997	Randomised trial of addition of lamivudine or lamivudine plus loviride to zidovudine-containing regimens for patients with HIV-1 infection: The CAESAR trial
24	Fischl	1997	Safety and antiviral activity of combination therapy with zidovudine, zalcitabine, and two doses of interferon-alpha2a in patients with HIV. AIDS Clinical Trials Group Study 197
25	Spector	1997	Comparative trial of two dosages of zalcitabine in zidovudine-experienced children with advanced human immunodeficiency virus disease. Pediatric AIDS Clinical Trials Group
26	Keiser	1998	An open-label pilot study of the efficacy and tolerability of once-daily didanosine versus twice-daily didanosine
27	Montaner	1998	A randomized, double-blind trial comparing combinations of nevirapine, didanosine, and zidovudine for HIV-infected patients: the INCAS Trial. Italy, The Netherlands, Canada and Australia Study
28	Haubrich	1998	Improved survival and reduced clinical progression in HIV-infected patients with advanced disease treated with saquinavir plus zalcitabine
29	Sadler	1999	Safety and Pharmacokinetics of Amprenavir (141W94), a Human Immunodeficiency Virus (HIV) Type 1 Protease Inhibitor, following Oral Administration of Single Doses to HIV-Infected Adults
30	Babiker	1999	A randomized trial comparing regimens of four reverse transcriptase inhibitors given together or cyclically in HIV-1 infection - The Quattro Trial
31	Friedland	1999	Efficacy and safety of delavirdine mesylate with zidovudine and didanosine compared with two-drug combinations of these agents in persons with HIV disease with CD4 counts of 100 to 500 cells/mm3 (ACTG 261)
32	Haubrich	1999	A phase II safety and efficacy study of amprenavir in combination with zidovudine and lamivudine in HIV-infected patients with limited antiretroviral experience. Amprenavir PROAB2002 Study Team
33	Mobley	1999	Virological and immunological responses to once-daily dosing of didanosine in combination with stavudine. AI454-143 Team
34	Monno	1999	Comparison of once and twice daily dosing of didanosine in combination with stavudine for the treatment of HIV-1 infection. AI 454-146 Team
35	Price	1999	Neurological outcomes in late HIV infection: Adverse impact of neurological impairment on survival and protective effect of antiviral therapy

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
36	Molina	1999	The ALBI trial: A randomized controlled trial comparing stavudine plus didanosine with zidovudine plus lamivudine and a regimen alternating both combinations in previously untreated patients infected with human immunodeficiency virus
37	Revicki	1999	Quality of life outcomes of saquinavir, zalcitabine and combination saquinavir plus zalcitabine therapy for adults with advanced HIV infection with CD4 counts between 50 and 300 cells/mm3
38	Been-Tiktak	1999	Efficacy and safety of combination therapy with delavirdine and zidovudine: a European/Australian phase II trial
39	NR	1999	Amprenavir study results released
40	Gatell	1999	AVANTI 1: randomized, double-blind trial to evaluate the efficacy and safety of zidovudine plus lamivudine versus zidovudine plus lamivudine plus loviride in HIV-infected antiretroviral-naive patients. AVANTI Study Group
41	Para	1999	ACTG 260: a randomized, phase I-II, dose-ranging trial of the anti-human immunodeficiency virus activity of delavirdine monotherapy
42	Gulick	2000	Randomized study of saquinavir with ritonavir or nelfinavir together with delavirdine, adefovir, or both in human immunodeficiency virus-infected adults with virologic failure on indinavir: AIDS Clinical Trials Group Study 359
43	Currier	2000	Differences between women and men in adverse events and CD4+ responses to nucleoside analogue therapy for HIV infection
44	Albrecht	2000	Effect of lamivudine in HIV-infected persons with prior exposure to zidovudine/didanosine or zidovudine/zalcitabine
45	García	2000	Comparison of twice-daily stavudine plus once- or twice-daily didanosine and nevirapine in early stages of HIV infection: the scan study
46	Girard	2000	Phase II placebo-controlled trial of fozivudine tidoxil for HIV infection: pharmacokinetics, tolerability, and efficacy
47	Kazatchkine	2000	Didanosine dosed once daily is equivalent to twice daily dosing for patients on double or triple combination antiretroviral therapy
48	Kroon	2000	A randomized, double-blind trial of half versus standard dose of zidovudine plus zalcitabine in Thai HIV-1-infected patients (study HIV-NAT 001). HIV Netherlands Australia Thailand Research Collaboration
49	Joly	2000	Delavirdine in combination with zidovudine in treatment of human immunodeficiency virus type 1-infected patients: evaluation of efficacy and emergence of viral resistance in a randomized, comparative phase III trial. The M/3331/0013B Study Group
50	Nachman	2000	Nucleoside analogs plus ritonavir in stable antiretroviral therapy-experienced HIV-infected children: a randomized controlled trial. Pediatric AIDS Clinical Trials Group 338 Study Team
51	Carr	2001	HIV protease inhibitor substitution in patients with lipodystrophy: a randomized, controlled, open-label, multicentre study
52	Fisher	2001	The safety and efficacy of adefovir dipivoxil in patients with advanced HIV disease: a randomized, placebo-controlled trial
53	Arasteh	2001	GW420867X administered to HIV-1-infected patients alone and in combination with lamivudine and zidovudine
54	Ruiz	2001	Antiretroviral treatment simplification with nevirapine in protease inhibitor-experienced patients with hiv-associated lipodystrophy: 1-year prospective follow-up of a multicenter, randomized, controlled study
55	Hammer	2002	Dual vs single protease inhibitor therapy following antiretroviral treatment failure: a randomized trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
56	ADHOC International Steering Committee	2002	A randomized placebo-controlled trial of adefovir dipivoxil in advanced HIV infection: the ADHOC trial
57	Burger	2003	Therapeutic drug monitoring of nelfinavir and indinavir in treatment-naive HIV-1-infected individuals
58	Simpson	2003	Lamotrigine for HIV-associated painful sensory neuropathies: a placebo-controlled trial
59	Nadler	2003	Twice-daily amprenavir 1200 mg versus amprenavir 600 mg/ritonavir 100 mg, in combination with at least 2 other antiretroviral drugs, in HIV-1-infected patients
60	Eron	2004	Short-term safety and antiretroviral activity of T-1249, a second-generation fusion inhibitor of HIV
61	Raguin	2004	Salvage therapy with amprenavir, lopinavir and ritonavir 200 mg/d or 400 mg/d in HIV-infected patients in virological failure
62	Pulido	2004	A randomized study investigating the efficacy and safety of amprenavir in combination with low-dose ritonavir in protease inhibitor-experienced HIV-infected adults
63	Cardiello	2005	A prospective, randomized trial of structured treatment interruption for patients with chronic HIV type 1 infection
64	Molina	2005	Simplification therapy with once-daily emtricitabine, didanosine, and efavirenz in HIV-1-infected adults with viral suppression receiving a protease inhibitor-based regimen: a randomized trial
65	Molina	2005	Didanosine in HIV-1-infected patients experiencing failure of antiretroviral therapy: a randomized placebo-controlled trial
66	Hernandez	2005	MexVir 1: comparison of two antiretroviral schemes including nelfinavir in Mexican patients with HIV infection: a national, multicenter, 48-week follow-up
67	Hernandez	2005	MexVir 1: comparison of two antiretroviral schemes including nelfinavir in Mexican patients with HIV infection: a national, multicenter, 48-week follow-up
68	Ananworanich	2006	CD4-guided scheduled treatment interruptions compared with continuous therapy for patients infected with HIV-1: results of the Staccato randomised trial
69	Cahn	2006	Ritonavir-boosted tipranavir demonstrates superior efficacy to ritonavir-boosted protease inhibitors in treatment-experienced HIV-infected patients: 24-week results of the RESIST-2 trial
70	Wang	2006	Randomized double-blinded and controlled clinical trial on treatment of HIV/AIDS by Zhongyan-4
71	Cahn	2006	Efficacy and tolerability of 10-day monotherapy with apricitabine in antiretroviral-naive, HIV-infected patients
72	Gripshover	2006	Amdoxovir versus placebo with enfuvirtide plus optimized background therapy for HIV-1-infected subjects failing current therapy (AACTG A5118)
73	Piketty	2006	Salvage therapy with atazanavir/ritonavir combined to tenofovir in HIV-infected patients with multiple treatment failures: randomized ANRS 107 trial
74	Sprinz	2006	Substitution with lopinavir/ritonavir improves patient-reported outcomes including quality of life in patients who were intolerant to their antiretroviral therapy
75	Ghosn	2007	Antiviral activity of low-dose alovudine in antiretroviral-experienced patients: results from a 4-week randomized, double-blind, placebo-controlled dose-ranging trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
76	Gulick	2007	Phase 2 study of the safety and efficacy of vicriviroc, a CCR5 inhibitor, in HIV-1-Infected, treatment-experienced patients: AIDS clinical trials group 5211
77	Winston	2007	The safety, efficacy, and pharmacokinetic profile of a switch in antiretroviral therapy to saquinavir, ritonavir, and atazanavir alone for 48 weeks and a switch in the saquinavir formulation
78	Schürmann	2007	Antiviral activity, pharmacokinetics and safety of vicriviroc, an oral CCR5 antagonist, during 14-day monotherapy in HIV-infected adults
79	Asboe	2007	A virological benefit from an induction/maintenance strategy: the Forte trial
80	Lowe	2007	Stavudine but not didanosine as part of HAART contributes to peripheral lipoatrophy: a substudy from the Antiretroviral Regimen Evaluation Study (ARES)
81	Maitland	2008	Switching from twice-daily abacavir and lamivudine to the once-daily fixed-dose combination tablet of abacavir and lamivudine improves patient adherence and satisfaction with therapy
82	Currier	2008	Antiviral activity and safety of aplaviroc with lamivudine/zidovudine in HIV-infected, therapy-naive patients: the ASCENT (CCR102881) study
83	Yeni	2009	Antiviral activity and safety of aplaviroc, a CCR5 antagonist, in combination with lopinavir/ritonavir in HIV-infected, therapy-naïve patients: results of the EPIC study (CCR100136)
84	Fätkenheuer	2009	Activity, pharmacokinetics and safety of lersivirine (UK-453,061), a next-generation nonnucleoside reverse transcriptase inhibitor, during 7-day monotherapy in HIV-1-infected patients
85	Gutiérrez-Valencia	2009	Stepped-dose versus full-dose efavirenz for HIV infection and neuropsychiatric adverse events: a randomized trial
86	Sension	2009	Improvement in lipid profiles in antiretroviral-experienced HIV-positive patients with hyperlipidemia after a switch to unboosted atazanavir
87	Mulenga	2010	Strategies for nevirapine initiation in HIV-infected children taking pediatric fixed-dose combination "baby pills" in Zambia: a randomized controlled trial
88	Murphy	2010	Antiviral activity and tolerability of amdoxovir with zidovudine in a randomized double-blind placebo-controlled study in HIV-1-infected individuals
89	Ratsela	2010	A randomized factorial trial comparing 4 treatment regimens in treatment-naive HIV-infected persons with AIDS and/or a CD4 cell count <200 cells/μL in South Africa
90	Read	2010	The effect of leflunomide on cycling and activation of T-cells in HIV-1-infected participants
91	Lalezari	2011	Safety, efficacy, and pharmacokinetics of TBR-652, a CCR5/CCR2 antagonist, in HIV-1-infected, treatment-experienced, CCR5 antagonist-naive subjects
92	Lake	2012	A randomized trial of Raltegravir replacement for protease inhibitor or non-nucleoside reverse transcriptase inhibitor in HIV-infected women with lipohypertrophy
93	Carey	2012	A randomized study of pharmacokinetics, efficacy, and safety of 2 raltegravir plus atazanavir strategies in ART-treated adults
94	Cotte	2013	Randomized placebo-controlled study of the safety, tolerability, antiviral activity, and pharmacokinetics of 10-day monotherapy with BMS-986001, a novel HIV NRTI, in treatment-experienced HIV-1-infected subjects

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
95	Wang	2013	Effect of Immune No. 2 (2) on the immune reconstitution in patients with HIV/AIDS after highly active antiretroviral treatment: a randomized double blind placebo controlled clinical trial
96	Wilkins	2013	SPIRIT: switching to rilpivirine/emtricitabine/tenofovir DF single-tablet regimen from boosted protease inhibitor maintains HIV suppression at week 48 regardless of viral load or CD4 + count prior to initiation of ARV therapy
97	Vernazza	2013	Efficacy and safety of lersivirine (UK-453,061) versus efavirenz in antiretroviral treatment-naive HIV-1-infected patients: week 48 primary analysis results from an ongoing, multicenter, randomized, double-blind, phase IIb trial
98	DeJesus	2014	Efficacy and safety of lersivirine versus etravirine for the treatment of HIV-1 infection in patients with prior non-nucleoside reverse transcriptase inhibitor (NNRTI) use and evidence of NNRTI resistance: a randomized phase 2B trial
99	Stellbrink	2014	Antiviral activity, pharmacokinetics, and safety of the HIV-1 protease inhibitor TMC310911, coadministered with ritonavir, in treatment-naive HIV-1-infected patients
100	Harrison	2015	HIV-1 Drug Resistance and Second-Line Treatment in Children Randomized to Switch at Low Versus Higher RNA Thresholds
101	Krystal	2015	BMS-955176: Antiviral activity/safety of a 2nd-generation HIV-1 maturation inhibitor
102	Gupta	2016	Efficacy, safety, bone and metabolic effects of HIV nucleoside reverse transcriptase inhibitor BMS-986001 (AI467003): a phase 2b randomised, controlled, partly blinded trial
103	Thompson	2016	A 48-week randomized phase 2b study evaluating cenicriviroc versus efavirenz in treatment-naive HIV-infected adults with C-C chemokine receptor type 5-tropic virus
104	Zhang	2016	Combination of long-acting HIV fusion inhibitor albuvirtide and LPV/r showed potent efficacy in HIV-1 patients
105	Lake	2016	STRIIVING: switching to abacavir/dolutegravir/lamivudine fixed dose combination (ABC/DTG/3TC FDC) from a PI, INI or NNRTI based regimen maintains HIV suppression at week 48
106	Gallant	2017	Antiviral Activity, Safety, and Pharmacokinetics of Bictegravir as 10-Day Monotherapy in HIV-1-Infected Adults
107	Hwang	2017	Antiviral Activity, Safety, and Exposure-Response Relationships of GSK3532795, a Second-Generation Human Immunodeficiency Virus Type 1 Maturation Inhibitor, Administered as Monotherapy or in Combination With Atazanavir With or Without Ritonavir in a Phase 2a Randomized, Dose-Ranging, Controlled Trial (AI468002)
108	Sax	2017	A randomized trial of bictegravir or dolutegravir with emtricitabine and tenofovir alafenamide (F/TAF) followed by open label switch to bictegravir/F/ TAF fixed dose combination
109	Sax	2017	Randomised trial of bictegravir or dolutegravir with FTC/TAF for initial HIV therapy
110	Sax	2017	Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380–1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial
111	Wijting	2017	Dolutegravir as maintenance monotherapy for HIV (DOMONO): a phase 2, randomised non-inferiority trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
112	Sax	2018	Coformulated bictegravir, emtricitabine, tenofovir alafenamide after initial treatment with bictegravir or dolutegravir and emtricitabine/tenofovir alafenamide
113	Stellbrink	2018	Phase III randomized, controlled clinical trial of bictegravir coformulated with FTC/TAF in a fixed-dose combination (B/F/TAF) versus dolutegravir (DTG) + F/TAF in treatmentnaive HIV-1 positive adults: week 96
114	Wohl	2018	A phase 3, randomized, controlled clinical trial of bictegravir in a fixed-dose combination, B/F/TAF, vs. ABC/DTG/3TC in treatment-naïve adults at week 96
115	Mora-Peris	2018	Changes in cerebral function parameters with maraviroc-intensified antiretroviral therapy in treatment naive HIV-positive individuals
116	Gatell	2019	Immediate Versus Deferred Switching From a Boosted Protease Inhibitor-based Regimen to a Dolutegravir-based Regimen in Virologically Suppressed Patients With High Cardiovascular Risk or Age ≥50 Years: Final 96-Week Results of the NEAT022 Study
117	Rutsaert	2019	Safety, tolerability and impact on viral reservoirs of the addition to antiretroviral therapy of ABX464, an investigational antiviral drug, in individuals living with HIV-1: a Phase IIa randomised controlled study
118	Sax	2019	Switching to a single-tablet regimen bictegravir, emtricitabine, and tenofovir alafenamide (B/F/TAF) from dolutegravir (DTG) plus emtricitabine and either tenofovir alafenamide or tenofovir disoproxil fumarate (F/TAF or F/TDF)
119	Stellbrink	2019	Co-formulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial
120	Wijting	2019	Changes in renal, bone, lipid, and inflammation markers in HIV-1 patients after combination antiretroviral therapy simplification to dolutegravir monotherapy
121	Wohl	2019	Bictegravir combined with emtricitabine and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial
122	Kityo	2019	Longer-term (96-week) efficacy and safety of switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in women
123	Sax	2020	Switching to bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with HIV
124	Su	2020	Efficacy and safety of the long-acting fusion inhibitor albuvirtide in antiretroviral-experienced adults with human immunodeficiency virus-1: interim analysis of the randomized, controlled, phase 3, non-inferiority TALENT study
125	Kumar	2020	Long-term treatment efficacy and safety following switch to doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF): week 144 results of the DRIVE-SHIFT trial
126	Luscombe	2020	Human immunodeficiency virus type-1 Vpu inhibitor, BIT225, in combination with 3-drug antiretroviral therapy modulates inflammation and immune cells functions
127	Lama	2021	Clinical and Immunologic Outcomes After Immediate or Deferred Antiretroviral Therapy Initiation During Primary Human Immunodeficiency Virus Infection: The Sabes Randomized Clinical Study

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV não mais utilizada na prática clínica ou compararem o mesmo esquema ARV iniciado em momentos diferentes			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
128	Nelson	2021	Efficacy, safety and central nervous system effects after switch from efavirenz/tenofovir/emtricitabine to doravirine/tenofovir/lamivudine
Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Fischl	1989	Prolonged zidovudine therapy in patients with AIDS and advanced AIDS-related complex
2	Fischl	1990	A randomized controlled trial of a reduced daily dose of zidovudine in patients with the acquired immunodeficiency syndrome.
3	Fischl	1990	The safety and efficacy of zidovudine (AZT) in the treatment of subjects with mildly symptomatic human immunodeficiency virus type 1 (HIV) infection. A double-blind, placebo-controlled trial. The AIDS Clinical Trials Group
4	Volberding	1990	Zidovudine in asymptomatic human immunodeficiency virus infection. A controlled trial in persons with fewer than 500 CD4-positive cells per cubic millimeter. The AIDS Clinical Trials Group of the National Institute of Allergy and Infectious Diseases
5	Merigan	1991	Placebo-controlled trial to evaluate zidovudine in treatment of human immunodeficiency virus infection in asymptomatic patients with hemophilia. NHF-ACTG 036 Study Group
6	Kimura	1992	A randomized trial of reduced doses of azidothymidine in Japanese patients with human immunodeficiency virus type 1 infection
7	Nordic Medical Research Councils' HIV Therapy Group	1992	Double blind dose-response study of zidovudine in AIDS and advanced HIV infection. Nordic Medical Research Councils' HIV Therapy Group
8	Gelber	1992	Quality-of-life evaluation in a clinical trial of zidovudine therapy in patients with mildly symptomatic HIV infection. The AIDS Clinical Trials Group
9	Davey	1993	Plasma viremia as a sensitive indicator of the antiretroviral activity of L-697,661
10	Cooper	1993	Zidovudine in persons with asymptomatic HIV infection and CD4+ cell counts greater than 400 per cubic millimeter. The European-Australian Collaborative Group
11	Wu	1993	Functional status and well-being in a placebo-controlled trial of zidovudine in early symptomatic HIV infection
12	Mannucci	1994	Randomized double-blind, placebo-controlled trial of twice-daily zidovudine in asymptomatic haemophiliacs infected with the human immunodeficiency virus type 1. European-Australian Haemophilia Collaborative Study Group
13	Yarchoan	1994	A randomized pilot study of alternating or simultaneous zidovudine and didanosine therapy in patients with symptomatic human immunodeficiency virus infection
14	Lenderking	1994	Evaluation of the quality of life associated with zidovudine treatment in asymptomatic human immunodeficiency virus infection. The AIDS Clinical Trials Group
15	Husson	1994	Zidovudine and didanosine combination therapy in children with human immunodeficiency virus infection
16	Eron	1995	Treatment with lamivudine, zidovudine, or both in HIV-positive patients with 200 to 500 CD4+ cells per cubic millimeter. North American HIV Working Party
17	Kitchen	1995	Safety and activity of saquinavir in HIV infection

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
18	Darbyshire	1996	Delta: A randomised double-blind controlled trial comparing combinations of zidovudine plus didanosine or zalcitabine with zidovudine alone in HIV-infected individuals
19	Brady	1996	Randomized study of the tolerance and efficacy of high- versus low-dose zidovudine in human immunodeficiency virus-infected children with mild to moderate symptoms (AIDS Clinical Trials group 128)
20	Staszewski	1996	Safety and efficacy of lamivudine-zidovudine combination therapy in zidovudine-experienced patients. A randomized controlled comparison with zidovudine monotherapy. Lamivudine European HIV Working Group
21	Englund	1997	Zidovudine, didanosine, or both as the initial treatment for symptomatic HIV-infected children. AIDS Clinical Trials Group (ACTG) Study 152 Team
22	Gulick	1997	Treatment with indinavir, zidovudine, and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral therapy
23	Hammer	1997	A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. AIDS Clinical Trials Group 320 Study Team
24	Simpson	1997	Analysis of myopathy in a placebo-controlled zidovudine trial
25	Shepp	1997	A comparative trial of zidovudine administered every four versus every twelve hours for the treatment of advanced HIV disease
26	Gulick	1998	Simultaneous vs sequential initiation of therapy with indinavir, zidovudine, and lamivudine for HIV-1 infection: 100-week follow-up
27	Cameron	1998	Randomised placebo-controlled trial of ritonavir in advanced HIV-1 disease. The Advanced HIV Disease Ritonavir Study Group
28	Foudraine	1998	Improvement of chronic diarrhoea in patients with advanced HIV-1 infection during potent antiretroviral therapy
29	Mitsuyasu	1998	Activity of the soft gelatin formulation of saquinavir in combination therapy in antiretroviral-naive patients. NV15355 Study Team
30	Kline	1998	A randomized comparative trial of stavudine (d4T) versus zidovudine (ZDV, AZT) in children with human immunodeficiency virus infection. AIDS Clinical Trials Group 240 Team
31	Markowitz	1998	A preliminary evaluation of nelfinavir mesylate, an inhibitor of human immunodeficiency virus (HIV)-1 protease, to treat HIV infection
32	Niu	1998	Zidovudine treatment in patients with primary (acute) human immunodeficiency virus type 1 infection: a randomized, double-blind, placebo-controlled trial. DATRI 002 Study Group. Division of AIDS Treatment Research Initiative
33	Gibb	1998	A randomized double-blind trial of the addition of lamivudine or matching placebo to current nucleoside analogue reverse transcriptase inhibitor therapy in HIV-infected children: The PENTA-4 trial
34	Hirsch	1999	A randomized, controlled trial of indinavir, zidovudine, and lamivudine in adults with advanced human immunodeficiency virus type 1 infection and prior antiretroviral therapy
35	Staszewski	1999	Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults. Study 006 Team
36	Kumar	1999	Safety and pharmacokinetics of abacavir (1592U89) following oral administration of escalating single doses in human immunodeficiency virus type 1-infected adults

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
37	Stuart	1999	Randomized trial comparing saquinavir soft gelatin capsules versus indinavir as part of triple therapy (CHEESE study)
38	Gisolf	2000	The effect of treatment intensification in HIV-infection: a study comparing treatment with ritonavir/saquinavir and ritonavir/saquinavir/stavudine. Prometheus Study Group
39	Lewi	2000	Randomized, double-blind trial comparing indinavir alone, zidovudine alone and indinavir plus zidovudine in antiretroviral therapy-naive HIV-infected individuals with CD4 cell counts between 50 and 250/mm3
40	Phanuphak	2000	A comparison of two dosing regimens of zidovudine in Thai adults with early symptomatic HIV infection. Conducting clinical HIV trials in South-East Asia
41	AVANTI	2000	AVANTI 2. Randomized, double-blind trial to evaluate the efficacy and safety of zidovudine plus lamivudine versus zidovudine plus lamivudine plus indinavir in HIV-infected antiretroviral-naive patients
42	Murphy	2001	ABT-378/ritonavir plus stavudine and lamivudine for the treatment of antiretroviral-naive adults with HIV-1 infection: 48-week results
43	Rozenbaum	2001	Treatment intensification with abacavir in HIV-infected patients with at least 12 weeks previous lamivudine/zidovudine treatment
44	Benson	2002	Safety and antiviral activity at 48 weeks of lopinavir/ritonavir plus nevirapine and 2 nucleoside reverse-transcriptase inhibitors in human immunodeficiency virus type 1-infected protease inhibitor-experienced patients
45	French	2002	Randomized, open-label, comparative trial to evaluate the efficacy and safety of three antiretroviral drug combinations including two nucleoside analogues and nevirapine for previously untreated HIV-1 Infection: the OzCombo 2 study
46	Núñez	2002	SENC (Spanish efavirenz vs. nevirapine comparison) trial: a randomized, open-label study in HIV-infected naive individuals
47	Lichterfeld	2002	Long-term efficacy and safety of ritonavir/indinavir at 400/400 mg twice a day in combination with two nucleoside reverse transcriptase inhibitors as first line antiretroviral therapy
48	Gerstoft	2003	Low efficacy and high frequency of adverse events in a randomized trial of the triple nucleoside regimen abacavir, stavudine and didanosine
49	Haas	2003	Therapy with atazanavir plus saquinavir in patients failing highly active antiretroviral therapy: a randomized comparative pilot trial
50	Murphy	2003	Dose-ranging, randomized, clinical trial of atazanavir with lamivudine and stavudine in antiretroviral-naive subjects: 48-week results
51	van Leeuwen	2003	A randomized trial to study first-line combination therapy with or without a protease inhibitor in HIV-1-infected patients
52	Martinez-Picado	2003	Alternation of antiretroviral drug regimens for HIV infection. A randomized, controlled trial
53	Kirk	2003	A randomized trial comparing initial HAART regimens of nelfinavir/nevirapine and ritonavir/saquinavir in combination with two nucleoside reverse transcriptase inhibitors
54	Lalezari	2003	A controlled Phase II trial assessing three doses of enfuvirtide (T-20) in combination with abacavir, amprenavir, ritonavir and efavirenz in non-nucleoside reverse transcriptase inhibitor-naive HIV-infected adults
55	Maggiolo	2003	Once-a-day therapy for HIV infection: a controlled, randomized study in antiretroviral-naive HIV-1-infected patients
56	Rousseau	2003	Prospective randomized trial of emtricitabine versus lamivudine short-term monotherapy in human immunodeficiency virus-infected patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
57	Negredo	2004	Alternation of antiretroviral drug regimens for HIV infection. Efficacy, safety and tolerability at week 96 of the Swatch Study
58	Ruane	2004	Pharmacodynamic effects of zidovudine 600 mg once/day versus 300 mg twice/day in therapy-naïve patients infected with human immunodeficiency virus
59	van Leth	2004	Comparison of first-line antiretroviral therapy with regimens including nevirapine, efavirenz, or both drugs, plus stavudine and lamivudine: a randomised open-label trial, the 2NN Study
60	Rhame	2004	Pharmacokinetics of indinavir and ritonavir administered at 667 and 100 milligrams, respectively, every 12 hours compared with indinavir administered at 800 milligrams every 8 hours in human immunodeficiency virus-infected patients
61	Caso	2005	A randomized controlled trial investigating the efficacy and safety of switching from a protease inhibitor to nevirapine in patients with undetectable viral load
62	Arasteh	2005	TMC114/ritonavir substitution for protease inhibitor(s) in a non-suppressive antiretroviral regimen: a 14-day proof-of-principle trial
63	Maitland	2005	Early virologic failure in HIV-1 infected subjects on didanosine/tenofovir/efavirenz: 12-week results from a randomized trial
64	Barrios	2005	Simplification therapy with once-daily didanosine, tenofovir and efavirenz in HIV-1-infected adults with viral suppression receiving a more complex antiretroviral regimen: final results of the EFADITE trial
65	Lowe	2005	Comparison of two once-daily regimens with a regimen consisting of nelfinavir, didanosine, and stavudine in antiretroviral therapy-naïve adults: 48-week results from the Antiretroviral Regimen Evaluation Study (ARES)
66	Sosa	2005	Abacavir and lamivudine fixed-dose combination tablet once daily compared with abacavir and lamivudine twice daily in HIV-infected patients over 48 weeks (ESS30008, SEAL)
67	Portsmouth	2005	Better maintained adherence on switching from twice-daily to once-daily therapy for HIV: a 24-week randomized trial of treatment simplification using stavudine prolonged-release capsules
68	Montaner	2006	Efficacy, safety and pharmacokinetics of once-daily saquinavir soft-gelatin capsule/ritonavir in antiretroviral-naive, HIV-infected patients
69	Ruane	2006	Pilot study of once-daily simplification therapy with abacavir/lamivudine/zidovudine and efavirenz for treatment of HIV-1 infection
70	DeJesus	2006	Antiviral activity, pharmacokinetics, and dose response of the HIV-1 integrase inhibitor GS-9137 (JTK-303) in treatment-naive and treatment-experienced patients
71	Gathe	2007	Efficacy and Safety of Three Doses of Tipranavir Boosted with Ritonavir in Treatment-Experienced HIV Type 1-Infected Patients
72	Brew	2007	Factor in AIDS dementia complex trial design: results and lessons from the abacavir trial
73	Fischl	2007	Randomized open-label trial of two simplified, class-sparing regimens following a first suppressive three or four-drug regimen
74	Nadler	2007	Efficacy and safety of etravirine (TMC125) in patients with highly resistant HIV-1: primary 24-week analysis
75	Podzamczer	2007	High-dose lopinavir/ritonavir in highly treatment-experienced HIV-1 patients: efficacy, safety, and predictors of response
76	Markowitz	2007	Long-term efficacy and safety of tipranavir boosted with ritonavir in HIV-1-infected patients failing multiple protease inhibitor regimens: 80-week data from a phase 2 study

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
77	Demeter	2008	Association of efavirenz hypersusceptibility with virologic response in ACTG 368, a randomized trial of abacavir (ABC) in combination with efavirenz (EFV) and indinavir (IDV) in HIV-infected subjects with prior nucleoside analog experience
78	Berenguer	2008	Didanosine, lamivudine, and efavirenz versus zidovudine, lamivudine, and efavirenz for the initial treatment of HIV type 1 infection: final analysis (48 weeks) of a prospective, randomized, noninferiority clinical trial, GESIDA 3903
79	Cohen	2008	Short-term safety and tolerability of a once-daily fixed-dose abacavir-lamivudine combination versus twice-daily dosing of abacavir and lamivudine as separate components: findings from the ALOHA study
80	Salazar	2008	Efficacy, safety and tolerability of tipranavir coadministered with ritonavir in HIV-1-infected children and adolescents
81	Montaner	2008	Safety, tolerability, and preliminary efficacy of 48 weeks of etravirine therapy in a phase IIb dose-ranging study involving treatment-experienced patients with HIV-1 infection
82	Blümer	2008	Zidovudine/lamivudine contributes to insulin resistance within 3 months of starting combination antiretroviral therapy
83	Wright	2008	Efficacy and safety of 48 weeks of enfuvirtide 180 mg once-daily dosing versus 90 mg twice-daily dosing in HIV-infected patients
84	Tebas	2009	Peripheral and visceral fat changes following a treatment switch to a non-thymidine analogue or a nucleoside-sparing regimen in HIV-infected subjects with peripheral lipoatrophy: results of ACTG A5110
85	van Vonderen	2009	Zidovudine/lamivudine for HIV-1 infection contributes to limb fat loss
86	Landman	2009	Efficacy and safety of ritonavir-boosted dual protease inhibitor therapy in antiretroviral-naive HIV-1-infected patients: the 2IP ANRS 127 study
87	Molina	2009	Fosamprenavir/ritonavir in advanced HIV disease (TRIAD): a randomized study of high-dose, dual-boosted or standard dose fosamprenavir/ritonavir in HIV-1-infected patients with antiretroviral resistance
88	van Vonderen	2009	First line zidovudine/lamivudine/lopinavir/ritonavir leads to greater bone loss compared to nevirapine/lopinavir/ritonavir
89	Moltó	2010	Treatment simplification to once daily darunavir/ritonavir guided by the darunavir inhibitory quotient in heavily pretreated HIV-infected patients
90	Goebel	2010	Pharmacokinetic characterization of three doses of tipranavir boosted with ritonavir on highly active antiretroviral therapy in treatment-experienced HIV-1 patients
91	Morello	2010	The benefit of simplification from tipranavir/ritonavir 500/200 bid to 500/100 bid guided by therapeutic drug monitoring
92	Eron	2011	Raltegravir once daily or twice daily in previously untreated patients with HIV-1: a randomised, active-controlled, phase 3 non-inferiority trial
93	Gazzard	2011	Phase 2 double-blind, randomized trial of etravirine versus efavirenz in treatment-naive patients: 48-week results
94	Nelson	2011	A comparison of neuropsychiatric adverse events during 12 weeks of treatment with etravirine and efavirenz in a treatment-naive, HIV-1-infected population
95	Fätkenheuer	2012	Lipid profiles for etravirine versus efavirenz in treatment-naive patients in the randomized, double-blind SENSE trial
96	van Lunzen	2012	Once daily dolutegravir (S/GSK1349572) in combination therapy in antiretroviral-naive adults with HIV: planned interim 48 week results from SPRING-1, a dose-ranging, randomised, phase 2b trial

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Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
97	Behrens	2012	Switching to tenofovir/emtricitabine from abacavir/lamivudine in HIV-infected adults with raised cholesterol: effect on lipid profiles
98	Nettles	2012	Pharmacodynamics, safety, and pharmacokinetics of BMS-663068, an oral HIV-1 attachment inhibitor in HIV-1-infected subjects
99	Di Perri	2013	Pharmacokinetics and pharmacodynamics of etravirine 400 mg once daily in treatment-naïve patients
100	Bertz	2013	Pharmacokinetics and pharmacodynamics of atazanavir-containing antiretroviral regimens, with or without ritonavir, in patients who are HIV-positive and treatment-naïve
101	Stellbrink	2013	Dolutegravir in antiretroviral-naive adults with HIV-1: 96-week results from a randomized dose-ranging study
102	Mills	2013	Maraviroc once-daily nucleoside analog-sparing regimen in treatment-naive patients: randomized, open-label pilot study
103	Lalezari	2014	Attachment Inhibitor Prodrug BMS-663068 in ARV-Experienced Subjects: week 24 Analysis
104	Lalezari	2014	Safety profile of HIV-1 attachment inhibitor prodrug BMS-663068 in antiretroviral-experienced subjects: week 24 analysis
105	Carey	2015	Efficacy and safety of efavirenz 400 mg daily versus 600 mg daily: 96-week data from the randomised, double-blind, placebo-controlled, non-inferiority ENCORE1 study
106	Moltó	2015	Reduced darunavir dose is as effective in maintaining HIV suppression as the standard dose in virologically suppressed HIV-infected patients: a randomized clinical trial
107	Nozza	2015	Maraviroc 150mg daily plus lopinavir/ritonavir, a nucleoside/nucleotide reverse transcriptase inhibitor-sparing regimen for HIV-infected naive patients: 48-week final results of VEMAN study
108	Orrell	2015	Pharmacokinetics of Etravirine Combined with Atazanavir/Ritonavir and a Nucleoside Reverse Transcriptase Inhibitor in Antiretroviral Treatment-Experienced, HIV-1-Infected Patients
109	Schürmann	2016	A randomized, double-blind, placebo-controlled, short-term monotherapy study of doravirine in treatment-naive HIV-infected individuals
110	Butler	2016	BREATHER (PENTA 16) short-cycle therapy (SCT) (5 days on/2 days off) in young people with chronic human immunodeficiency virus infection: an open, randomised, parallel-group Phase II/III trial
111	Margolis	2016	Cabotegravir+rilpivirine as long-acting maintenance therapy: lATTE-2 week 48 results
112	Thompson	2017	Safety and efficacy of the HIV-1 attachment inhibitor prodrug fostemsavir in antiretroviral-experienced subjects: week 48 analysis of AI438011, a Phase IIb, randomized controlled trial
113	Rossetti	2017	Switch to maraviroc with darunavir/r, both QD, in patients with suppressed HIV-1 was well tolerated but virologically inferior to standard antiretroviral therapy: 48-week results of a randomized trial
114	Venter	2018	Non-inferior efficacy for darunavir/ritonavir 400/100 mg once daily versus lopinavir/ritonavir, for patients with HIV RNA below 50 copies/mL in South Africa: the 48-week WRHI 052 study
115	Morón-López	2019	Switching From a Protease Inhibitor–based Regimen to a Dolutegravir-based Regimen: A Randomized Clinical Trial to Determine the Effect on Peripheral Blood and Ileum Biopsies From Antiretroviral Therapy–suppressed Human Immunodeficiency Virus–infected Individuals
116	Chen	2020	Efficacy and safety of lower dose tenofovir disoproxil fumarate and efavirenz versus standard dose in HIV-infected, antiretroviral-naive adults: a multicentre, randomized, noninferiority trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por avaliarem TARV em doses não mais utilizadas na prática clínica			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
117	Chen	2020	Pharmacogenomics and pharmacokinetics of efavirenz 400 or 600 mg in 184 treatment-naive HIV-infected patients in China
118	Quercia	2020	ATLAS-2M subanalysis based on prior injection exposure: efficacy, ISRs, and preference of cabotegravir + rilpivirine every 2 months
119	Overton	2021	Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study
Estudos excluídos por não descreverem eventos adversos de interesse para essa revisão			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Schmitt	1988	Neuropsychological outcome of zidovudine (AZT) treatment of patients with AIDS and AIDS-related complex
2	Parks	1988	HIV-1 inhibition by azidothymidine in a concurrently randomized placebo-controlled trail
3	Bass	1992	The effect of zidovudine treatment on serum neopterin and beta 2-microglobulin levels in mildly symptomatic, HIV type 1 seropositive individuals
4	Danner	1995	A short-term study of the safety, pharmacokinetics, and efficacy of ritonavir, an inhibitor of HIV-1 protease. European-Australian Collaborative Ritonavir Study Group
5	Perrella	1996	Combined therapy with zidovudine, recombinant granulocyte colony stimulating factors and erythropoietin in asymptomatic HIV patients
6	Schapiro	1996	The effect of high-dose saquinavir on viral load and CD4+ T-cell counts in HIV-infected patients
7	Brouwers	1997	Effect of combination therapy with zidovudine and didanosine on neuropsychological functioning in patients with symptomatic HIV disease: A comparison of simultaneous and alternating regimens
8	Havlir	1998	Maintenance antiretroviral therapies in HIV infected patients with undetectable plasma HIV RNA after triple-drug therapy. AIDS Clinical Trials Group Study 343 Team
9	Foudraine	1998	An open randomized controlled trial of zidovudine plus lamivudine versus stavudine plus lamivudine
10	Moyle	1998	Safety, pharmacokinetics, and antiretroviral activity of the potent, specific human immunodeficiency virus protease inhibitor nelfinavir: results of a phase I/II trial and extended follow-up in patients infected with human immunodeficiency virus
11	Pollard	1999	Safety and antiretroviral effects of combined didanosine and stavudine therapy in HIV-infected individuals with CD4 counts of 200 to 500 cells/mm3
12	Katlama	2000	The role of abacavir (ABC, 1592) in antiretroviral therapy-experienced patients: results from a randomized, double-blind, trial. CNA3002 European Study Team
13	Kuritzkes	2000	Continued lamivudine versus delavirdine in combination with indinavir and zidovudine or stavudine in lamivudine-experienced patients: results of Adult AIDS Clinical Trials Group protocol 370
14	McDowell	2000	Multiple-dose pharmacokinetics and pharmacodynamics of abacavir alone and in combination with zidovudine in human immunodeficiency virus-infected adults
15	Carosi	2001	Antiviral potency of HAART regimens and clinical success are not strictly coupled in real life conditions: evidence from the MASTER-1 study
16	Smith	2001	A randomized trial of nelfinavir, ritonavir, or delavirdine in combination with saquinavir-SGC and stavudine in treatment-experienced HIV-1-infected patients

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Estudos excluídos por não descreverem eventos adversos de interesse para essa revisão			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
17	Røge	2001	Comparison of p-triglyceride levels among patients with human immunodeficiency virus on randomized treatment with ritonavir, indinavir or ritonavir/saquinavir
18	Saag	2001	Randomized, double-blind comparison of two nelfinavir doses plus nucleosides in HIV-infected patients (Agouron study 511)
19	Negredo	2002	Virological, immunological, and clinical impact of switching from protease inhibitors to nevirapine or to efavirenz in patients with human immunodeficiency virus infection and long-lasting viral suppression
20	Hoy	2004	Changes in mitochondrial DNA in peripheral blood mononuclear cells from HIV-infected patients with lipoatrophy randomized to receive abacavir
21	Garcia-Benayas	2004	Benefits in the lipid profile after substitution of abacavir for stavudine: a 48-week prospective study
22	MacManus	2004	GW433908/ritonavir once daily in antiretroviral therapy-naive HIV-infected patients: absence of protease resistance at 48 weeks
23	Dubé	2007	Effects of potent antiretroviral therapy on free testosterone levels and fat-free mass in men in a prospective, randomized trial: A5005s, a substudy of AIDS clinical trials group study 384
24	Green	2007	Lamivudine/abacavir maintains virological superiority over zidovudine/lamivudine and zidovudine/abacavir beyond 5 years in children
25	Chêne	2007	Changes in the peripheral blood mtDNA levels in naive patients treated by different nucleoside reverse transcriptase inhibitor combinations and their association with subsequent lipodystrophy
26	Milinkovic	2007	The impact of reducing stavudine dose versus switching to tenofovir on plasma lipids, body composition and mitochondrial function in HIV-infected patients
27	Schackman	2007	Racial differences in virologic failure associated with adherence and quality of life on efavirenz-containing regimens for initial HIV therapy: results of ACTG A5095
28	Lafaurie	2008	Switch from zidovudine- to non-zidovudine-containing regimens is associated with modest haematological improvement and no obvious clinical benefit: a substudy of the ANRS 099 ALIZE trial
29	Arenas-Pinto	2008	The risk of developing peripheral neuropathy induced by nucleoside reverse transcriptase inhibitors decreases over time: evidence from the Delta trial
30	Seoane	2008	Lipid and apoprotein profile in HIV-1-infected patients after CD4-guided treatment interruption
31	Grant	2009	Maintaining reduced viral fitness and CD4 response in HIV-infected patients with viremia receiving a boosted protease inhibitor
32	Haubrich	2009	Metabolic outcomes in a randomized trial of nucleoside, nonnucleoside and protease inhibitor-sparing regimens for initial HIV treatment
33	McComsey	2009	Changes in body composition with ritonavir-boosted and unboosted atazanavir treatment in combination with Lamivudine and Stavudine: a 96-week randomized, controlled study
34	Duvivier	2009	Greater decrease in bone mineral density with protease inhibitor regimens compared with nonnucleoside reverse transcriptase inhibitor regimens in HIV-1 infected naive patients
35	Boothby	2009	Adipocyte differentiation, mitochondrial gene expression and fat distribution: differences between zidovudine and tenofovir after 6 months
36	Brown	2009	Loss of bone mineral density after antiretroviral therapy initiation, independent of antiretroviral regimen

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Estudos excluídos por não descreverem eventos adversos de interesse para essa revisão			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
37	Nguemaim	2010	Changes in lipid profiles in two groups of HIV-1 infected patients in cameroon on two treatment regimens with either efavirenz or nevirapine, in association with reverse transcriptase inhibitors
38	Murphy	2010	Change to atazanavir/ritonavir treatment improves lipids but not endothelial function in patients on stable antiretroviral therapy
39	Patricia	2010	Saquinavir/ritonavir monotherapy as a new nucleoside-sparing maintenance strategy in long-term virologically suppressed HIV-infected patients
40	Campo	2010	Switch from protease inhibitor- to efavirenz-based antiretroviral therapy improves quality of life, treatment satisfaction and adherence with low rates of virological failure in virologically suppressed patients
41	Moyle	2010	Phase 2a randomized controlled trial of short-term activity, safety, and pharmacokinetics of a novel nonnucleoside reverse transcriptase inhibitor, RDEA806, in HIV-1-positive, antiretroviral-naive subjects
42	Hatano	2011	A randomized, controlled trial of raltegravir intensification in antiretroviral-treated, HIV-infected patients with a suboptimal CD4+ T cell response
43	Hulgan	2011	European mitochondrial DNA haplogroups and metabolic changes during antiretroviral therapy in AIDS Clinical Trials Group Study A5142
44	Lazzarin	2011	Pharmacokinetic (PK) and pharmacodynamic analyses of once- and twice-daily darunavir/ritonavir (DRV/r) in the odin trial
45	Martin	2011	Predictors of limb fat gain in HIV positive patients following a change to tenofovir-emtricitabine or abacavir-lamivudine
46	McComsey	2011	Peripheral and central fat changes in subjects randomized to abacavir-lamivudine or tenofovir-emtricitabine with atazanavir-ritonavir or efavirenz: ACTG Study A5224s
47	Nguyen	2011	A randomized crossover study to compare efavirenz and etravirine treatment
48	Vrouenraets	2011	Persistent decline in estimated but not measured glomerular filtration rate on tenofovir may reflect tubular rather than glomerular toxicity
49	Cooper	2011	Beliefs about antiretroviral therapy, treatment adherence and quality of life in a 48-week randomised study of continuation of zidovudine/lamivudine or switch to tenofovir DF/emtricitabine, each with efavirenz
50	Briot	2011	Prospective one-year bone loss in treatment-naïve HIV+ men and women on single or multiple drug HIV therapies
51	MacInnes	2011	Maraviroc can improve lipid profiles in dyslipidemic patients with HIV: results from the MERIT trial
52	Sax	2011	Abacavir/lamivudine versus tenofovir DF/emtricitabine as part of combination regimens for initial treatment of HIV: final results
53	McComsey	2011	Bone mineral density and fractures in antiretroviral-naive persons randomized to receive abacavir-lamivudine or tenofovir disoproxil fumarate-emtricitabine along with efavirenz or atazanavir-ritonavir: Aids Clinical Trials Group A5224s, a substudy of ACTG A5202
54	Hatano	2012	A randomized controlled trial assessing the effects of raltegravir intensification on endothelial function in treated HIV infection
55	Trinh	2012	Lopinavir/ritonavir (LPV/r) combined with raltegravir (RAL) or tenofovir/emtricitabine (TDF/FTC) in antiretroviral-naive subjects: 96-week safety and efficacy results of the PROGRESS study
56	Orkin	2012	Changes in patient-reported neuropsychiatric outcomes during the SENSE trial: first-line treatment with two nucleoside analogues plus etravirine or efavirenz

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos de interesse para essa revisão			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
57	Feeney	2012	Zidovudine/lamivudine but not nevirapine in combination with lopinavir/ritonavir decreases subcutaneous adipose tissue mitochondrial DNA
58	Robertson	2012	Improved neuropsychological and neurological functioning across three antiretroviral regimens in diverse resource-limited settings: AIDS Clinical Trials Group study a5199, the International Neurological Study
59	Kuhn	2012	Switching children previously exposed to nevirapine to nevirapine-based treatment after initial suppression with a protease-inhibitor-based regimen: Long-term follow-up of a randomised, open-label trial
60	Wilkins	2013	STaR Study: single tablet regimen rilpivirine/emtricitabine/ tenofovir DF is non-inferior to efavirenz/emtricitabine/ tenofovir DF in ART-naive adults regardless of baseline viral load and CD4 + count
61	Martin	2013	HIV lipodystrophy in participants randomised to lopinavir/ritonavir (LPV/r) +2-3 nucleoside/nucleotide reverse transcriptase inhibitors (N(t)RTI) or LPV/r + raltegravir as second-line antiretroviral therapy
62	Menezes	2013	The early effects of stavudine compared with tenofovir on adipocyte gene expression, mitochondrial DNA copy number and metabolic parameters in South African HIV-infected patients: a randomized trial
63	ENCORE1 Study Group	2014	Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial
64	Guaraldi	2014	Switching to darunavir/ritonavir monotherapy vs. triple-therapy on body fat redistribution and bone mass in HIV-infected adults: the Monarch randomized controlled trial
65	Haskelberg	2014	Bone mineral density over 96 weeks in adults failing first-line therapy randomized to raltegravir/lopinavir/ritonavir compared with standard second-line therapy
66	Hulgan	2014	Urinary eicosanoid metabolites in HIV-infected women with central obesity switching to raltegravir: An analysis from the women, integrase, and fat accumulation trial
67	Wyatt	2014	Changes in proteinuria and albuminuria with initiation of antiretroviral therapy: data from a randomized trial comparing tenofovir disoproxil fumarate/emtricitabine versus abacavir/lamivudine
68	Langebeek	2014	A simplified combination antiretroviral therapy regimen enhances adherence, treatment satisfaction and quality of life: results of a randomized clinical trial
69	Smith	2014	Outcomes by sex following treatment initiation with atazanavir plus ritonavir or efavirenz with abacavir/lamivudine or tenofovir/emtricitabine
70	Shiau	2014	Sex differences in responses to antiretroviral treatment in south african HIV-infected children on ritonavir-boosted lopinavir- and nevirapine-based treatment
71	Hsieh	2015	Increased bone resorption during tenofovir plus lopinavir/ritonavir therapy in Chinese individuals with HIV
72	Brunetta	2015	Patient-Reported Outcomes After a Switch to a Single-Tablet Regimen of Rilpivirine, Emtricitabine, and Tenofovir DF in HIV-1-Positive, Virologically Suppressed Individuals: Additional Findings From a Randomized, Open-Label, 48-Week Trial
73	Santos	2015	The Lipid-Lowering Effect of Tenofovir/Emtricitabine: a Randomized, Crossover, Double-Blind, Placebo-Controlled Trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos de interesse para essa revisão			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
74	Satchell	2015	A prospective, randomised study to assess safety, changes in platelet reactivity, plasma cardiac biomarkers, immunological and metabolic parameters in HIV-1-infected subjects undergoing switch in antiretroviral therapy
75	Tiraboschi	2015	The impact of boosted darunavir monotherapy on neurocognitive function and quality of life: results from a prospective randomised study
76	Ofotokun	2015	Comparison of the metabolic effects of ritonavir-boosted darunavir or atazanavir versus raltegravir, and the impact of ritonavir plasma exposure: ACTG 5257
77	Gates	2016	Maraviroc-intensified combined antiretroviral therapy improves cognition in virally suppressed HIV-associated neurocognitive disorder
78	Crespo	2016	Improvement of BMD after Switching from Lopinavir/R Plus Two Nucleos(T)ide Reverse Transcriptase Inhibitors to Lopinavir/R Plus Lamivudine: OLE-LIP Substudy
79	Kambugu	2016	Neurocognitive Function at the First-Line Failure and on the Second-Line Antiretroviral Therapy in Africa: Analyses From the EARNEST Trial
80	Karris	2016	A randomized controlled clinical trial on the impact of CCR5 blockade with maraviroc in early infection on T-cell dynamics
81	Martinez	2017	Switching from boosted protease inhibitors (PI/r) to dolutegravir (DTG) in virologically suppressed HIV-infected patients with high cardiovascular risk: 48-week effects on subclinical cardiovascular disease
82	Saumoy	2017	Atherogenic properties of LDL particles after switching from Truvada or Kivexa plus lopinavir/r to lamivudine plus lopinavir/r: OLE-MET substudy
83	Spinner	2017	Pharmacokinetics of once-daily dolutegravir and ritonavir-boosted darunavir in HIV patients: the DUALIS study
84	Walmsley	2017	Sword 1 and 2: subgroup analysis of 48 week results by age, race and gender
85	Wohl	2017	Viral blips were infrequent in HIV-1-infected virologically-suppressed adults treated with tenofovir alafenamide or tenofovir df rilpivirine-containing regimens
86	Kelesidis	2017	Changes in plasma levels of oxidized lipoproteins and lipoprotein subfractions with atazanavir-, raltegravir-, darunavir-based initial antiviral therapy and associations with common carotid artery intima-media thickness: ACTG 5260s
87	Shikuma	2018	Sleep and neuropsychological performance in HIV+ subjects on efavirenz-based therapy and response to switch in therapy
88	Vos	2018	Lipid levels, insulin resistance and cardiovascular risk over 96 weeks of antiretroviral therapy: a randomised controlled trial comparing low-dose stavudine and tenofovir
89	Morales-Ramirez	2018	Safety, efficacy, and dose response of the maturation inhibitor GSK3532795 (formerly known as BMS-955176) plus tenofovir/emtricitabine once daily in treatment-naive HIV-1-infected adults: Week 24 primary analysis from a randomized Phase IIb trial
90	Robertson	2018	Similar neurocognitive outcomes after 48 weeks in HIV-1-infected participants randomized to continue tenofovir/emtricitabine + atazanavir/ritonavir or simplify to abacavir/lamivudine + atazanavir
91	El Kamari	2019	Lower Pretreatment Gut Integrity Is Independently Associated With Fat Gain on Antiretroviral Therapy
92	Hamzah	2019	Early safety of tenofovir alafenamide in patients with a history of tubulopathy on tenofovir disoproxil fumarate: a randomized controlled clinical trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos de interesse para essa revisão			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
93	Bednasz	2019	Race/Ethnicity and Protease Inhibitor Use Influence Plasma Tenofovir Exposure in Adults Living with HIV-1 in AIDS Clinical Trials Group Study A5202
94	Sculier	2019	Dolutegravir/emtricitabine dual therapy is non-inferior to standard combination antiretroviral therapy in maintaining HIV suppression throughout 48 weeks (SIMPL'HIV study)
95	Wang	2019	Switching from a 3-drug tenofovir alafenamide (TAF)-based regimen (TBR) to a 2-drug dolutegravir/lamivudine (2DR, DTG/3TC FDC) was not associated with a higher frequency of intermittent viremia in suppressed patients in the TANGO study
96	Landman	2019	ANRS 170 QUATUOR 4/7 days maintenance strategy in antiretroviral treated adults with HIV-1 infection: an open randomised parallel non-inferiority phase III trial
97	Debroy	2020	Antiretroviral therapy initiation is associated with decreased visceral and subcutaneous adipose tissue density in people living with HIV
98	Hu	2020	Correlation between cardiovascular risk factors in hiv-infected patients and three highly active anti-retroviral therapy regimens
99	Olliges	2021	Health-related quality-of-life in people living with HIV after switching to dual therapy with ritonavir-boosted darunavir + dolutegravir: a DUALIS sub-study
Estudos excluídos por serem de análise post-hoc			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Fisac	2003	A comparison of the effects of nevirapine and nelfinavir on metabolism and body habitus in antiretroviral-naive human immunodeficiency virus-infected patients: a randomized controlled study
2	Lafeuillade	2003	Comparison of metabolic abnormalities and clinical lipodystrophy 48 weeks after switching from HAART to Trizivir versus continued HAART: the Trizal study
3	Ananworanich	2005	Incidence and risk factors for rash in Thai patients randomized to regimens with nevirapine, efavirenz or both drugs
4	Malan	2010	Gastrointestinal tolerability and quality of life in antiretroviral-naive HIV-1-infected patients: data from the CASTLE study
5	Sierra-Madero	2010	Efficacy and safety of maraviroc versus efavirenz, both with zidovudine/lamivudine: 96-week results from the MERIT study
6	Winston	2010	Neuropsychiatric adverse events with ritonavir-boosted darunavir monotherapy in HIV-infected individuals: a randomised prospective study
7	Squires	2011	Comparative gender analysis of the efficacy and safety of atazanavir/ritonavir and lopinavir/ritonavir at 96 weeks in the CASTLE study
8	Uy	2011	Treatment of advanced HIV disease in antiretroviral-naïve HIV-1-infected patients receiving once-daily atazanavir/ritonavir or twice-daily lopinavir/ritonavir, each in combination with tenofovir disoproxil fumarate and emtricitabine
9	Fox	2011	Improvement in vitamin D deficiency following antiretroviral regime change: Results from the MONET trial
10	Kolta	2011	Fat tissue distribution changes in HIV-infected patients treated with lopinavir/ritonavir. Results of the MONARK trial
11	Focà	2012	Prospective evaluation of bone markers, parathormone and 1,25-$(OH)_2$ vitamin D in HIV-positive patients after the initiation of tenofovir/emtricitabine with atazanavir/ritonavir or efavirenz

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por serem de análise post-hoc			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
12	Bunupuradah	2012	Neurocognitive impairment in patients randomized to second-line lopinavir/ritonavir-based antiretroviral therapy vs. lopinavir/ritonavir monotherapy
13	Erlandson	2013	Weight and lean body mass change with antiretroviral initiation and impact on bone mineral density
14	Martínez	2013	Abacavir/lamivudine versus tenofovir/emtricitabine in virologically suppressed patients switching from ritonavir-boosted protease inhibitors to raltegravir
15	Erlandson	2014	Impact of randomized antiretroviral therapy initiation on glucose metabolism
16	Arribas	2014	Simplification to Stribild vs continuation of RTV-boosted DRV with FTC and TDF in virologically suppressed HIV adults: a STRATEGY-PI subgroup analysis
17	Romo	2014	Renal and metabolic toxicities following initiation of HIV-1 treatment regimen in a diverse, multinational setting: a focused safety analysis of ACTG PEARLS (A5175)
18	Girard	2014	Comparison of renal changes with lopinavir/ritonavir plus raltegravir or tenofovir/emtricitabine in the PROGRESS study
19	Bernardino	2015	Bone mineral density and inflammatory and bone biomarkers after darunavir-ritonavir combined with either raltegravir or tenofovir-emtricitabine in antiretroviral-naive adults with HIV-1: a substudy of the NEAT001/ANRS143 randomised trial
20	Brown	2015	Changes in Bone Mineral Density After Initiation of Antiretroviral Treatment With Tenofovir Disoproxil Fumarate/Emtricitabine Plus Atazanavir/Ritonavir, Darunavir/Ritonavir, or Raltegravir
21	Bwakura-Dangarembizi	2015	Prevalence of lipodystrophy and metabolic abnormalities in HIV-infected African children after 3 years on first-line antiretroviral therapy
22	Cahn	2015	Dolutegravir versus raltegravir in ARV-experienced INI-naive HIV+ adults: 48-week subgroup analysis of Latin American subjects in the SAILING study
23	Achan	2016	Growth recovery among HIV-infected children randomized to lopinavir/ritonavir or NNRTI-based antiretroviral therapy
24	Gallant	2017	Atazanavir Plus Cobicistat: Week 48 and Week 144 Subgroup Analyses of a Phase 3, Randomized, Double-Blind, Active-Controlled Trial
25	Squires	2017	Influence of sex/gender and race on responses to raltegravir combined with tenofovir-emtricitabine in treatment-naive human immunodeficiency virus-1 infected patients: pooled analyses of the STARTMRK and QDMRK studies
26	Squires	2017	Response by gender of HIV-1-infected subjects treated with abacavir/lamivudine plus atazanavir, with or without ritonavir, for 144 weeks
27	Post	2017	Efficacy and safety of emtricitabine/tenofovir alafenamide (FTC/TAF) vs. emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) as a backbone for treatment of HIV-1 infection in virologically suppressed adults: subgroup analysis by third agent of a randomized, double-blind, activecontrolled phase 3 trial
28	Goldstein	2017	Week 96 efficacy and safety of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF) in older, hivinfected virologically-suppressed adults
29	Arenas-Pinto	2018	Risk of Suicidal Behavior With Use of Efavirenz: Results from the Strategic Timing of Antiretroviral Treatment Trial
30	Colella	2018	Potential associations between atazanavir exposure and clinical outcome: a pharmacokinetic sub-study from the MODAt randomized trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por serem de análise post-hoc			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
31	Bernardino	2019	Body composition and adipokines changes after initial treatment with darunavir-ritonavir plus either raltegravir or tenofovir disoproxil fumarate-emtricitabine: A substudy of the NEAT001/ANRS143 randomised trial
32	Ackerman	2021	Long-term efficacy and safety of fostemsavir among subgroups of heavily treatment-experienced adults with HIV-1
33	Kumar	2021	Brief Report: Switching to DOR/3TC/TDF Maintains HIV-1 Virologic Suppression Through Week 144 in the DRIVE-SHIFT Trial
Estudos excluídos por usarem múltiplos esquemas ARV nos seus braços			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Orkin	2018	Efficacy and safety of switching from boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide at 48 weeks in adults with virologically suppressed HIV-1 (EMERALD): a phase 3, randomised, non-inferiority trial
2	Sax	2009	Abacavir-lamivudine versus tenofovir-emtricitabine for initial HIV-1 therapy
3	Bonnet	2013	Early loss of bone mineral density is correlated with a gain of fat mass in patients starting a protease inhibitor containing regimen: the prospective Lipotrip study
4	John	2003	Randomized, controlled, 48-week study of switching stavudine and/or protease inhibitors to combivir/abacavir to prevent or reverse lipoatrophy in HIV-infected patients
5	Schooley	2002	Tenofovir DF in antiretroviral-experienced patients: results from a 48-week, randomized, double-blind study
6	Waters	2010	A Phase IV, double-blind, multi-centre, randomised, placebo-controlled, pilot study to assess the feasibility of switching individuals receiving efavirenz (EFV) with continuing central nervous system (CNS) adverse events (AE) to once-daily etravirine (ETR
Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	Richman	1987	The toxicity of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial
2	NR	1989	The Safety and Effectiveness of Zidovudine (AZT) in the Treatment of HIV Infection in Patients With AIDS and Advanced ARC
3	NR	1990	A Multi-Center Clinical Trial To Evaluate Azidothymidine (AZT) in the Treatment of Human Immunodeficiency Virus (HIV) Infection in Patients With AIDS Post First Episode PCP
4	Bozzette	1991	Peripheral nerve function in persons with asymptomatic or minimally symptomatic HIV disease: absence of zidovudine neurotoxicity
5	Fischl	1993	Zalcitabine compared with zidovudine in patients with advanced HIV-1 infection who received previous zidovudine therapy
6	Mulder	1994	Zidovudine twice daily in asymptomatic subjects with HIV infection and a high risk of progression to AIDS: a randomized, double-blind placebo-controlled study. The European-Australian Collaborative Group (Study 017)
7	NR	1994	The Safety of Different Dose Levels of Zidovudine in HIV-Infected Children

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
8	Dolin	1995	Zidovudine compared with didanosine in patients with advanced HIV type 1 infection and little or no previous experience with zidovudine. AIDS Clinical Trials Group
9	Fischl	1995	Combination and monotherapy with zidovudine and zalcitabine in patients with advanced HIV disease
10	Montaner	1995	Didanosine compared with continued zidovudine therapy for HIV-infected patients with 200 to 500 CD4 cells/mm3: A double-blind, randomized, controlled trial
11	Petersen	1995	Dose-related activity of stavudine in patients infected with human immunodeficiency virus
12	Kinloch-De Loës	1995	A controlled trial of zidovudine in primary human immunodeficiency virus infection
13	Bartlett	1996	Lamivudine plus zidovudine compared with zalcitabine plus zidovudine in patients with HIV infection. A randomized, double-blind, placebo-controlled trial. North American HIV Working Party
14	Carr	1996	A controlled trial of nevirapine plus zidovudine versus zidovudine alone in p24 antigenaemic HIV-infected patients. The Dutch-Italian-Australian Nevirapine Study Group
15	D'Aquila	1996	Nevirapine, zidovudine, and didanosine compared with zidovudine and didanosine in patients with HIV-1 infection. A randomized, double-blind, placebo-controlled trial. National Institute of Allergy and Infectious Diseases AIDS Clinical Trials Group Protocol 241 Investigators
16	Katlama	1996	Safety and efficacy of lamivudine-zidovudine combination therapy in antiretroviral-naive patients. A randomized controlled comparison with zidovudine monotherapy. Lamivudine European HIV Working Group
17	Spruance	1997	Clinical efficacy of monotherapy with stavudine compared with zidovudine in HIV-infected, zidovudine-experienced patients. A randomized, double-blind, controlled trial. Bristol-Myers Squibb Stavudine/019 Study Group
18	Sudre	1997	Low doses of zidovudine plus didanosine are less effective than higher doses of didanosine monotherapy: a randomized trial in patients pretreated with zidovudine
19	Cohen	1998	A randomized trial of the effect of ritonavir in maintaining quality of life in advanced HIV disease
20	Henry	1998	A randomized, controlled, double-blind study comparing the survival benefit of four different reverse transcriptase inhibitor therapies (three-drug, two-drug, and alternating drug) for the treatment of advanced AIDS
21	McKinney	1998	A randomized study of combined zidovudine-lamivudine versus didanosine monotherapy in children with symptomatic therapy-naive HIV-1 infection. The Pediatric AIDS Clinical Trials Group Protocol 300 Study Team
22	Montaner	1998	The effects of lamivudine treatment on HIV-1 disease progression are highly correlated with plasma HIV-1 RNA and CD4 cell count
23	Saag	1998	Antiretroviral effect and safety of abacavir alone and in combination with zidovudine in HIV-infected adults. Abacavir Phase 2 Clinical Team
24	Staszewski	1998	A dose-ranging study to evaluate the safety and efficacy of abacavir alone or in combination with zidovudine and lamivudine in antiretroviral treatment-naive subjects
25	Pialoux	1998	A randomized trial of three maintenance regimens given after three months of induction therapy with zidovudine, lamivudine, and indinavir in previously untreated HIV-1-infected patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
26	NR	1998	A Phase IIIb, Randomized, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of 2NRTI/Abacavir versus Continued 2NRTI/PI Treatment in HIV-1 Infected Subjects with Undetectable Plasma HIV-1 RNA Levels
27	García	1999	A randomized study comparing triple versus double antiretroviral therapy or no treatment in HIV-1-infected patients in very early stage disease: the Spanish Earth-1 study
28	Krown	1999	Phase II, randomized, open-label, community-based trial to compare the safety and activity of combination therapy with recombinant interferon-alpha2b and zidovudine versus zidovudine alone in patients with asymptomatic to mildly symptomatic HIV infection
29	Kirk	1999	Combination therapy containing ritonavir plus saquinavir has superior short-term antiretroviral efficacy: a randomized trial
30	NR	1999	A Study of T-20 in HIV-Positive Adults
31	NR	1999	A Study to Compare the Effectiveness of Two Anti-HIV Drug Combinations
32	NR	1999	The Safety and Effectiveness of Three Anti-HIV Drug Combinations in HIV-Infected Patients Who Have Taken AZT
33	NR	1999	The Effectiveness of Three Anti-HIV Drug Combinations in HIV-Infected Patients Who Have Never Used Anti-HIV Drugs
34	NR	1999	A Multicenter, Open-Label, Randomized, 24-Week Study to Compare the Safety and Activity of Indinavir Sulfate, 800 Mg q 8 h Versus 1,200 Mg q 12 h in Combination With Zidovudine and 3TC
35	NR	1999	The Safety and Effectiveness of Lamivudine Plus Stavudine or Zidovudine in HIV-Infected Patients Who Have Taken Zidovudine
36	NR	1999	Comparison of Ro 31-8959 Plus Zidovudine (AZT) Versus AZT Plus Zalcitabine (ddC) Versus Ro 31-8959 Plus AZT Plus ddC
37	NR	1999	A Study to Find the Best Dosing Schedule for Delavirdine, Zidovudine, and Indinavir in HIV-Positive Patients
38	NR	1999	Virologic and Immunologic Activity of Continued Lamivudine (3TC) vs Delavirdine (DLV) in Combination With Indinavir (IDV) and Zidovudine (ZDV) or Stavudine (d4T) in 3TC-Experienced Subjects
39	NR	1999	A Comparison of Zidovudine (AZT) Used Alone or in Combination With Didanosine (ddI) or Dideoxycytidine (ddC) in HIV-Infected Patients
40	NR	1999	A Six-Month Safety and Antiviral Study in HIV-1 Seropositive, AZT-Experienced Patients With CD4 Counts Less Than or Equal to 50 Cells/mm3 to Evaluate MK-639 Alone Versus Zidovudine (AZT) and 3TC Versus the Combination of MK-639 With AZT/3TC
41	NR	1999	A Study of Indinavir Taken With or Without DMP 266
42	NR	1999	The Safety and Effectiveness of Zidovudine in the Treatment of HIV-Infected Children With Mild to Moderate Symptoms
43	NR	1999	A Study of Viracept in HIV-Positive Women
44	NR	1999	A Study of Indinavir Sulfate Given Together With Stavudine to HIV-Positive Patients
45	NR	1999	A Comparison of Lamivudine and Zidovudine, Used Alone and Together, in HIV-Infected Patients Who Have Not Used Zidovudine in the Past
46	NR	1999	A Comparison of Zidovudine Plus Lamivudine Versus ddI Used Alone or in Combination With Zidovudine in HIV-1 Infected Children
47	NR	1999	The Safety and Effectiveness of Nevirapine and Zidovudine, Given Separately and Together, in HIV-1 Infected Patients Who Have No Symptoms of the Disease

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
48	NR	1999	Safety and Effectiveness of Giving Indinavir and Nelfinavir to HIV-Infected Patients
49	NR	1999	A Study on the Safety and Effectiveness of Adefovir Dipivoxil in Combination With Anti-HIV Therapy (HAART) in HIV-Positive Patients
50	NR	1999	A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Adefovir Dipivoxil When Added to Standard Antiretroviral Therapy for the Treatment of HIV-Infected Patients With CD4 Cell Counts >= 200/mm3
51	NR	1999	The Safety and Effectiveness of Indinavir Sulfate Plus Efavirenz
52	NR	1999	A Comparison of 141W94 and Indinavir in HIV-Infected Patients
53	NR	1999	A Comparison of Two Dose Levels of Indinavir Combined With Two Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs) in HIV-Infected Patients
54	NR	1999	A Randomized, Parallel Arm, Comparative, Open Label, Multicenter Study of the Activity and Safety of Two Formulations of Saquinavir in Combination With Other Antiretroviral Drugs
55	NR	1999	A Comparison of Saquinavir Hard- and Soft-Gelatin Capsules in HIV-Infected Patients
56	NR	1999	A Study to Compare the Safety and Effectiveness of Indinavir Combined With Stavudine and Lamivudine
57	NR	1999	A Phase III Randomized Double-Blind, Multicenter Study to Evaluate the Safety and Efficacy of 3TC/ZDV/1592U89 and 3TC/ZDV/IDV in HIV-1 Infected Antiretroviral Therapy-Naive Subjects
58	NR	1999	A Study Comparing Two Forms of Didanosine in HIV-infected Patients
59	NR	1999	The Safety and Effectiveness of Adefovir Dipivoxil Plus Indinavir Combined With Zidovudine or Lamivudine or Stavudine in HIV-Infected Patients Who Have Not Taken Anti-HIV Drugs
60	NR	1999	A Study to Compare the Safety and Effectiveness of Two Dosing Schedules of Lamivudine in Combination With Two Other Anti-HIV Drugs
61	NR	1999	A Study of Three Drug Combination Therapies in HIV-Infected Patients Who Have Never Been Treated With Anti-HIV Drugs
62	NR	1999	A Comparison of Two Triple-Drug Combinations in Patients Who Have Never Been Treated With Anti-HIV Drugs
63	NR	1999	A Study of Two Anti-HIV Drug Combinations in HIV-Infected Patients
64	NR	1999	The Safety and Effectiveness of Lamivudine Plus Zidovudine, Used With and Without 1592U89, in HIV-1 Infected Patients Who Have Never Taken Anti-HIV Drugs
65	NR	1999	The Safety and Effectiveness of Zidovudine Plus Lamivudine, Used With and Without 1592U89, in HIV-1 Infected Children Who Have Taken Anti-HIV-1 Drugs
66	NR	1999	A Study to Compare the Effects of Two Anti-HIV Drug Combinations on the Immune Systems of HIV-Infected Patients
67	NR	1999	The Safety and Effectiveness of MK-639 and Zidovudine, Used Alone and Together, in HIV-Infected Patients Who Have Never Taken Anti-HIV Drugs
68	NR	1999	A Study of 1592U89 in Combination With Protease Inhibitors in HIV-Infected Patients Who Have Never Taken Anti-HIV Drugs
69	NR	1999	Safety and Effectiveness of Four Anti-HIV Drug Combinations in HIV-Infected Children and Teens
70	NR	1999	Study of a New Protease Inhibitor, BMS-232632, in Combination With Other Anti-HIV Drugs

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
71	NR	1999	A Phase III Study to Evaluate the Safety, Tolerance, and Efficacy of Early Treatment With Zidovudine (AZT) in Asymptomatic Infants With HIV Infection
72	NR	1999	A Randomized, Double-Blind, Four-Arm Study Comparing Combination Nucleoside, Alternating Nucleoside, and Triple-Drug Therapy for the Treatment of Advanced HIV Disease (CD4 <= 50/mm3)
73	NR	1999	A Comparison of Zidovudine (AZT) and Stavudine in HIV-Infected Patients
74	NR	1999	A Study of Several Anti-HIV Drug Combinations in HIV-Infected Patients Who Have Used Indinavir
75	NR	1999	A Randomized Trial of the Efficacy and Safety of a Strategy of Starting With Nelfinavir Versus Ritonavir Added to Background Antiretroviral (AR) Nucleoside Therapy in HIV-Infected Individuals With CD4+ Cell Counts Less Than or Equal to 200/mm3
76	NR	1999	A Study of Three Different Anti-HIV Drug Combinations in HIV-Infected Patients
77	NR	1999	The Effectiveness of Nelfinavir and Efavirenz, Used Alone or Together, Combined With Other Anti-HIV Drugs in Patients Who Have Taken Anti-HIV Drugs
78	NR	1999	ABT-378/Ritonavir in Combination With Reverse Transcriptase Inhibitors in Antiretroviral Naïve HIV-Infected Subjects
79	NR	1999	A Study to Compare Three Doses of T-20 When Given in Combination With Abacavir, Amprenavir, Ritonavir, and Efavirenz to HIV-Infected Adults
80	NR	1999	A Study of Azidothymidine in HIV-Infected Children
81	NR	1999	Safety and Effectiveness of Giving Combinations of Three or Four Anti-HIV Drugs to HIV-Infected Patients
82	NR	1999	The Safety and Effectiveness of Retrovir Plus HIVID Combined With Either Nevirapine or Invirase in the Treatment of HIV Infection
83	NR	1999	A Randomized Comparative Trial of Zidovudine (AZT) Versus 2',3'-Dideoxyinosine (ddI) Versus AZT Plus ddI in Symptomatic HIV-Infected Children
84	NR	1999	A Phase II Efficacy Study Comparing 2',3'-Dideoxyinosine (ddI) (BMY-40900) and Zidovudine Therapy of Patients With HIV Infection Who Have Been on Long Term Zidovudine Treatment
85	NR	1999	Comparison of ddI Versus Zidovudine in HIV-Infected Patients
86	NR	1999	A Randomized Trial to Evaluate the Safety and Efficacy of Combination Therapy With Retrovir (AZT) and HIVID (ddC) Versus Retrovir, HIVID, and Wellferon (Interferon Alfa-n1) for the Treatment of HIV Infection
87	NR	1999	A Study of the Safety and Effectiveness of Different Doses of 1592U89 in HIV-Infected Patients
88	NR	1999	The Safety and Effects of 1592U89 Used Alone or in Combination With Other Anti-HIV Drugs in HIV-Infected Infants and Children
89	NR	1999	A Phase I/II, Open Label Study to Evaluate the Antiviral Potential of Combination Zidovudine and 2' 3'-Dideoxyinosine (Didanosine) in Patients With Asymptomatic HIV Disease
90	NR	1999	Safety and Effectiveness of Combining Hydroxyurea (HU) With Didanosine (ddI) and Stavudine (d4T) for Treatment of HIV-Infected Adults

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
91	NR	1999	A Randomized, Double Blind, Comparative Study of Dideoxycytidine (ddC) Alone or ddC/AZT Combination Versus Zidovudine (ZDV) Alone in Patients With HIV Infection Who Have Received Prior ZDV Therapy
92	NR	1999	Safety and Efficacy of Zidovudine for Asymptomatic HIV-Infected Individuals
93	NR	1999	The Safety and Effectiveness of Nevirapine Plus Lamivudine Plus Other Anti-HIV Drugs
94	NR	1999	A Randomized Phase II Efficacy, Activity and Safety Study of GLQ223 Alone and in Combination With Zidovudine in Symptomatic HIV-Infected Patients Without Prior Treatment With GLQ223 or Trichosanthin
95	NR	1999	A Study of Stavudine in HIV-Infected Patients Who Have Not Had Success With Other Anti-HIV Drugs
96	NR	1999	Dideoxycytidine (Ro 24-2027) A Randomized, Open-Label, Comparative Study of Dideoxycytidine (ddC) Versus Zidovudine (AZT) in Patients With AIDS or Advanced ARC Who Have Received Long-Term AZT Therapy
97	NR	1999	Safety and Effectiveness of Giving Adefovir (Preveon) Plus Other Anti-HIV Drugs to HIV-Infected Patients Who Have Not Responded to Other Anti-HIV Drug Combinations
98	NR	1999	(Ro 24-2027) A Randomized, Double-Blind, Comparative Study of Dideoxycytidine (ddC) Versus Zidovudine (AZT) in Patients With AIDS or Advanced ARC
99	NR	1999	A Pilot, Open-Label, Phase II, Randomized Study to Determine the Effects of Viracept on the Outcome of Cutaneous and Mucosal KS in AIDS Patients With CD4 <= 500 Cells/mm3
100	NR	1999	Double-Blind Comparison of the Efficacy of Continued Zidovudine Versus 2',3'-Dideoxyinosine (ddI) (BMY-40900) for the Treatment of Patients With AIDS or AIDS-Related Complex and Increasing Symptomatology Despite Treatment With Zidovudine
101	NR	1999	The Safety and Effectiveness of Zidovudine in the Treatment of Patients With Early AIDS Related Complex
102	NR	1999	The Antiviral Efficacy of Concurrent Zidovudine and 2',3'-Dideoxyinosine or 2',3'-Dideoxycytidine in Patients With Human Immunodeficiency Virus Disease
103	NR	1999	A Phase III, Randomized, Double-Blind, Multicentre Study to Evaluate the Safety and Efficacy of 1592U89 in Patients With AIDS Dementia Complex
104	Carr	2000	A randomised, open-label comparison of three highly active antiretroviral therapy regimens including two nucleoside analogues and indinavir for previously untreated HIV-1 infection: the OzCombo1 study
105	Eron	2000	Efficacy, safety, and adherence with a twice-daily combination lamivudine/zidovudine tablet formulation, plus a protease inhibitor, in HIV infection
106	Eron	2000	A comparison of stavudine, didanosine and indinavir with zidovudine, lamivudine and indinavir for the initial treatment of HIV-1 infected individuals: selection of thymidine analog regimen therapy (START II)
107	Floridia	2000	A randomized trial comparing the introduction of ritonavir or indinavir in 1251 nucleoside-experienced patients with advanced HIV infection
108	Goodgame	2000	Amprenavir in combination with lamivudine and zidovudine versus lamivudine and zidovudine alone in HIV-1-infected antiretroviral-naive adults. Amprenavir PROAB3001 International Study Team

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
109	Haas	2000	Comparative studies of two-times-daily versus three-times-daily indinavir in combination with zidovudine and lamivudine
110	Katzenstein	2000	Virologic and CD4+ cell responses to new nucleoside regimens: switching to stavudine or adding lamivudine after prolonged zidovudine treatment of human immunodeficiency virus infection. ACTG 302 Study Team. AIDS Clinical Trials Group
111	Moyle	2000	The SPICE study: 48-week activity of combinations of saquinavir soft gelatin and nelfinavir with and without nucleoside analogues. Study of Protease Inhibitor Combinations in Europe
112	Opravil	2000	Effects of early antiretroviral treatment on HIV-1 RNA in blood and lymphoid tissue: a randomized trial of double versus triple therapy
113	Roca	2000	A randomized, comparative study of lamivudine plus stavudine, with indinavir or nelfinavir, in treatment-experienced HIV-infected patients
114	Squires	2000	A comparison of stavudine plus lamivudine versus zidovudine plus lamivudine in combination with indinavir in antiretroviral naive individuals with HIV infection: selection of thymidine analog regimen therapy (START I)
115	Wiznia	2000	Combination nucleoside analog reverse transcriptase inhibitor(s) plus nevirapine, nelfinavir, or ritonavir in stable antiretroviral therapy-experienced HIV-infected children: week 24 results of a randomized controlled trial--PACTG 377. Pediatric AIDS Clinical Trials Group 377 Study Team
116	NR	2000	A randomised phase II trial to compare the toxicity, tolerability and activity of 2-drug combinations of the nucleoside analogue reverse transcriptase inhibitors (NRTIs) lamivudine ((-)2'-deoxy-3'thiacytidine, 3tc), zidovudine (ZDV) and 1592U89
117	NR	2000	An open randomised trial to evaluate the activity and tolerability of combinations of reverse transcriptase and protease inhibitors, including induction therapy, in individuals with Human Immunodeficiency Virus-1 (HIV-1) infection and CD4 cell counts grea
118	NR	2000	The Safety and Effectiveness of Indinavir Plus Ritonavir Plus Two NRTIs in HIV-Infected Patients Who Need Early Intervention Treatment
119	NR	2000	The Safety and Effectiveness of (+)-Calanolide A in HIV-Infected Patients Who Have Never Taken Anti-HIV Drugs
120	NR	2000	Effectiveness and Safety of Epivir/Ziagen/Zerit (3TC/ABC/d4T) Versus Epivir/Ziagen/Sustiva (3TC/ABC/EFV) Versus Epivir/Ziagen/Agenerase/Norvir (3TC/ABC/APV/RTV) in HIV Patients Who Have Never Received Treatment
121	NR	2000	Effectiveness and Safety of Two Forms of Stavudine in HIV-Infected Patients
122	NR	2000	A Comparison of Three Anti-HIV Drug Combinations in HIV-Infected Patients
123	NR	2000	Safety and Effectiveness of 3 Anti-HIV Treatments in Patients Who Have Failed Previous Treatments Containing Nelfinavir
124	NR	2000	Safety and Effectiveness of Lamivudine When Given Once a Day Versus Twice a Day in Combination With Other Anti-HIV Drugs in HIV-Infected Adults Who Have Never Received Anti-HIV Drugs
125	NR	2000	Safety and Effectiveness of a Combination Anti-HIV Drug Treatment
126	NR	2000	Safety and Effectiveness of a New Anti-HIV Drug (AG1549) in Combination With Other Anti-HIV Drugs in HIV-Infected Patients
127	NR	2000	Safety and Tolerance of Indinavir Plus Ritonavir in HIV-Positive Patients Failing Therapy With Amprenavir, Nelfinavir, or Saquinavir

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
128	NR	2000	A Comparison of Emtricitabine and Stavudine Used With Didanosine Plus Efavirenz in HIV-Infected Patients Who Have Not Taken Anti-HIV Drugs
129	Clumeck	2001	Simplification with abacavir-based triple nucleoside therapy versus continued protease inhibitor-based highly active antiretroviral therapy in HIV-1-infected patients with undetectable plasma HIV-1 RNA
130	Florence	2001	Ritonavir/saquinavir plus one nucleoside reverse transcriptase inhibitor (NRTI) versus indinavir plus two NRTIs in protease inhibitor-naive HIV-1-infected adults (IRIS study)
131	Gartland	2001	AVANTI 3: a randomized, double-blind trial to compare the efficacy and safety of lamivudine plus zidovudine versus lamivudine plus zidovudine plus nelfinavir in HIV-1-infected antiretroviral-naive patients
132	Albrecht	2001	Nelfinavir, efavirenz, or both after the failure of nucleoside treatment of HIV infection
133	Jensen-Fangel	2001	The effect of nevirapine in combination with nelfinavir in heavily pretreated HIV-1-infected patients: a prospective, open-label, controlled, randomized study
134	Smeaton	2001	ACTG (AIDS Clinical Trials Group) 384: a strategy trial comparing consecutive treatments for HIV-1
135	Staszewski	2001	Abacavir-lamivudine-zidovudine vs indinavir-lamivudine-zidovudine in antiretroviral-naive HIV-infected adults: A randomized equivalence trial
136	Ungsedhapand	2001	A randomized, open-label, comparative trial of zidovudine plus lamivudine versus zidovudine plus lamivudine plus didanosine in antiretroviral-naive HIV-1-infected Thai patients
137	Katlama	2001	Intensification of stable background therapy with abacavir in antiretroviral therapy experienced patients: 48-week data from a randomized, double-blind trial
138	Michelet	2001	Ritonavir-saquinavir dual protease inhibitor compared to ritonavir alone in human immunodeficiency virus-infected patients
139	McMahon	2001	Antiretroviral activity and safety of abacavir in combination with selected HIV-1 protease inhibitors in therapy-naive HIV-1-infected adults
140	NR	2001	A Comparison of BMS-232632 With Efavirenz, Each in Combination With Zidovudine-Lamivudine
141	NR	2001	Safety and Tolerability of Z-100 in Patients With Early HIV Infection
142	NR	2001	Comparison of Two Dosing Regimens of GW433908/Ritonavir Versus Lopinavir/Ritonavir for 48 Weeks in HIV Patients Who Have Taken Protease Inhibitors and Experienced Virological Failure
143	NR	2001	A Comparison of Atazanavir and Nelfinavir, Each in Combination With 2 NRTIs, in Patients Who Have Failed Treatments Without a Protease Inhibitor
144	NR	2001	Comparison of GW433908/Ritonavir to Nelfinavir When Used With Abacavir and Lamivudine in Patients That Have Not Taken Antiretroviral Drugs
145	NR	2001	Comparing Side Effects of Two Forms of Videx in HIV-Infected Adults
146	NR	2001	T-20 in HIV Patients With Prior Drug Treatment and/or Resistance to Each of the Three Classes of Anti-HIV Drugs
147	NR	2001	Comparison of GW433908 and Nelfinavir in HIV Patients Who Have Not Had Antiretroviral Therapy
148	NR	2001	Safety and Effectiveness of TRIZIVIR (Abacavir/Lamivudine/Zidovudine) With Efavirenz in HIV-Infected Patients Who Have Never Taken Anti-HIV Drugs

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
149	NR	2001	Atazanavir Versus Lopinavir/Ritonavir (LPV/RTV) in Patients Who Have Not Had Success With Protease Inhibitor-Containing HAART Regimen(s)
150	NR	2001	Simplified Drug Regimens for HIV Patients in ACTG 388 or Patients Who Responded to A First Potent Combination Regimen
151	Podzamczer	2002	A randomized clinical trial comparing nelfinavir or nevirapine associated to zidovudine/lamivudine in HIV-infected naive patients (the Combine Study)
152	Gathe	2002	Antiviral activity of enteric-coated didanosine, stavudine, and nelfinavir versus zidovudine plus lamivudine and nelfinavir
153	Carr	2002	Abacavir substitution for nucleoside analogs in patients with HIV lipoatrophy: a randomized trial
154	Walmsley	2002	Lopinavir-ritonavir versus nelfinavir for the initial treatment of HIV infection
155	Joly	2002	Efficacy of zidovudine compared to stavudine, both in combination with lamivudine and indinavir, in human immunodeficiency virus-infected nucleoside-experienced patients with no prior exposure to lamivudine, stavudine, or protease inhibitors (novavir trial)
156	Opravil	2002	A randomized trial of simplified maintenance therapy with abacavir, lamivudine, and zidovudine in human immunodeficiency virus infection
157	Sension	2002	Lamivudine 300 mg QD versus continued lamivudine 150 mg BID with stavudine and a protease inhibitor in suppressed patients
158	NR	2002	Efficacy and Safety of Tenofovir DF/Atazanavir Enhanced With Low Dose of Ritonavir in HIV-Infected Patients
159	NR	2002	A Study Comparing 4 Doses Of GW810781 Versus Placebo In HIV-Infected Patients
160	NR	2002	Safety and Antiviral Study of ACH-126, 443 (Beta-L-Fd4C) in the Treatment of Adults With HIV Infection and Modestly Detectable Viral Load
161	NR	2002	Lopinavir/Ritonavir in Combination With Saquinavir Mesylate or Lamivudine/Zidovudine to Explore Metabolic Toxicities in Antiretroviral HIV-Infected Subjects
162	NR	2002	Study to Explore Safety And Tolerability of Fosamprenavir With or Without Ritonavir in Combination With TRIZIVIR or COMBIVIR
163	NR	2002	Study of Lopinavir, Ritonavir, Tenofovir and Emtricitabine in HIV-Infected Antiretroviral Naïve Subjects
164	NR	2002	A Dose Escalation Study of Tenofovir Alafenamide in Treatment-Naive Patients
165	NR	2002	Comparing the Safety, Effectiveness, and Tolerability of Three Anti-HIV Drug Regimens for Treatment-Naive Patients
166	NR	2002	CSP #512 - Options in Management With Anti-Retrovirals
167	NR	2002	A HIV Study Of A Fixed-Dose Combination Tablet In Antiretroviral Experienced Patients
168	Dragsted	2003	Randomized trial to evaluate indinavir/ritonavir versus saquinavir/ritonavir in human immunodeficiency virus type 1-infected patients: the MaxCmin1 Trial
169	Fischl	2003	Twice-daily Trizivir versus Combivir-abacavir in antiretroviral-experienced adults with human immunodeficiency virus-1 infection: a formulation-switch trial
170	Fischl	2003	A randomized trial of 2 different 4-drug antiretroviral regimens versus a 3-drug regimen, in advanced human immunodeficiency virus disease
171	Arnaiz	2003	Continued indinavir versus switching to indinavir/ritonavir in HIV-infected patients with suppressed viral load

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
172	Squires	2003	Tenofovir disoproxil fumarate in nucleoside-resistant HIV-1 infection: a randomized trial
173	Matheron	2003	Triple nucleoside combination zidovudine/lamivudine/abacavir versus zidovudine/lamivudine/nelfinavir as first-line therapy in HIV-1-infected adults: a randomized trial
174	Moyle	2003	A 48-week, randomized, open-label comparison of three abacavir-based substitution approaches in the management of dyslipidemia and peripheral lipoatrophy
175	Sáez-Llorens	2003	Forty-eight-week evaluation of lopinavir/ritonavir, a new protease inhibitor, in human immunodeficiency virus-infected children
176	Katlama	2003	TRIZAL study: switching from successful HAART to Trizivir (abacavir-lamivudine-zidovudine combination tablet): 48 weeks efficacy, safety and adherence results
177	Lalezari	2003	Enfuvirtide, an HIV-1 fusion inhibitor, for drug-resistant HIV infection in North and South America
178	Lazzarin	2003	Efficacy of enfuvirtide in patients infected with drug-resistant HIV-1 in Europe and Australia
179	Maggiolo	2003	Outcome of 2 simplification strategies for the treatment of human immunodeficiency virus type 1 infection
180	Martínez	2003	Substitution of nevirapine, efavirenz, or abacavir for protease inhibitors in patients with human immunodeficiency virus infection
181	NR	2003	TMC114-C202: a Study of Safety, Efficacy, and Tolerability of TMC114 and Low Dose Ritonavir in HIV-1 Infected Patients
182	NR	2003	Safety and Efficacy of BAY 50-4798 in Patients With HIV Infection
183	NR	2003	Randomized Evaluation of Strategic Intervention in Multidrug Resistant Patients With Tipranavir (RESIST)
184	DeJesus	2004	Abacavir versus zidovudine combined with lamivudine and efavirenz, for the treatment of antiretroviral-naive HIV-infected adults
185	DeJesus	2004	Once-daily versus twice-daily lamivudine, in combination with zidovudine and efavirenz, for the treatment of antiretroviral-naive adults with HIV infection: a randomized equivalence trial
186	Eron	2004	Once-daily versus twice-daily lopinavir/ritonavir in antiretroviral-naive HIV-positive patients: a 48-week randomized clinical trial
187	Gallant	2004	Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naive patients: a 3-year randomized trial
188	Gulick	2004	Triple-nucleoside regimens versus efavirenz-containing regimens for the initial treatment of HIV-1 infection
189	Benson	2004	A randomized study of emtricitabine and lamivudine in stably suppressed patients with HIV
190	Gathe	2004	SOLO: 48-week efficacy and safety comparison of once-daily fosamprenavir /ritonavir versus twice-daily nelfinavir in naive HIV-1-infected patients
191	Vibhagool	2004	Triple nucleoside treatment with abacavir plus the lamivudine/zidovudine combination tablet (COM) compared to indinavir/COM in antiretroviral therapy-naïve adults: results of a 48-week open-label, equivalence trial (CNA3014)
192	Perez	2004	A randomized clinical trial comparing nelfinavir and ritonavir in patients with advanced HIV disease (CPCRA 042/CTN 102)
193	Rodriguez-French	2004	The NEAT study: a 48-week open-label study to compare the antiviral efficacy and safety of GW433908 versus nelfinavir in antiretroviral therapy-naive HIV-1-infected patients
194	Saag	2004	Efficacy and safety of emtricitabine vs stavudine in combination therapy in antiretroviral-naive patients: a randomized trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
195	Gaytan	2004	Nevirapina o efavirenz en combinación com dos análogos de nucleósidos em pacientes com infécción por el VIH sin tratamiento previo
196	NR	2004	Phase IV-III, open-label, randomized, comparative study, to evaluate the safety and efficacy of the nucleoside supression of a triple therapy based on lopinavir-ritonavir vs. continuous triple therapy on patients infected by HIV that have maintained unde
197	NR	2004	A Phase III, Randomized, Controlled, Open-label, Multicentre, Three Arm Study to Compare the Efficacy and Safety of a Dual-boosted HIV-1 Protease Inhibitor (PI) regimen of Fosamprenavir (FPV)/ Lopinavir (LPV)/Ritonavir (RTV)/1400mg/533mg/133mg Twice Dail
198	NR	2004	Monotherapy Versus Placebo Over 7 Days-Non-Nucleoside Reverse Transcriptase Inhibitor-Experienced HIV1 Infected Adults
199	NR	2004	GW873140 to Treat HIV-1 Infected Adults
200	NR	2004	TNX-355 With Optimized Background Therapy (OBT) in Treatment-Experienced Subjects With HIV-1
201	NR	2004	Safety of Saquinavir and High Doses of Lopinavir/Ritonavir in Children With HIV
202	NR	2004	A Study Comparing Safety Of Abacavir And Lamivudine Administered Once-Daily As A Single Tablet Versus The Same Drugs Administered Twice-Daily As Separate Tablets (ALOHA Study)
203	NR	2004	Safety and Effectiveness of the Oral HIV Entry Inhibitor Vicriviroc in HIV Infected Patients
204	NR	2004	NNRTI vs PI Regimens for HIV Infected Women After They Have Taken Nevirapine to Prevent Mother-To-Child HIV Transmission
205	NR	2004	Pharmacokinetics and Safety Study of Tipranavir in Combination With Low Dose Ritonavir in Human Immunodeficiency Virus (HIV)-Infected Children
206	NR	2004	Trial of Maraviroc (UK-427,857) in Combination With Optimized Background Therapy Versus Optimized Background Therapy Alone for the Treatment of HIV-1 Infected Subjects
207	NR	2004	Trial of Maraviroc (UK-427,857) in Combination With Optimized Background Therapy Versus Optimized Background Therapy Alone for the Treatment of Antiretroviral-Experienced NonCCR5-Tropic HIV-1 Infected Subjects
208	NR	2004	Trial of Maraviroc (UK-427,857) in Combination With Zidovudine/Lamivudine Versus Efavirenz in Combination With Zidovudine/Lamivudine
209	NR	2004	A Study Comparing The Safety, Tolerability and Efficacy of Trizivir VS Combivir & Atazanavir In Subjects With HIV
210	NR	2004	Fosamprenavir Versus Other Protease Inhibitors
211	NR	2004	KALETRA Or LEXIVA With Ritonavir Combined With EPIVIR And Abacavir In Naive Subjects Over 48 Weeks
212	NR	2004	A Study to Evaluate the Safety and Efficacy of an Investigational Drug in HIV Infected Patients (0518-004)(COMPLETED)
213	Dragsted	2005	A randomized trial to evaluate lopinavir/ritonavir versus saquinavir/ritonavir in HIV-1-infected patients: the MaxCmin2 trial
214	Cohen	2005	Comparison of atazanavir with lopinavir/ritonavir in patients with prior protease inhibitor failure: a randomized multinational trial
215	Arribas	2005	Lopinavir/ritonavir as single-drug therapy for maintenance of HIV-1 viral suppression: 48-week results of a randomized, controlled, open-label, proof-of-concept pilot clinical trial (OK Study)

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
216	Bonjoch	2005	Antiretroviral treatment simplification with 3 NRTIs or 2 NRTIs plus nevirapine in HIV-1-infected patients treated with successful first-line HAART
217	Markowitz	2005	Induction with abacavir/lamivudine/zidovudine plus efavirenz for 48 weeks followed by 48-week maintenance with abacavir/lamivudine/zidovudine alone in antiretroviral-naive HIV-1-infected patients
218	Negredo	2005	Lopinavir/ritonavir plus nevirapine as a nucleoside-sparing approach in antiretroviral-experienced patients (NEKA study)
219	Izzedine	2005	Long-term renal safety of tenofovir disoproxil fumarate in antiretroviral-naive HIV-1-infected patients. Data from a double-blind randomized active-controlled multicentre study
220	Justesen	2005	The long-term pharmacokinetics and safety of adding low-dose ritonavir to a nelfinavir 1,250 mg twice-daily regimen in HIV-infected patients
221	Keiser	2005	Substituting abacavir for hyperlipidemia-associated protease inhibitors in HAART regimens improves fasting lipid profiles, maintains virologic suppression, and simplifies treatment
222	NR	2005	ASK-500
223	NR	2005	The STEAL Study
224	NR	2005	A Phase III, randomised, double-blind, placebo-controlled, multicentre, parallel group study to compare the efficacy and safety of GW873140 400mg BID in combination with a ritonavir-containing optimised background therapy (OBT) regimen versus placebo plu
225	NR	2005	Large, Simple Trial Comparing Two Strategies for Management of Anti-Retroviral Therapy (The SMART Study) - SMART
226	NR	2005	A Phase IIb randomized, partially blinded, dose-finding trial of TMC278 in antiretroviral naive HIV-1 infected subjects. - N/A
227	NR	2005	Randomized, double-blind, placebo-controlled 7 day monotherapy Phase IIa study to evaluate the antiviral activity and safety of oral administered RTV-boosted BILR 355 (75 mg and 150 mg twice daily) in HIV-1-infected, NNRTI-experienced patients, followed
228	NR	2005	A Phase IV, Open-Label, Randomized, Multicenter Trial Assessing the Efficacy of a Treatment Maintenance Phase with Unboosted vs. Boosted Reyataz After an Induction Phase with Reyataz and Ritonavir in Treatment Naive HIV Patients Revised Protocol 03 Incor
229	NR	2005	A Phase 3, Randomized, Open-label, Study of Lopinavir/ritonavir Tablets Versus Soft Gel Capsules and Once Daily Versus Twice Daily Administration, when Coadministered with NRTIs in Antiretroviral Naïve HIV-1 Infected Subjects
230	NR	2005	Ensayo randomizado para determinar el tratamiento óptimo de pacientes con infección por VIH en quienes la terapia con TARGA de primera y segunda línea ha fracasado - Options in management with antiretrovirals
231	NR	2005	ESTUDIO DE LOS CAMBIOS EN EL RECUENTO DE LINFOCITOS CD4 TRAS LA SUSTITUCIÓN DE TENOFOVIR POR ABACAVIR EN PACIENTES CON UNA PAUTA HAART QUE INCLUYA DDI + TENOFOVIR Y CON SUPRESIÓN VIRAL
232	NR	2005	Safety and Efficacy of SCH-417690 in HIV-infected Treatment-Naive Subjects - N/A
233	NR	2005	Multicenter, Double-Blind, Randomized, Dose-Ranging, Placebo-Controlled Study to Evaluate the Safety, Pharmacokinetics, and Antiretroviral Activity of Raltegravir in Combination With an Optimized Background Therapy (OBT), Versus Optimized Background Ther

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
234	NR	2005	A randomized, controlled, open-label trial to compare the efficacy, safety and tolerability of TMC114/RTV versus LPV/RTV in treatment-experienced HIV-1 infected subjects
235	NR	2005	A Phase III, randomized, double-blind, placebo-controlled, multicenter, parallel group study to compare the efficacy and safety of GW873140 400mg BID in combination with a ritonavir-containing optimized background therapy (OBT) regimen versus placebo plu
236	NR	2005	A Randomized, Open Label Study Assessing Safety, Tolerability, and Efficacy of an Induction/Maintenance Treatment Strategy Including Lopinavir/ritonavir (LPV/r) plus Tenofovir Disoproxil Fumarate (TDF) and Emtricitabine (FTC) versus Efavirenz (EFV) plus
237	NR	2005	An open-label trial with TMC125 in HIV-1 infected subjects, who were randomized to a TMC125 treatment arm in a sponsor-selected TMC125 trial and were treated for at least 48 weeks. - N/A
238	NR	2005	Vicriviroc (SCH 417690) in Combination Treatment with Optimized ART Regimen in Experienced Subjects (VICTOR-E1) - VICTOR-E1
239	NR	2005	GEMINI Study - A Study of Saquinavir/Ritonavir in Treatment-Naive Patients With HIV-1 Infection
240	NR	2005	Open-label randomized multicenter study of once daily antiretroviral treatment regimen comparing ritonavir boosted atazanavir to efavirenz
241	NR	2005	A Study Exploring an Induction-Maintenance Kaletra-Based Therapy Versus a Sustiva-Based Regimen in Previously Non-Treated, HIV-1/HCV Co-Infected Subjects
242	NR	2005	Efficacy and Safety of Kaletra Monotheraphy Compared to Kaletra Based Triple Therapy to Treat HIV in Antiretroviral Naïve Patients
243	NR	2005	GEMINI Study - A Study of Saquinavir/Ritonavir in Treatment-Naive Patients With HIV-1 Infection
244	NR	2005	A Study of an Oral Entry Inhibitor, SP01A, in Treatment-Experienced HIV-Infected Patients
245	NR	2005	TMC114-C214: trial of TMC114 Administered With Low Dose Ritonavir (RTV) in HIV-1 Infected Treatment Experienced Patients
246	NR	2005	A Pilot Study of Atazanavir/Ritonavir/Efavirenz as a Nucleoside Sparing Regimen
247	NR	2005	Abacavir/Lamivudine Versus Emtricitabine/Tenofovir Both In Combination With Lopinavir/Ritonavir For The Treatment Of HIV
248	NR	2005	A Randomised, Open-label Trial to Assess the Safety and Efficacy of Switching to Tenofovir-emtricitabine or Abacavir-lamivudine: the STEAL Study
249	NR	2005	TMC114-C211: trial of an Investigational Protease Inhibitor TMC114 With Ritonavir (TMC114/r") in HIV-1 Infected Patients Who Have Never Been Treated With Antiretroviral Medications"
250	NR	2005	Comparing a Nucleoside-Analogue-Sparing Regimen and a Protease-Inhibitor-Sparing Regimen in HIV Infected Patients
251	NR	2005	Tipranavir/Ritonavir vs. Genotypically Defined Protease Inhibitor/Ritonavir in HIV Patients (RESIST-2)
252	NR	2005	A Randomised Trial to Evaluate the Antiviral Efficacy and Safety of Treatment With 500 mg Tipranavir (TPV) Plus 100 mg or 200 mg Ritonavir (RTV) p.o. BID in Comparison to 400 mg Lopinavir (LPV) Plus 100 mg RTV p.o. BID in Combination With Standard Backgr
253	NR	2005	Combination of Efavirenz and Truvada - COMET Study
254	NR	2005	Salvage Therapy With Amprenavir, Lopinavir and Ritonavir in HIV-Infected Patients in Virological Failure
255	NR	2005	Induction-maintenance of Lopinavir/r in HIV-infected Subjects

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
256	NR	2005	MEDICLAS Study (Metabolic Effects of Different Classes of AntiretroviralS)
257	NR	2005	DART II - A Phase IV Study of 3 Antiretroviral Medicines in Combination, in HIV Patients Who Have Not Been Previously Treated With Antiretroviral Therapy
258	NR	2005	Lopinavir/r Monotherapy as Maintenance Therapy After Long Term Viral Suppression
259	NR	2005	A Phase IIIb Study Comparing Two Boosted Protease Inhibitor-based HAART Regimens in HIV-infected Patients Experiencing Their First Virologic Failure While Receiving an NNRTI-containing HAART Regimen
260	NR	2005	Once Daily Antiretroviral Therapy in HIV Infected Adults Treated With HAART
261	NR	2005	Once Daily 3TC, Efavirenz and ddI for HIV Infection
262	NR	2005	A 48 Week Study Comparing Treatment With Saquinavir + Lopinavir/Ritonavir in Combination With Enfuvirtide HAART Versus Saquinavir + Lopinavir/Ritonavir + Other Nucleoside Combinations to See the Efficacy of These Treatments in Patients Infected With HIV
263	NR	2005	The Once A Day Protease Inhibitor Regimens""
264	NR	2005	A Comparison of Two Anti-HIV Drug Regimens for Youth Who Have Failed Prior Therapy
265	NR	2005	Study Comparing Racivir and Lamivudine in Treatment-Experienced HIV Subjects
266	NR	2005	Dual Boosted Protease Inhibitor Regimens Without Any Additional Antiretroviral Therapy in HIV-1 Infected Patients (ANRS127)
267	NR	2005	Effect of Tenofovir Disoproxil Fumarate on Lipid Levels in HIV Infected Adults on Stable Anti-HIV Drug Therapy
268	NR	2005	Study of Treatment of Antiretroviral-naive, HIV-1-Infected Patients Comparing Tenofovir Disoproxil Fumarate Administered in Combination With Lamivudine and Efavirenz vs. Stavudine, Lamivudine and Efavirenz
269	NR	2005	Tenofovir Disoproxil Fumarate/Emtricitabine/Efavirenz Versus Combivir/Efavirenz in Antiretroviral-Naive HIV-1 Infected Subjects
270	NR	2005	Once a Day (QD) - Twice a Day (BID) Clinical Trial: didanosine, Lamivudine and Efavirenz Versus Zidovudine, Lamivudine and Efavirenz in the Starting Treatment of HIV
271	NR	2005	Anti-HIV Drugs for Treating Infants Who Acquired HIV Infection at Birth
272	NR	2005	A Study of TMC278 in Human Immunodeficiency Virus Type 1 Infected Patients, Who Are Not Treated With Antiretroviral Medicines
273	NR	2005	Vicriviroc, a CCR5 Inhibitor, Added to an Optimized Antiretroviral Therapy for Previously Treated HIV (VICTOR-E2) (Study P04285)(TERMINATED)
274	NR	2005	Safety and Efficacy of an Investigational Drug in Human Immunodeficiency Virus (HIV)-Infected Patients Failing Current Antiretroviral Therapies (0518-005)(COMPLETED)
275	NR	2005	Study of Lopinavir/Ritonavir Tablets Versus Soft Gel Capsules and Once Daily Versus Twice Daily Administration, When Coadministered With Nucleoside Reverse Transcriptase Inhibitors in Antiretroviral Naive Human Immunodeficiency Virus Type 1 Infected Subj
276	NR	2005	Randomised open multicentre trial comparing stavudine versus abacavir, both combined with lamivudine/efavirenz, in Human Immunodeficiency Virus (HIV) infected antiretroviral naïve patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
277	NR	2005	Therapeutic Drug Monitoring in HIV-Infected Children Starting a New Anti-Retroviral Regime
278	NR	2005	Randomised, multicentre, open clinical trial assessing the effectiveness and safety of simplification to atazanavir + ritonavir versus continuation of a stable antiretroviral regimen on lopinavir/ritonavir
279	Eron	2006	The KLEAN study of fosamprenavir-ritonavir versus lopinavir-ritonavir, each in combination with abacavir-lamivudine, for initial treatment of HIV infection over 48 weeks: a randomised non-inferiority trial
280	Gallant	2006	Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV
281	Gathe	2006	Efficacy of the protease inhibitors tipranavir plus ritonavir in treatment-experienced patients: 24-week analysis from the RESIST-1 trial
282	Martínez	2006	Clinical trial comparing efficacy and safety of four highly active antiretroviral therapy (HAART) in antiretroviral-naive treatment with advanced HIV infection
283	Gulick	2006	Three- vs four-drug antiretroviral regimens for the initial treatment of HIV-1 infection: a randomized controlled trial
284	Markowitz	2006	Antiretroviral activity, pharmacokinetics, and tolerability of MK-0518, a novel inhibitor of HIV-1 integrase, dosed as monotherapy for 10 days in treatment-naive HIV-1-infected individuals
285	Yeni	2006	Virological and immunological outcomes at 3 years after starting antiretroviral therapy with regimens containing non-nucleoside reverse transcriptase inhibitor, protease inhibitor, or both in INITIO: open-label randomised trial
286	Jemsek	2006	Body fat and other metabolic effects of atazanavir and efavirenz, each administered in combination with zidovudine plus lamivudine, in antiretroviral-naive HIV-infected patients
287	Kumar	2006	A prospective, 96-week study of the impact of Trizivir, Combivir/nelfinavir, and lamivudine/stavudine/nelfinavir on lipids, metabolic parameters and efficacy in antiretroviral-naive patients: effect of sex and ethnicity
288	MacArthur	2006	A comparison of three highly active antiretroviral treatment strategies consisting of non-nucleoside reverse transcriptase inhibitors, protease inhibitors, or both in the presence of nucleoside reverse transcriptase inhibitors as initial therapy (CPCRA 058 FIRST Study): a long-term randomised trial
289	Goebel	2006	Short-term antiviral activity of TMC278--a novel NNRTI--in treatment-naive HIV-1-infected subjects
290	Johnson	2006	96-week comparison of once-daily atazanavir/ritonavir and twice-daily lopinavir/ritonavir in patients with multiple virologic failures
291	Moyle	2006	A randomized comparative trial of tenofovir DF or abacavir as replacement for a thymidine analogue in persons with lipoatrophy
292	Bartlett	2006	Long-term results of initial therapy with abacavir and Lamivudine combined with Efavirenz, Amprenavir/Ritonavir, or Stavudine
293	Lamarca	2006	Efficacy and safety of a once-daily fixed-dose combination of abacavir/lamivudine compared with abacavir twice daily and lamivudine once daily as separate entities in antiretroviral-experienced HIV-1-infected patients (CAL30001 Study)
294	Boyd	2006	Boosted versus unboosted indinavir with zidovudine and lamivudine in nucleoside pre-treated patients: a randomized, open-label trial with 112 weeks of follow-up (HIV-NAT 005)

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
295	Moyle	2006	An open-label, randomized comparative pilot study of a single-class quadruple therapy regimen versus a 2-class triple therapy regimen for individuals initiating antiretroviral therapy
296	Pozniak	2006	Tenofovir disoproxil fumarate, emtricitabine, and efavirenz versus fixed-dose zidovudine/lamivudine and efavirenz in antiretroviral-naive patients: virologic, immunologic, and morphologic changes--a 96-week analysis
297	NR	2006	A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Antiretroviral Activity of MK-0518 in Combination With an Optimized Background Therapy (OBT), Versus Optimized Background Therapy Alone, in HIVInfected Patients
298	NR	2006	Open-label, randomised clinical trial to compare the virological efficacy and safety of Atazanavir/Ritonavir on a background of Tenofovir and Emtricitabine vs. Nevirapine on same background, in HIV-1-infected patients who have received no previous antire
299	NR	2006	A Multicenter, Double-Blind, Randomized, Active-Controlled Study to Evaluate the Safety and Antiretroviral Activity of MK- 0518 Versus Efavirenz in Treatment Naïve HIV-Infected Patients, Each in Combination With TRUVADA™ - MK-0518 safety and efficacy stu
300	NR	2006	Pilot phase IV, multicenter, randomized, open-label and controlled study to assess the evolution of peripheral body fat distribution after switching from AZT containing backbone to Truvada in HIV-1-infected patients on HAART (RECOMB Study) - RECOMB
301	NR	2006	A randomised, controlled, opel-label trial to compare the efficacy, safety and tolerability of a treatment simplification by darunavir/ritonavir (DRV/r) 800/100 mg O.D. versus a triple combination therapy containing DRV/r in HIV-1 infected subjects with
302	NR	2006	A 24-week, randomised, open-label, 2-arm study to compare the tolerability and efficacy of saquinavir tablets with ritonavir versus lopinavir/ritonavir tablets in HIV 1 infected adults switching from Kaletra capsules - LoCKIT Study
303	NR	2006	Host genetic factors influencing drug disposition and response to HIV treatment - Pharmacogenetics of HIV Therapy
304	NR	2006	A Randomized, Double-Blind, Phase II Study Comparing the Anti-Retroviral Safety and Efficacy of Dexelvucitabine (DFC) 200 mg Once Daily to Lamivudine (3TC) 300 mg Once Daily in Addition to Optimized Background Therapy in HIV-1 Infected Subjects Who Have
305	NR	2006	A Randomized, Controlled, Open-Label, 48-Week Study of Continuing Successfully Suppressive Treatment in HIV-1 Infected Adults with First-Line Twice-Daily Zidovudine and Lamivudine-Based Regimens versus Proactively Replacing of Zidovudine and Lamivudine b
306	NR	2006	A Phase IIIB, Randomized, Open-Label, Multicenter Study of the Safety and Efficacy of GW433908 700mg BID plus ritonavir 100mg BID Versus Lopinavir/ritonavir 400mg/100mg BID when Administered in Combination with the Abacavir/Lamivudine 600mg/300mg Fixed-D
307	NR	2006	A 96 Week Phase IIIB Study Comparing the Antiviral Efficacy and Safety of Atazanavir/ritonavir ATV/RTV with Lopinavir/ritonavir LPV/RTV , Each in Combination with Fixed Dose Tenofovir-Emtricitabine in HIV-1 infected treatment naive subjects. - Castle
308	NR	2006	A multicenter, randomized, prospective, controlled study to evaluate the efficacy and the tolerability of a switch to a two different-dosed, nevirapine-based HAARTs in HIV-1 infected patients with undetectable plasma viremia. - SNODO
309	NR	2006	Safety and Efficacy of Tenofovir DF in HIV-1 Infected Adolescents Failing Their Current Antiretroviral Therapy

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
310	NR	2006	Randomized, Double-Blind Study Comparing Dexelvucitabine (DFC) to Lamivudine (3TC) in Subjects With Resistance to NRTIs, PIs, and NNRTIs
311	NR	2006	Evaluation of two Trizivir-based strategies of induction-maintenance in antiretroviral-naive HIV-infected patients
312	NR	2006	TMC125-C203: phase II Randomized (Patients Are Assigned Different Treatments Based on Chance), Placebo Controlled Dose Escalating Trial of TMC125 in HIV-1 Infected Patients
313	NR	2006	Safety Study of Elvucitabine in HIV-1 Subjects
314	NR	2006	A Randomized, Prospective Study of the Efficacy, Safety and Tolerability of Two Doses of GW433908Ritonavir Given With Abacavir/Lamivudine Fixed Dose Combination
315	NR	2006	BMS-Reyataz Study in Treatment in Naive Subjects to Compare the Efficacy and Safety Between Boosted Reyataz and Kaletra When in Combination With Fixed Dose Truvada
316	NR	2006	Trial to Evaluate Steady State Pharmacokinetic Parameters, Efficacy and Safety of Nevirapine in Antiretroviral Drug naïve Pediatric Patients
317	NR	2006	Phase II Study on the Antiviral Activity and Safety of BILR 355 BS in HIV-1 Infected, NNRTI-treated Patients
318	NR	2006	Study to Evaluate the Effectiveness of ABC+3TC +EFV in Once-Daily Regimens Versus KLT in Twice-Daily Regimens in Naive HIV Patients
319	NR	2006	3 TPV/RTV Doses in Multiple ARV Experienced Patients - Tipranavir Dose Defining Study
320	NR	2006	Study Comparing Reducing the Dose of Stavudine Versus Switching to Tenofovir in HIV-Infected Patients Receiving Antiretroviral Therapy
321	NR	2006	Immuno-Virological Efficacy of Combination With Trizivir +Tenofovir in Multiresistant HIV Patients
322	NR	2006	Safety and Effectiveness of Short-Term Anti-HIV Drug Therapy for Recent HIV-1 Infection
323	NR	2006	Comparing the Effectiveness Between Ritonavir Boosted Atazanavir and Efavirenz for the First HIV Treatment
324	NR	2006	A Study to Evaluate the Safety and Efficacy of Raltegravir (MK0518) in HIV-Infected Patients Failing Current Antiretroviral Therapies (MK0518-018 EXT2)
325	NR	2006	A Study to Evaluate the Safety and Antiretroviral Activity of MK-0518 Versus Efavirenz in Treatment Naive HIV-Infected Patients, Each in Combination With TRUVADA (0518-021 EXT)
326	NR	2006	A Study to Evaluate the Safety and Efficacy of Raltegravir (MK0518) in HIV-Infected Patients Failing Current Antiretroviral Therapies (0518-019)
327	NR	2006	Single Tablet Regimen (STR) Simplification Study for HIV-1 Infected Patients
328	NR	2006	Elvucitabine/Efavirenz/Tenofovir vs. Lamivudine/Efavirenz/Tenofovir in HIV-1 Infected, Treatment Naive Subjects
329	NR	2006	Study on the Effect of Kaletra + Nevirapine as Maintenance Bitherapy Compared to a Triple Therapy Including Kaletra + Analogues in HIV Patients
330	NR	2006	Nevirapine or Atazanavir/Ritonavir Given With Emtricitabine/Tenofovir in Human Immunodeficiency Virus (HIV)-1-infected Treatment Naive Adults
331	NR	2006	A Study of an Investigational Regimen Combining FDA Approved HIV Drugs in HIV-Infected Subjects
332	NR	2006	ALTAIR - Alternative Antiretroviral Strategies : a Comparison of Three Initial Regimens

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
333	NR	2006	Monotherapy Versus Placebo Over 10 Days in Integrase Naive HIV-1 Infected Adults
334	NR	2006	SP01A: the Study of an Oral Entry Inhibitor in Treatment-Experienced HIV Patients
335	NR	2006	Study of Lopinavir/Ritonavir Tablets Comparing Once-Daily Versus Twice-Daily Administration When Coadministered With Nucleoside/Nucleotide Reverse Transcriptase Inhibitors in Antiretroviral-Experienced Human Immunodeficiency Virus Type 1 Infected Subject
336	Gatell	2007	Efficacy and safety of atazanavir-based highly active antiretroviral therapy in patients with virologic suppression switched from a stable, boosted or unboosted protease inhibitor treatment regimen: the SWAN Study (AI424-097) 48-week results
337	Grinsztejn	2007	Safety and efficacy of the HIV-1 integrase inhibitor raltegravir (MK-0518) in treatment-experienced patients with multidrug-resistant virus: a phase II randomised controlled trial
338	Lazzarin	2007	Efficacy and safety of TMC125 (etravirine) in treatment-experienced HIV-1-infected patients in DUET-2: 24-week results from a randomised, double-blind, placebo-controlled trial
339	Madruga	2007	Efficacy and safety of darunavir-ritonavir compared with that of lopinavir-ritonavir at 48 weeks in treatment-experienced, HIV-infected patients in TITAN: a randomised controlled phase III trial
340	Madruga	2007	Efficacy and safety of TMC125 (etravirine) in treatment-experienced HIV-1-infected patients in DUET-1: 24-week results from a randomised, double-blind, placebo-controlled trial
341	Mallolas	2007	A randomized trial comparing the efficacy and tolerability of two HAART strategies at two years in antiretroviral naive patients
342	Parienti	2007	Efavirenz to nevirapine switch in HIV-1-infected patients with dyslipidemia: a randomized, controlled study
343	Gulick	2007	Intensification of a triple-nucleoside regimen with tenofovir or efavirenz in HIV-1-infected patients with virological suppression
344	Haubrich	2007	Week 24 efficacy and safety of TMC114/ritonavir in treatment-experienced HIV patients
345	Katlama	2007	Efficacy and safety of TMC114/ritonavir in treatment-experienced HIV patients: 24-week results of POWER 1
346	Molina	2007	A lopinavir/ritonavir-based once-daily regimen results in better compliance and is non-inferior to a twice-daily regimen through 96 weeks
347	Loutfy	2007	Randomized controlled trial of once-daily tenofovir, lamivudine, and lopinavir/ritonavir versus remaining on the same regimen in virologically suppressed HIV-infected patients on their first PI-containing HAART regimen
348	Markowitz	2007	Rapid and durable antiretroviral effect of the HIV-1 Integrase inhibitor raltegravir as part of combination therapy in treatment-naive patients with HIV-1 infection: results of a 48-week controlled study
349	Podzamczer	2007	Less lipoatrophy and better lipid profile with abacavir as compared to stavudine: 96-week results of a randomized study
350	NR	2007	Vicriviroc in Combination Treatment with an Optimized ART Regimen in HIV-Infected Treatment-Experienced Subjects (VICTOR-E4) - VICTOR-E4
351	NR	2007	Study of Once-Daily Versus Twice-Daily Fosamprenavir plus Ritonavir, Administered with Abacavir/Lamivudine Once-Daily in Antiretroviral-Naïve HIV-1 Infected Adult Subjects. - Merit

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
352	NR	2007	Effect and safety of switching from zidovudin to either tenofovir or abacavir in patients suffering from HIV. An open label study. - SWAP-TA
353	NR	2007	IMPACTO DE LA INTENSIFICACIÓN CON RALTEGRAVIR EN LA LATENCIA VIRAL DE VIH-1 EN PACIENTES CON SUPRESIÓN VIRAL COMPLETA (IMPACT OF RALTEGRAVIR INTENSIFICATION ON HIV-1 VIRAL LATENCY IN PATIENTS WITH PREVIOUS COMPLETE VIRAL SUPPRESSION). - INTEGRAL
354	NR	2007	A Multicenter, Double-Blind, Randomized, Active-Controlled Study to Evaluate the Safety and Antiretroviral Activity of MK-0518 Versus KALETRA™ in HIV-Infected Patients Switched from a Stable KALETRA™-Based Regimen - Study A
355	NR	2007	A randomised prospective study assessing changes in neuro-cognitive function, using a computerised test battery, in treatment naïve HIV-1 positive subjects commencing two different antiretroviral regimens. - CogNaive Study
356	NR	2007	A randomized, open-label trial to compare the efficacy, safety and tolerability of DRV/rtv (800/100 mg) q.d. versus DRV/rtv (600/100 mg) b.i.d. in early treatment-experienced HIV-1 infected subjects. - Once-daily Darunavir In treatment-experieNced patien
357	NR	2007	A phase IV study to assess the feasibility of substituting double ritonavir-boosted protease inhibitors (PI) with ritonavir-boosted darunavir (DRV/r) in HIV-infected individuals with viral suppression on highly active antiretroviral therapy (HAART) - Dou
358	NR	2007	A Phase 4, Open Label, Randomized, Controlled Study to Assess the Effect on Lipid Profile of Switching from a Stable HAART Regimen of fixed dose Abacavir/Lamivuidine (Kivexa) Plus Efavirenz, to Once Daily Atripla in Adult HIV-1 Infected Subjects With Rai
359	NR	2007	A Phase III, Randomised, Open- Label Study Comparing the Safety and Efficacy of Switching Stavudine or Zidovudine to Tenofovir Disoproxil Fumarate versus Continuing Stavudine or Zidovudine in Virologically Suppressed HIV-Infected Children Taking Highly A
360	NR	2007	A randomised open-label study comparing the safety and efficacy of three different combination antiretroviral regimens as initial therapy for HIV infection. - Altair
361	NR	2007	Randomized, controlled, multicentric trial to evaluate efficacy and safety of the switch from a LPV/r based therapy to an ATV/r or a NVP based treatment in association with ABC/3TC, in HIV patient with undetectable viral load
362	NR	2007	Randomized, monocentric trial on sintoms, adherence,toxicity of alternate antiretrovirale regimen - ND
363	NR	2007	A pilot, randomized trial to evaluate the lipid profile after antiretroviral regimens including nevirapine or atazanavir boosted with ritonavir in HIV-positive patients naive for antiretrovirals - STAR2
364	NR	2007	Efficacy and Safety of VICRIVIROC in HIV-Infected Treatment-Naïve Subjects - P04875
365	NR	2007	Study of Once-Daily Abacavir/Lamivudine versus Tenofovir/Emtricitabine, Administered with Efavirenz in Antiretroviral-Naive, HIV-1 Infected Adult Subjects - CNA109586
366	NR	2007	Early Access of MK-0518 in Combination With an Optimized Background Antiretroviral Therapy (OBT) in Highly Treatment Experienced HIV-1 Infected Patients With Limited to No Treatment Options

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
367	NR	2007	Second-line Anti-Retroviral therapy in Africa: a randomised trial to evaluate the feasibility of maintenance monotherapy with ritonavir-boosted lopinavir (Aluvia® tablets) following initiation with 24 weeks of combination therapy in second-line anti-retr
368	NR	2007	Efficacy and Safety of VICRIVIROC in HIV-Infected Treatment-Naïve Subjects (Study P04875)
369	NR	2007	A Study of Indinavir Plus Ritonavir Plus Two NRTIs vs. Nelfinavir Plus Two NRTIs in HIV Positive Patients (0639-112)(COMPLETED)
370	NR	2007	Comparison of TPV/r to DRV/r in Triple Class Experienced Patient With Resistance to > 1 PI
371	NR	2007	Incidence and Severity of Neuropsychiatric Adverse Events of Efavirenz Given as a Stepped Dosage vs. the Usual Dosage
372	NR	2007	SPRING: safety, Efficacy, Pharmacokinetics of tipRanavir/r IN Race/Gender HIV+ Patients Randomized to TDM or SoC
373	NR	2007	Lopinavir Capsules to Kaletra or Invirase Tablets
374	NR	2007	Tipranavir/Ritonavir Low Dose Pharmacokinetics in Treatment Naive Patients
375	NR	2007	VERxVE Study on Efficacy and Safety of Nevirapine XR in Comparison to Nevirapine IR With Truvada in Naive HIV+ Patients
376	NR	2007	Effect of Atazanavir on Endothelial Function in HIV-Infected Patients
377	NR	2007	Nevirapine vs. Atazanavir Boosted With Ritonavir on a Background of Truvada in Human Immunodeficiency Virus (HIV) Infected Naive Patients (NEwArT)
378	NR	2007	Study Comparing Efficacy and Safety of Darunavir Boosted With Ritonavir to HART With 2 NRTI and Darunavir Boosted With Ritonavir in HIV-1 Infected Patients ANRS136
379	NR	2007	Safety and Efficacy of Switching From Stavudine or Zidovudine to Tenofovir DF in HIV-1 Infected Children
380	NR	2007	Comparison of Epzicom and Truvada for the Initial Once Daily HIV Treatment
381	NR	2007	Switching From PI to RALtegravir in HIV Stable Patients
382	NR	2007	Once-daily Antiretroviral Therapy in HIV-1 Infected Patients With CD4+ Cell Counts Below 100 Cells/Mcl
383	NR	2007	TMC278-TiDP6-C215: a Clinical Trial in Treatment Naive HIV-subjects Patients Comparing TMC278 to Efavirenz in Combination With 2 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors
384	NR	2007	Standard Antiretroviral v. Multi-class Therapy in Acutely HIV-1 Infected Antiretroviral-Naïve Subjects (ADARC 2007-01)
385	NR	2007	A Study to Evaluate the Safety and Efficacy of Adding Enfuvirtide to Oral Highly Active Antiretroviral Therapy (HAART) in Human Immunodeficiency Virus (HIV) Patients With Prior Treatment Experience
386	NR	2007	Vicriviroc in HIV(R5/X4)-Treatment Experienced Subjects (Study P05057AM5)(COMPLETED)
387	NR	2007	Vicriviroc in HIV-Treatment Experienced Subjects (Study P04405AM5)
388	NR	2007	A Study to Compare Effectiveness and Safety of Darunavir/Ritonavir (DRV/Rtv) 800mg/100mg Once Daily Versus DRV/Rtv 600mg/100mg Twice Daily in Early Treatment-Experienced HIV-1 Infected Patients (ODIN)
389	NR	2007	Vicriviroc in HIV-Treatment Experienced Subjects (Study P04889AM8)(COMPLETED)

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
390	NR	2007	Treatment Simplification by Darunavir/Ritonavir 800/100 mg Once a Day Versus a Triple Combination Therapy With Darunavir/Ritonavir
391	NR	2007	Induction/Simplification With Atazanavir + Ritonavir + Abacavir/Lamivudine Fixed-Dose Combination In HIV-1 Infection
392	Dart Trial Team	2008	Twenty-four-week safety and tolerability of nevirapine vs. abacavir in combination with zidovudine/lamivudine as first-line antiretroviral therapy: a randomized double-blind trial (NORA)
393	Duvivier	2008	Initial therapy with nucleoside reverse transcriptase inhibitor-containing regimens is more effective than with regimens that spare them with no difference in short-term fat distribution: Hippocampe-ANRS 121 Trial
394	Clotet	2008	A randomized, controlled study evaluating an induction treatment strategy in which enfuvirtide was added to an oral, highly active antiretroviral therapy regimen in treatment-experienced patients: the INTENSE study
395	Smith	2008	Fosamprenavir or atazanavir once daily boosted with ritonavir 100 mg, plus tenofovir/emtricitabine, for the initial treatment of HIV infection: 48-week results of ALERT
396	McComsey	2008	Effect of reducing the dose of stavudine on body composition, bone density, and markers of mitochondrial toxicity in HIV-infected subjects: a randomized, controlled study
397	Molina	2008	Once-daily atazanavir/ritonavir versus twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1-infected patients: 48 week efficacy and safety results of the CASTLE study
398	Riddler	2008	Class-sparing regimens for initial treatment of HIV-1 infection
399	Carr	2008	Effects of boosted tipranavir and lopinavir on body composition, insulin sensitivity and adipocytokines in antiretroviral-naive adults
400	Delfraissy	2008	Lopinavir/ritonavir monotherapy or plus zidovudine and lamivudine in antiretroviral-naive HIV-infected patients
401	Mallolas	2008	Induction therapy with trizivir plus efavirenz or lopinavir/ritonavir followed by trizivir alone in naive HIV-1-infected adults
402	Ortiz	2008	Efficacy and safety of once-daily darunavir/ritonavir versus lopinavir/ritonavir in treatment-naive HIV-1-infected patients at week 48
403	Tashima	2008	Efficacy and tolerability of long-term efavirenz plus nucleoside reverse transcriptase inhibitors for HIV-1 infection
404	Collier	2008	Randomized study of dual versus single ritonavir-enhanced protease inhibitors for protease inhibitor-experienced patients with HIV
405	Arribas	2008	Tenofovir disoproxil fumarate, emtricitabine, and efavirenz compared with zidovudine/lamivudine and efavirenz in treatment-naive patients: 144-week analysis
406	Malan	2008	Efficacy and safety of atazanavir, with or without ritonavir, as part of once-daily highly active antiretroviral therapy regimens in antiretroviral-naive patients
407	Walmsley	2008	Pharmacokinetics, safety, and efficacy of tipranavir boosted with ritonavir alone or in combination with other boosted protease inhibitors as part of optimized combination antiretroviral therapy in highly treatment-experienced patients (BI Study 1182.51)
408	van den Berg-Wolf	2008	Virologic, immunologic, clinical, safety, and resistance outcomes from a long-term comparison of efavirenz-based versus nevirapine-based antiretroviral regimens as initial therapy in HIV-1-infected persons
409	NR	2008	Safety and Pharmacokinetics Study of Multiple Dose Administration of Sifuvirtide in HIV-infected volunteers (FS0103)

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
410	NR	2008	Efficacy, safety, and pharmacokinetics study of Sifuvirtide for Injection in combination with HAART therapy in HIV infected subjects
411	NR	2008	A Phase 4, Open Label, Randomized, Controlled Study to Assess the Effect on Lipid Profile of Switching a Stable HAART Regimen of fixed dose Abacavir/Lamivudine (Kivexa) Plus Lopinavir/Ritonavir (Kaletra), to Emtricitabine/Tenofovir Disoproxil Fumarate (T
412	NR	2008	An open label, phase IIIb, randomized parallel group study to assess the efficacy and safety of switching HIV-1 infected patients successfully treated with a Nevirapine IR based regimen to Nevirapine XR 400 mg QD or remaining on Nevirapine IR 200 mg BIDb
413	NR	2008	CLINICAL TRIAL ASSESSING ONCE DAILY RALTEGRAVIR ADMINISTRATION (800 mg QD) IN HIV-1-INFECTED PATIENTS RECEIVING UNBOOSTED ATAZANAVIR (400 mg QD)-BASED ANTIRETROVIRAL THERAPY (ENSAYO CLÍNICO PARA EVALUAR LA ADMINISTRACIÓN DE RALTEGRAVIR UNA VEZ AL DÍA (80
414	NR	2008	A Multicenter, Randomized, Open-Label, Active-Controlled Pilot Study to Evaluate the Safety and Antiretroviral Activity of Unboosted Atazanavir BID Plus Raltegravir BID and Boosted Atazanavir QD in Combination with Tenofovir/Emtricitabine QD in Treatment
415	NR	2008	A phase IV, two-arm, open-label, single-centre randomised pilot study to assess the feasibility of immeidate or deferred switching of HIV-infected individuals intolerant of efavirenz, ritonavir-boosted lopinavir or ritonavir-boosted atazanavir, to ritona
416	NR	2008	A Multicenter, Randomized, Double-Blind, Phase 2b Trial to Determine The Efficacy, Tolerability And Safety Of 3 Dose Regimens Of RDEA806 and Open-Label Efavirenz as Active Control in HIV 1-Infected, Antiretroviral Naïve Subjects - Dose Response Naive Eff
417	NR	2008	A phase III, double blind, multi centre, randomised placebo controlled, pilot study to assess the feasibility of switching individuals receiving efavirenz with continuing Central Nervous System (CNS) toxicity to TMC125 - Efavirenz taxicity switch to etra
418	NR	2008	A clinical investigation study comparing elvitegravir with raltegravir, each administred with a background treatment in HIV-1 infected patients already on treatment with antiretroviral medicinal products
419	NR	2008	A randomised, controlled, open-label trial to compare brachial artery reactivity and cardiovascular risk of a treatment simplification by darunavir/ritonavir (DRV/r) 800/100 mg O.D. versus a triple combination therapy containing DRV/r in HIV-1 infected s
420	NR	2008	A randomized, open-label, study of lopinavir/ritonavir 400/100 mg tablet twice-daily + co-formulated emtricitabine/tenofovir disoproxil fumarate 200/300 mg once-daily versus lopinavir/ritonavir 400/100 mg tablet twice-daily + raltegravir 400 mg twice-dai
421	NR	2008	A Phase III Multicenter, Double-Blind, Randomized, Active Comparator-Controlled Clinical Trial to Study the Safety and Efficacy of Once Daily Raltegravir (MK-0518) Versus Twice Daily Raltegravir, Each in Combination With TRUVADA™, in Treatment-Naïve HIV
422	NR	2008	A phase 2b/3, randomized, double blind, dose confirming study of the safety, efficacy and tolerability of apricitabine versus lamivudine in treatment-experienced HIV-1 infected patients with the M184V/I mutation in reverse transcriptase - AVX-301
423	NR	2008	A Phase III, randomized, double-blind trial of TMC278 25 mg q.d. versus efavirenz 600 mg q.d. in combination with a fixed background regimen consisting of tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naïve HIV-1 infected subjects - E

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
424	NR	2008	A Double-Blind, Randomized, Multi-Center Trial to Evaluate the Safety and Efficacy of the Combination of 1592U89/Zidovudine (ZDV)/Lamivudine (3TC) Versus the Combination of Zidovudine (ZDV)/Lamivudine (3TC) in HIV-1 Therapy-Experienced
425	NR	2008	Safety and clinical effects of IDX12899 in HIV-1 infection
426	NR	2008	TMC114-C213: a Phase II Randomized, Controlled, Partially Blinded Trial to Investigate Dose-response of TMC114/RTV in 3-class-experienced HIV-1 Infected Patients, Followed by an Open-label Period on the Recommended Dose of TMC114/RTV
427	NR	2008	Efficacy and Safety of MK-0518 in Treatment-Experienced HIV-1 Infected Adult Patients With Hemophilia
428	NR	2008	Safety and Pharmacokinetic Study of Fixed Dose Combination of Zidovudine, Lamivudine, and Nevirapine in HIV-Infected Children in Thailand
429	NR	2008	Kaletra-isentress Treatment Evaluation
430	NR	2008	Efficacy and Safety of Switching From Retrovir to Tenofovir or Abacavir in HIV-infected Patients
431	NR	2008	Tenofovir DF + Efavirenz (TDF+EFV) Versus Tenofovir DF + Efavirenz + Lamivudine (TDF+EFV+3TC) Maintenance Regimen in Virologically Controlled Patients: COOL Trial
432	NR	2008	Pilot Study Switching Individuals Receiving EFV With Continuing Central Nervous System Toxicity to TMC125
433	NR	2008	Changes in Triglyceride and Other Lipids (Levels of Fats Found in Blood) When Taking Darunavir Compared to Atazanavir in HIV-infected Patients That Have Never Received Treatment
434	NR	2008	Safety and Efficacy Study of Switching From Epzicom to Truvada
435	NR	2008	Pharmacokinetics, Pharmacodynamics, And Safety Of Maraviroc (UK-427,857) In Patients With Human Immunodeficiency Virus
436	NR	2008	INNOVE Study: a Study of 3 Months Induction With Fuzeon (Enfuvirtide) + Optimized Background (OB) Versus OB Alone in HIV-1 Infected Patients With Virological Failure
437	NR	2008	Phase IIB Pilot of Atazanavir + Raltegravir
438	NR	2008	Second-line Therapy Antiretroviral in Patients Who Failed Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) - Based Regimens
439	NR	2008	Raltegravir vs. Atazanavir in Combination With Truvada® for the Treatment of Antiretroviral naïve HIV Infected Patients
440	NR	2008	Raltegravir vs. Lopinavir/Ritonavir, Both in Combination With Truvada, in HIV+ Treatment Naive Individuals
441	NR	2008	Multicenter, Randomized, Double-Blind, Double-Dummy, Phase 3 Study of the Safety and Efficacy of Elvitegravir Versus Raltegravir
442	NR	2008	Pilot Study of Raltegravir/Truvada Versus Efavirenz/Truvada for Adults With Acute IV-1 Infection
443	NR	2008	Raltegravir And Darunavir Antiretroviral in Antiretroviral Naive Patients
444	NR	2008	Raltegravir + Lopinavir/Ritonavir Versus Efavirenz + Tenofovir + Emtricitabine in Treatment Naive Patients
445	NR	2008	Raltegravir Therapy for Women With HIV and Fat Accumulation
446	NR	2008	Study Comparing Lopinavir/Ritonavir (LPV/r) + Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) With a Nucleoside Sparing Regimen Consisting of Lopinavir/Ritonavir + Raltegravir (RAL)
447	NR	2008	Phase IIa Dose-ranging Study of GSK1349572 in HIV-1 Infected Adults

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
448	NR	2008	Raltegravir (Isentress/MK-0518) and HIV-1 Infected CD4 Cells During Acute/Early HIV-1
449	NR	2008	Pilot Study of a Raltegravir Based NRTI Sparing Regimen
450	Pedro	2008	Raltegravir Added to Stable HAART in HIV-1 Infected Subjects With Viral Suppression and Low CD4 Recovery
451	NR	2008	TMC278-TiDP6-C209: A Clinical Trial in Treatment Naive HIV-1 Patients Comparing TMC278 to Efavirenz in Combination With Tenofovir + Emtricitabine
452	Negredo	2009	Improvement of Mitochondrial Toxicity in Patients Receiving a Nucleoside Reverse-Transcriptase Inhibitor–Sparing Strategy: Results from the Multicenter Study with Nevirapine and Kaletra (MULTINEKA)
453	De Castro	2009	Switch from enfuvirtide to raltegravir in virologically suppressed multidrug-resistant HIV-1-infected patients: a randomized open-label trial
454	Flammer	2009	Effect of atazanavir versus other protease inhibitor-containing antiretroviral therapy on endothelial function in HIV-infected persons: randomised controlled trial
455	Arribas	2009	Lopinavir-ritonavir monotherapy versus lopinavir-ritonavir and 2 nucleosides for maintenance therapy of HIV: 96-week analysis
456	Bussmann	2009	Response to zidovudine/didanosine-containing combination antiretroviral therapy among HIV-1 subtype C-infected adults in Botswana: two-year outcomes from a randomized clinical trial
457	Saag	2009	A double-blind, placebo-controlled trial of maraviroc in treatment-experienced patients infected with non-R5 HIV-1
458	Stanley	2009	Effects of switching from lopinavir/ritonavir to atazanavir/ritonavir on muscle glucose uptake and visceral fat in HIV-infected patients
459	Kumar	2009	A randomized, controlled trial of initial anti-retroviral therapy with abacavir/lamivudine/zidovudine twice-daily compared to atazanavir once-daily with lamivudine/zidovudine twice-daily in HIV-infected patients over 48 weeks (ESS100327, the ACTION Study)
460	Lennox	2009	Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naive patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial
461	Martin	2009	Simplification of antiretroviral therapy with tenofovir-emtricitabine or abacavir-Lamivudine: a randomized, 96-week trial
462	Pulido	2009	Long-term efficacy and safety of fosamprenavir plus ritonavir versus lopinavir/ritonavir in combination with abacavir/lamivudine over 144 weeks
463	Rey	2009	High rate of early virological failure with the once-daily tenofovir/lamivudine/nevirapine combination in naive HIV-1-infected patients
464	Mills	2009	Once-daily darunavir/ritonavir vs. lopinavir/ritonavir in treatment-naive, HIV-1-infected patients: 96-week analysis
465	Smith	2009	Randomized, double-blind, placebo-matched, multicenter trial of abacavir/lamivudine or tenofovir/emtricitabine with lopinavir/ritonavir for initial HIV treatment
466	Calza	2009	Efficacy and safety of atazanavir-ritonavir plus abacavir-lamivudine or tenofovir-emtricitabine in patients with hyperlipidaemia switched from a stable protease inhibitor-based regimen including one thymidine analogue
467	Carosi	2009	Study of once-daily versus twice-daily fosamprenavir plus ritonavir administered with abacavir/lamivudine once daily in antiretroviral-naïve HIV-1-infected adult subjects

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
468	Nunes	2009	Monotherapy with Lopinavir/Ritonavir as maintenance after HIV-1 viral suppression: results of a 96-week randomized, controlled, open-label, pilot trial (KalMo study)
469	Dejesus	2009	Simplification of antiretroviral therapy to a single-tablet regimen consisting of efavirenz, emtricitabine, and tenofovir disoproxil fumarate versus unmodified antiretroviral therapy in virologically suppressed HIV-1-infected patients
470	Fisher	2009	A randomized comparative trial of continued zidovudine/lamivudine or replacement with tenofovir disoproxil fumarate/emtricitabine in efavirenz-treated HIV-1-infected individuals
471	Mallolas	2009	Efficacy and safety of switching from boosted lopinavir to boosted atazanavir in patients with virological suppression receiving a LPV/r-containing HAART: the ATAZIP study
472	Martínez	2009	A simplification trial switching from nucleoside reverse transcriptase inhibitors to once-daily fixed-dose abacavir/lamivudine or tenofovir/emtricitabine in HIV-1-infected patients with virological suppression
473	Walmsley	2009	Gemini: A noninferiority study of saquinavir/ritonavir versus lopinavir/ritonavir as initial HIV-I therapy in adults
474	Hicks	2009	Comparison of once-daily fosamprenavir boosted with either 100 or 200 mg of ritonavir, in combination with abacavir/lamivudine: 96-week results from COL100758
475	NR	2009	Randomized, Open label, Multiple-Dose Study to Evaluate the Pharmacodynamics, Safety and Pharmacokinetics of BMS-663068 in HIV-1 Infected Subjects
476	NR	2009	PILOT STUDY TO ASSESS THE EFFICACY AND SAFETY OF SWITCHING PROTEASE INHIBITOR TO ETRAVIRINE IN HIV-1-INFECTED SUBJECTS WITH VIREMIA SUPPRESSION (ESTUDIO PILOTO PARA EVALUAR LA EFICACIA Y SEGURIDAD DE LA SIMPLIFICACIÓN DE UN INHIBIDOR DE LA PROTEASA A ETR
477	NR	2009	RANDOMISED AND PROSPECTIVE CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF LOPINAVIR/RITONAVIR MONOTHERAPY VS DARUNAVIR/RITONAVIR MONOTHERAPIES AS SIMPLIFICATION SWITCHING STRATEGIES OF PI/NNRTI-TRIPLE THERAPY BASED-REGIMENS
478	NR	2009	ENSAYO CLÍNICO PILOTO PARA EVALUAR LA SEGURIDAD Y EFICACIA DE CAMBIAR EL ITINAN O EL IP A MARAVIROC EN PACIENTES INFECTADOS POR EL VIH-1 CON CARGA VIRAL INDETECTABLE Y DISLIPEMIA ASOCIADA A LOS ANTIRETROVIRALES (PILOT STUDY TO ASSESS THE SAFETY AND EFICA
479	NR	2009	PILOT STUDY OF NOVEL COMBINATION OF MARAVIROC +ATAZANAVIR/RITONAVIR VS ATAZANAVIR/RITONAVIR +EMTRICITABINE/TENOFOVIR FOR THE TREATMENT OF TREATMENT NAÏVE HIV-INFECTED PATIENTS WITH R5 HIV-1
480	NR	2009	PRotease-Inhibitors MOnotherapy Strategies as maintenance therapy in persons with fully suppressed HIV replication: results from an open-label randomized comparative trial (PRIMO Trial) - PRIMO Trial
481	NR	2009	A Phase IIb study to select a once daily oral dose of GSK1349572 administered with either abacavir/lamivudine or tenofovir/emtricitabine in HIV-1 infected antiretroviral therapy naïve adult subjects. - ND

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
482	NR	2009	Exploratory study on inflammatory immune response related to endothelial dysfunction in HIV-infected na?ve patients treated with abacavir compared to tenofovir-based regimens. - ABRACADABRA
483	NR	2009	Phase IIb pilot study for the evaluation of the safety and the feasibility of treatment simplification to tenofovir+emtricitabina+raltegravir or to lamivudine+abacavir+raltegravir in patients with optimal virological control and toxicity to the current c
484	NR	2009	Evaluation of Three Strategies of Second-line Antiretroviral Treatment in Africa (Dakar - Bobo-Dioulasso - Yaoundé)
485	NR	2009	Study of the Safety and Efficacy of Stribild Versus Atripla in Human Immunodeficiency Virus, Type 1 (HIV-1) Infected, Antiretroviral Treatment-Naive Adults
486	NR	2009	A Clinical Trial Comparing the Tolerability of Etravirine to Efavirenz in Combination With 2 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors in Treatment-naive HIV-1 Infected Patients
487	NR	2009	Artery Elasticity After Switch From Epzicom to Truvada
488	NR	2009	A Study Of Different Doses Of UK-453, 061 Plus Truvada Compared To Efavirenz Plus Truvada In Patients Who Have Not Been Previously Treated For HIV-1
489	NR	2009	Clinical Study to Evaluate the Efficacy and Safety of Lopinavir/Ritonavir Monotherapy Versus Darunavir/Ritonavir Monotherapies as Simplification Switching Strategies of PI/NNRTI-Triple Therapy Based-Regimens
490	NR	2009	Safety and Efficacy of Cobicistat-boosted Atazanavir Compared to Ritonavir-boosted Atazanavir in Combination With Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 Infected, Antiretroviral Treatment-Naive Adults
491	NR	2009	Switching From Protease Inhibitor (PI) to Etravirine in HIV-1 Infected Subjects With Viremia Suppression
492	NR	2009	A Trial of 2 Options for Second Line Combination Antiretroviral Therapy Following Virological Failure of a Standard Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)+2N(t)RTI First Line Regimen
493	NR	2009	BATAR: individuals Currently Taking Boosted Atazanavir as Part of an HIV Treatment Regimen Will be Evaluated to See if Substituting Raltegravir for Nucleoside Transcriptase Inhibitors Will be Safe and Well Tolerated
494	NR	2009	Safety and Efficacy of Reduced Dose Efavirenz (EFV) With Standard Dose EFV Plus Two Nucleotide Reverse Transcriptase Inhibitors (N(t)RTI) in Antiretroviral-naïve HIV-infected Individuals
495	NR	2009	Lopinavir/r Monotherapy Versus Abacavir/Lamivudine and Lopinavir/r for Limb Fat Recovery in Persons With Lipoatrophy
496	NR	2009	Raltegravir Switch for Toxicity or Adverse Events
497	NR	2009	Switching the Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) or Protease Inhibitor (PI) to Maraviroc in HIV Subjects
498	NR	2009	A Pilot Study Of A Novel Treatment Regimen, Maraviroc + Ritonavir Boosted Atazanavir, In Treatment Naive HIV-Infected Patients
499	NR	2009	Study on the Antiviral Therapy and Immune Reconstitution of Chinese HIV/AIDS Patients
500	NR	2009	Safety and Efficacy of ADAPTAVIR's Ability to Eliminate Treatment-Resistant Infectious Virus in Peripheral Blood Mononuclear Cells (PBMCs)

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
501	NR	2009	PENTA18: Pharmacokinetics, safety and efficacy of lopinavir/ritonavir tablets in combination antiretroviral therapy in human immunodeficiency virus-1 (HIV-1) infected children
502	NR	2009	Study to Compare the Safety and Anti-HIV Effect of GSK1265744 Versus Placebo in HIV-1 Infected Adults (ITZ112929)
503	Palumbo	2010	Antiretroviral Treatment for Children with Peripartum Nevirapine Exposure
504	Hammer	2010	A randomized, placebo-controlled trial of abacavir intensification in HIV-1-infected adults with virologic suppression on a protease inhibitor-containing regimen
505	Cooper	2010	Maraviroc versus efavirenz, both in combination with zidovudine-lamivudine, for the treatment of antiretroviral-naive subjects with CCR5-tropic HIV-1 infection
506	Stellbrink	2010	Comparison of changes in bone density and turnover with abacavir-lamivudine versus tenofovir-emtricitabine in HIV-infected adults: 48-week results from the ASSERT study
507	Suleiman	2010	Vicriviroc in combination therapy with an optimized regimen for treatment-experienced subjects: 48-week results of the VICTOR-E1 phase 2 trial
508	Wilkin	2010	Three-year safety and efficacy of vicriviroc, a CCR5 antagonist, in HIV-1-infected treatment-experienced patients
509	Yeh	2010	Vicriviroc and peripheral neuropathy: results from AIDS Clinical Trials Group 5211
510	Josephson	2010	The relation between treatment outcome and efavirenz, atazanavir or lopinavir exposure in the NORTHIV trial of treatment-naïve HIV-1 infected patients
511	Lennox	2010	Raltegravir versus Efavirenz regimens in treatment-naive HIV-1-infected patients: 96-week efficacy, durability, subgroup, safety, and metabolic analyses
512	Malan	2010	96-week efficacy and safety of atazanavir, with and without ritonavir, in a HAART regimen in treatment-naive patients
513	Meynard	2010	Lopinavir/ritonavir monotherapy versus current treatment continuation for maintenance therapy of HIV-1 infection: the KALESOLO trial
514	Arribas	2010	The MONET trial: darunavir/ritonavir with or without nucleoside analogues, for patients with HIV RNA below 50 copies/ml
515	Katlama	2010	Efficacy of darunavir/ritonavir maintenance monotherapy in patients with HIV-1 viral suppression: a randomized open-label, noninferiority trial, MONOI-ANRS 136
516	Martínez	2010	Substitution of raltegravir for ritonavir-boosted protease inhibitors in HIV-infected patients: the SPIRAL study
517	Pozniak	2010	Efficacy and safety of TMC278 in antiretroviral-naive HIV-1 patients: week 96 results of a phase IIb randomized trial
518	Squires	2010	Similar efficacy and tolerability of atazanavir compared with atazanavir/ritonavir, each with abacavir/lamivudine after initial suppression with abacavir/lamivudine plus ritonavir-boosted atazanavir in HIV-infected patients
519	Wester	2010	Non-nucleoside reverse transcriptase inhibitor outcomes among combination antiretroviral therapy-treated adults in Botswana
520	Hodder	2010	Patient-reported outcomes in virologically suppressed, HIV-1-Infected subjects after switching to a simplified, single-tablet regimen of efavirenz, emtricitabine, and tenofovir DF
521	Sprenger	2010	Abacavir/lamivudine/zidovudine maintenance after standard induction in antiretroviral therapy-naïve patients: FREE randomized trial interim results

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
522	Edén	2010	Differential effects of efavirenz, lopinavir/r, and atazanavir/r on the initial viral decay rate in treatment naïve HIV-1-infected patients
523	González-García	2010	Short communication: Comparable safety and efficacy with once-daily versus twice-daily dosing of lopinavir/ritonavir tablets with emtricitabine + tenofovir DF in antiretroviral-naïve, HIV type 1-infected subjects: 96 week final results of the randomized trial M05-730
524	Miró	2010	Immune reconstitution in severely immunosuppressed antiretroviral-naive HIV type 1-infected patients using a nonnucleoside reverse transcriptase inhibitor-based or a boosted protease inhibitor-based antiretroviral regimen: three-year results (The Advanz Trial): a randomized, controlled trial
525	Ghosn	2010	Unboosted atazanavir-based therapy maintains control of HIV type-1 replication as effectively as a ritonavir-boosted regimen
526	Echeverría	2010	Similar antiviral efficacy and tolerability between efavirenz and lopinavir/ritonavir, administered with abacavir/lamivudine (Kivexa), in antiretroviral-naïve patients: a 48-week, multicentre, randomized study (Lake Study)
527	Molina	2010	Once-daily atazanavir/ritonavir compared with twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1-infected patients: 96-week efficacy and safety results of the CASTLE study
528	Munderi	2010	Nevirapine/zidovudine/lamivudine has superior immunological and virological responses not reflected in clinical outcomes in a 48-week randomized comparison with abacavir/zidovudine/lamivudine in HIV-infected Ugandan adults with low CD4 cell counts
529	Pinola	2010	Lopinavir/ritonavir + tenofovir Dual Therapy versus Lopinavir/ritonavir-Based Triple Therapy in HIV-Infected Antiretroviral Naïve Subjects: the Kalead Study
530	Post	2010	Randomized comparison of renal effects, efficacy, and safety with once-daily abacavir/lamivudine versus tenofovir/emtricitabine, administered with efavirenz, in antiretroviral-naive, HIV-1-infected adults: 48-week results from the ASSERT study
531	Puls	2010	Efavirenz versus boosted atazanavir or zidovudine and abacavir in antiretroviral treatment-naive, HIV-infected subjects: week 48 data from the Altair study
532	Sierra-Madero	2010	Prospective, randomized, open label trial of efavirenz vs lopinavir/ritonavir in HIV+ treatment-naive subjects with CD4+<200 cell/mm3 in Mexico
533	Winston	2010	Neuropsychiatric Adverse Events With Ritonavir-Boosted Darunavir Monotherapy in HIV-Infected Individuals: A Randomised Prospective Study
534	NR	2010	ALTAIR - Alternative Antiretroviral Strategies: a Comparison of Three Initial Regimens
535	NR	2010	A phase 3 clinical trial to compare the safety and effectiveness of GSK1349572 and abacavir/lamivudine compared to Atripla over 96 weeks in patients with HIV infection who have not previously received treatment
536	NR	2010	Study to test a new drug dolutegravir vs. raltegravir for HIV patients who have never taken HIV medication
537	NR	2010	A phase II, double blind, exploratory, parallel-group, placebo-controlled clinical study to assess two dosing regimens of GSK2402968 for efficacy, safety, tolerability and pharmacokinetics in ambulant subjects with Duchenne muscular dystrophy

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
538	NR	2010	A randomised, open label, prospective study to assess two different therapeutic strategies following first treatment failure in HIV-1 infected subjects. 'The First Failure Study' : 'FAST' - The First Failure Study
539	NR	2010	A randomised open-label study comparing the safety and efficacy of ritonavir boosted lopinavir and 2-3N(t)RTI backbone versus ritonavir boosted lopinavir and raltegravir in participants virologically failing first-line NNRTI/2N(t)RTI therapy: the SECOND
540	NR	2010	A randomised, double-blind, placebo-controlled, clinical trial to compare the safety and efficacy of reduced dose efavirenz (EFV) with standard dose EFV plus two nucleotide reverse transcriptase inhibitors (N(t)RTI) in antiretroviral-naïve HIV-infected i
541	NR	2010	A prospective, randomised study to assess safety, changes in platelet reactivity, plasma cardiac biomarkers and metabolic parameters over 48 weeks in HIV-1 infected subjects undergoing a switch in antiretroviral therapy. - The St. Marys and The Mater Swi
542	NR	2010	Efficacy of atazanavir/ritonavir monotherapy as maintenance in patients with viral suppression. Randomized, open label non inferiority trial. (MODAt STUDY) - ND
543	NR	2010	Randomized multicenter study on security and efficacy of therapeutic switch to maraviroc + darunavir/ritonavir once daily in patients who are in triple antiretroviral regimen with three drugs belonging at least to one of the three historical classes and
544	NR	2010	An open-label randomised two-year trial comparing two first-line regimens in HIV-infected antiretroviral naïve subjects: darunavir/r + tenofovir/emtricitabine vs. darunavir/r + raltegravir - NEAT 001/ANRS143
545	NR	2010	Effectiveness of generic split adult tablets and paediatric fixed dose combination (FDC) of d4T/3TC/NVP in the treatment of HIV infected Malawian children
546	NR	2010	Children with human immunodeficiency virus (HIV) in Africa - pharmacokinetics and acceptability/adherence of simple antiretroviral regimens (CHAPAS-3 trial)
547	NR	2010	A Trial With TMC278-TIDP6-C222 for Continued TMC278 Access in Patients Infected With Human Immunodeficiency Virus-1
548	NR	2010	Low Dose Atazanavir/r Versus Standard Dose Atazanavir/r (LASA)
549	NR	2010	Study of Lopinavir/ Ritonavir and Lamivudine Versus Standard Therapy in Naïve HIV-1 Infected Subjects
550	NR	2010	Switching From Efavirenz to Atazanavir/ Ritonavir in HIV-infected Subjects With Good Virologic Suppression
551	NR	2010	Safety and Efficacy of COBI-boosted Atazanavir Versus Ritonavir-boosted Atazanavir Each Administered With Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 Infected, Antiretroviral Treatment-Naive Adults
552	NR	2010	Effect of Maraviroc (MCV) on the Immunological Recovery of HIV-1 Discordant Patients With CD4 Lymphocyte Counts Below 200 Cells/mm3
553	NR	2010	Study to Evaluate the Safety and Efficacy of Stribild Versus Atripla in Human Immunodeficiency Virus, Type 1 (HIV-1) Infected, Antiretroviral Treatment-Naive Adults
554	NR	2010	Post-prandial Lipid Effects of Raltegravir (RAL) vs Ritonavir -Boosted Darunavir (DRV-r) in Anti-retroviral Therapy (ART)- Naive Adults or Adults Recommencing ART
555	NR	2010	A Simplification Study of Unboosted Reyataz With Epzicom (ASSURE)

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
556	NR	2010	Protease Inhibitor Monotherapy Versus Ongoing Triple-therapy in the Long Term Management of HIV Infection (PIVOT)
557	NR	2010	COMPARISM BETWEEN ONCE DAILY AND TWICE DAILY LPV/RTR CO-ADMINISTERED WITH TENOFOVIR AND EMTRICITOBIN AMONG HIV INFECTED PATIENTS DURING MUSLIM RAMADAN
558	NR	2010	A Study of GSK1349572 Versus Raltegravir (RAL) With Investigator Selected Background Regimen in Antiretroviral-Experienced, Integrase Inhibitor-Naive Adults
559	Elgadi	2011	Boosted tipranavir versus darunavir in treatment-experienced patients: observational data from the randomized POTENT trial
560	Gallien	2011	Efficacy and safety of raltegravir in treatment-experienced HIV-1-infected patients switching from enfuvirtide-based regimens: 48 week results of the randomized EASIER ANRS 138 trial
561	Harrison	2011	First-line antiretroviral therapy with a protease inhibitor versus non-nucleoside reverse transcriptase inhibitor and switch at higher versus low viral load in HIV-infected children: An open-label, randomised phase 2/3 trial
562	Cahn	2011	Pilot, randomized study assessing safety, tolerability and efficacy of simplified LPV/r maintenance therapy in HIV patients on the 1 PI-based regimen
563	Cohen	2011	Rilpivirine versus efavirenz with two background nucleoside or nucleotide reverse transcriptase inhibitors in treatment-naive adults infected with HIV-1 (THRIVE): a phase 3, randomised, non-inferiority trial
564	Soliman	2011	Boosted protease inhibitors and the electrocardiographic measures of QT and PR durations
565	Ulbricht	2011	A Multicenter, Open Labeled, Randomized, Phase III Study Comparing Lopinavir/Ritonavir Plus Atazanavir to Lopinavir/Ritonavir Plus Zidovudine and Lamivudine in Naive HIV-1-Infected Patients: 48-Week Analysis of the LORAN Trial
566	Vrouenraets	2011	Randomized comparison of metabolic and renal effects of saquinavir/r or atazanavir/r plus tenofovir/emtricitabine in treatment-naïve HIV-1-infected patients
567	Li	2011	[Safety study of 52-week highly active antiretroviral therapy in 198 HIV/AIDS Chinese patients]
568	Molina	2011	Rilpivirine versus efavirenz with tenofovir and emtricitabine in treatment-naive adults infected with HIV-1 (ECHO): a phase 3 randomised double-blind active-controlled trial
569	Cahn	2011	Week 48 analysis of once-daily vs. twice-daily darunavir/ritonavir in treatment-experienced HIV-1-infected patients
570	Cohen	2011	Randomized, phase 2 evaluation of two single-tablet regimens elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate for the initial treatment of HIV infection
571	Elion	2011	Phase 2 study of cobicistat versus ritonavir each with once-daily atazanavir and fixed-dose emtricitabine/tenofovir df in the initial treatment of HIV infection
572	Min	2011	Antiviral activity, safety, and pharmacokinetics/pharmacodynamics of dolutegravir as 10-day monotherapy in HIV-1-infected adults
573	Gathe	2011	Efficacy and safety of nevirapine extended-release once daily versus nevirapine immediate-release twice-daily in treatment-naive HIV-1-infected patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
574	Soriano	2011	Nevirapine versus atazanavir/ritonavir, each combined with tenofovir disoproxil fumarate/emtricitabine, in antiretroviral-naive HIV-1 patients: the ARTEN Trial
575	Reynes	2011	Examination of noninferiority, safety, and tolerability of lopinavir/ritonavir and raltegravir compared with lopinavir/ritonavir and tenofovir/ emtricitabine in antiretroviral-naïve subjects: the progress study, 48-week results
576	Dejesus	2011	A randomised comparison of safety and efficacy of nevirapine vs. atazanavir/ritonavir combined with tenofovir/emtricitabine in treatment-naïve patients
577	Podzamczer	2011	Lipid profiles for nevirapine vs. atazanavir/ritonavir, both combined with tenofovir disoproxil fumarate and emtricitabine over 48 weeks, in treatment-naïve HIV-1-infected patients (the ARTEN study)
578	Rasmussen	2011	Evaluation of cardiovascular biomarkers in HIV-infected patients switching to abacavir or tenofovir based therapy
579	Rockstroh	2011	Long-term treatment with raltegravir or efavirenz combined with tenofovir/emtricitabine for treatment-naive human immunodeficiency virus-1-infected patients: 156-week results from STARTMRK
580	Maserati	2011	Once-a-day (QD) vs. twice-daily (BID) nevirapine as simplification in PI-treated patients after 2 mos. of BID induction
581	Daar	2011	Atazanavir plus ritonavir or efavirenz as part of a 3-drug regimen for initial treatment of HIV-1
582	Honda	2011	Open-label randomized multicenter selection study of once daily antiretroviral treatment regimen comparing ritonavir-boosted atazanavir to efavirenz with fixed-dose abacavir and lamivudine
583	NR	2011	A randomised, open-label study to evaluate the efficacy and safety of maraviroc (MVC) as a switch for either nucleoside or nucleotide analogue reverse transcriptase inhibitors (N(t)RTI) or boosted protease inhibitors (PI/r) in HIV-1 infected individuals
584	NR	2011	Clinical study on Tolerability, pharmacodynamics and pharmacokinetics of multiple doses of Albuvirtide injection in HIV-infected patients
585	NR	2011	An Open-Label, Randomized Study Evaluating a Switch from a Regimen of Two Nucleoside Reverse Transcriptase Inhibitors plus any Third Agent to either a Regimen of Atazanavir/Ritonavir Once Daily and Raltegravir Twice Daily or to a Regimen of Atazanavir/Ri
586	NR	2011	EFFECT OF SWITCHING FROM NRTIS TO MARAVIROC ON NRTI-ASSOCIATED MITCHONDRIAL TOXICITY AND IMMUNE ACTIVATION
587	NR	2011	Study to assess the lipid-lowering effect of adding tenofovir/emtricitabine co-formulation vs placebo to HIV-1 infected subjects with dyslipidemia and sustained viral load suppression under monotherapy with ritonavir-boosted protease inhibitors
588	NR	2011	This clinical research study will assess the effectiveness (how well it works), safety, tolerability (how well the body stands the drug) and blood levels of combined doses of BMS-663068, Raltegravir and Tenofovir
589	NR	2011	A study to find out whether maraviroc given once daily is as effective as Truvada given once daily in treating HIV-infected patients never previously treated with maraviroc
590	NR	2011	PROTEA: a clinical trial comparing the efficacy of darunavir/ritonavir 800/100 mg monotherapy versus a triple combination therapy containing darunavir/ritonavir 800/100 mg and 2 nucleoside/nucleotide reverse transcriptase inhibitors in patients with unde
591	NR	2011	MARCH

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
592	NR	2011	This open label trial will recruit patients with HIV who are already receiving anti-HIV treatment which includes ritonavir and emtricitabine/tenofovir disoproxil fumurate (Truvada). Patients will be randomised to either remain on the same anti-HIV drugs
593	NR	2011	A Phase 3B, Randomized, Open-label Study to Evaluate the Safety and Efficacy of a Single Tablet Regimen of Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate Compared with a Single Tablet Regimen of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumar
594	Juan	2011	Study to Evaluate the Activity and Tolerability of Lopinavir/Ritonavir and Lamivudine Bitherapy in HIV Patients With Viral Suppression
595	Kirby	2011	Maraviroc Switch Collaborative Study
596	NR	2011	Study of MK-1972 in Human Immunodeficiency Virus (HIV)-1 Infected Participants Who Have Not Previously Received Antiretroviral Therapy (MK-1972-003)
597	NR	2011	Efficacy, Safety, and Tolerability of Cenicriviroc (CVC) in Combination With Truvada or Sustiva Plus Truvada in HIV 1-infected, Antiretroviral Treatment-naïve, Adult Patients Infected With Only CCR5-tropic Virus
598	NR	2011	Switch to Unboosted Atazanavir With Tenofovir Study
599	NR	2011	DRIVESHAFT: darunavir/Ritonavir In HIV-infected Virologically-suppressed Experienced Subjects
600	NR	2011	Pediatric Study for Appropriate Dose of Ritonavir Boosted Lopinavir in Thai HIV-infected Children (PEARL)
601	NR	2011	Effects of Switching Efavirenz to Raltegravir on Vascular Function and Bone Markers in HIV-infected Patients
602	NR	2011	Study to Evaluate the Safety and Efficacy of a Single Tablet Regimen of Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate Compared With a Single Tablet Regimen of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 Infected, Antiretrovir
603	NR	2011	Immuno-stimulation With Maraviroc Combined to Antiretroviral Therapy in Advanced Late Diagnosed HIV-1 Infected Patients
604	NR	2011	Clinical Trial of Brain-Penetrating HIV Drugs to Prevent Cognitive Impairment in China
605	NR	2011	Atazanavir/Ritonavir, Once Daily + Raltegravir, Twice Daily, Switch Study in HIV-1—Infected Patients
606	NR	2011	Study to Evaluate Switching From Regimens Consisting of a Ritonavir-boosted Protease Inhibitor Plus Emtricitabine/Tenofovir Fixed-Dose Combination to the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir DF Single-Tablet Regimen in Virologically Suppressed
607	NR	2011	Study to Evaluate Switching From Regimens Consisting of a Nonnucleoside Reverse Transcriptase Inhibitor Plus Emtricitabine and Tenofovir DF to the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir DF Single-Tablet Regimen in Virologically Suppressed, HIV-1
608	NR	2011	Safety and Efficacy of E/C/F/TAF (Genvoya®) Versus E/C/F/TDF (Stribild®) in HIV-1 Infected, Antiretroviral Treatment-Naive Adults
609	NR	2011	Cobicistat-containing Highly Active Antiretroviral Regimens in HIV-1 Infected Patients With Mild to Moderate Renal Impairment
610	NR	2011	A Study to Compare Brachial Artery Reactivity and Cardiovascular Risk of a Treatment Simplification by Darunavir/Ritonavir (DRV/r) 800/100 mg Versus a Triple Combination Therapy Containing DRV/r in HIV-1 Infected Patients

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
611	NR	2011	Dolutegravir Compared to Darunavir/Ritonavir , Each in Combination With Dual Nucleoside Reverse Transcriptase Inhibitors (NRTIs) in ART-naive Subjects
612	NR	2011	Antiretroviral Treatment Strategies in Relation to Adherence, Resistance and Virological Treatment Failure
613	NR	2011	A PHASE IIB RANDOMIZED, CONTROLLED, PARTIALLY-BLINDED TRIAL TO INVESTIGATE SAFETY, EFFICACY AND DOSE-RESPONSE OF BMS-663068 IN TREATMENT-EXPERIENCED HIV-1 SUBJECTS, FOLLOWED BY AN OPEN-LABEL PERIOD ON THE RECOMMENDED DOSE
614	NR	2011	A PHASE 3, RANDOMIZED, OPEN LABEL, CONTROLLED STUDY OF LOPINAVIR/RITONAVIR AND LAMIVUDINE VERSUS STANDARD THERAPY IN NAÏVE HIV-1 INFECTED SUBJECTS
615	NR	2011	Investigation of The Effect of Cenicriviroc (CVC) Plus FTC/TDF on Cardiovascular Disease Risk Factors
616	NR	2011	Effects of Intensive cART During Acute/Early HIV Infection
617	NR	2011	A Study to Assess Dolutegravir in HIV-infected Subjects With Treatment Failure on an Integrase Inhibitor Containing Regimen
618	NR	2011	A Trial Comparing GSK1349572 50mg Plus Abacavir/Lamivudine Once Daily to Atripla (Also Called The SINGLE Trial)
619	DeJesus	2012	Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate versus ritonavir-boosted atazanavir plus co-formulated emtricitabine and tenofovir disoproxil fumarate for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3, non-inferiority trial
620	Aberg	2012	Metabolic effects of darunavir/ritonavir versus atazanavir/ritonavir in treatment-naive, HIV type 1-infected subjects over 48 weeks
621	Albini	2012	A randomized, pilot trial to evaluate glomerular filtration rate by creatinine or cystatin C in naive HIV-infected patients after tenofovir/emtricitabine in combination with atazanavir/ritonavir or efavirenz
622	Arasteh	2012	Twenty-four-week efficacy and safety of switching virologically suppressed HIV-1-infected patients from nevirapine immediate release 200 mg twice daily to nevirapine extended release 400 mg once daily (TRANxITION)
623	Arribas	2012	The MONET trial: week 144 analysis of the efficacy of darunavir/ritonavir (DRV/r) monotherapy versus DRV/r plus two nucleoside reverse transcriptase inhibitors, for patients with viral load < 50 HIV-1 RNA copies/mL at baseline
624	Sax	2012	Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks
625	Lambert-Niclot	2012	Long-term efficacy of darunavir/ritonavir monotherapy in patients with hiv-1 viral suppression: week 96 results from the MONOI ANRS 136 study
626	Molina	2012	Efficacy and safety of once daily elvitegravir versus twice daily raltegravir in treatment-experienced patients with HIV-1 receiving a ritonavir-boosted protease inhibitor: randomised, double-blind, phase 3, non-inferiority study

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
627	Skiest	2012	Efficacy and safety of switching suppressed patients with elevated triglycerides from lopinavir/ritonavir or fosamprenavir/ritonavir to atazanavir/ritonavir or darunavir/ritonavir based therapy: the LARD study
628	Curran	2012	Body composition changes after switching from protease inhibitors to raltegravir: SPIRAL-LIP substudy
629	Curran	2012	Changes in body composition and mitochondrial DNA in HIV-1-infected patients switching to fixed-dose abacavir/lamivudine or tenofovir/emtricitabine: a substudy of the BICOMBO trial
630	Llibre	2012	Treatment intensification with raltegravir in subjects with sustained HIV-1 viraemia suppression: a randomized 48-week study
631	Moyle	2012	A randomized comparative 96-week trial of boosted atazanavir versus continued boosted protease inhibitor in HIV-1 patients with abdominal adiposity
632	Bánhegyi	2012	Week 96 efficacy, virology and safety of darunavir/r versus lopinavir/r in treatment-experienced patients in TITAN
633	Gotti	2012	Increase in standard cholesterol and large HDL particle subclasses in antiretroviral-naïve patients prescribed efavirenz compared to atazanavir/ritonavir
634	Kozal	2012	A nucleoside- and ritonavir-sparing regimen containing atazanavir plus raltegravir in antiretroviral treatment-naïve HIV-infected patients: SPARTAN study results
635	Squires	2012	ARIES 144 week results: durable virologic suppression in HIV-infected patients simplified to unboosted atazanavir/abacavir/lamivudine
636	Gotuzzo	2012	Sustained efficacy and safety of raltegravir after 5 years of combination antiretroviral therapy as initial treatment of HIV-1 infection: final results of a randomized, controlled, phase II study (Protocol 004)
637	Della Negra	2012	A randomized study of tenofovir disoproxil fumarate in treatment-experienced HIV-1 infected adolescents
638	Ofotokun	2012	A switch in therapy to a reverse transcriptase inhibitor sparing combination of lopinavir/ritonavir and raltegravir in virologically suppressed HIV-infected patients: a pilot randomized trial to assess efficacy and safety profile: the KITE study
639	Phanuphak	2012	A 72-week randomized study of the safety and efficacy of a stavudine to zidovudine switch at 24 weeks compared to zidovudine or tenofovir disoproxil fumarate when given with lamivudine and nevirapine
640	Rasmussen	2012	Comparison of bone and renal effects in HIV-infected adults switching to abacavir or tenofovir based therapy in a randomized trial
641	NR	2012	The Efavirenz (EFV) central nervous system exposure sub-study
642	NR	2012	A randomised, double-blind, placebo-controlled, clinical trial to compare the safety and efficacy of reduced dose efavirenz (EFV) with standard dose EFV plus 2N(t)RTI in antiretroviral-naive HIV-infected individuals over 96 weeks. Encore1 intensive pharm
643	NR	2012	The Neurocognitive Sub Study of Encore1: a Randomised, Double-Blind, Placebo-Controlled, Clinical Trial to Compare the Safety and Efficacy of Reduced Dose Efavirenz (EFV) With Standard Dose EFV Plus 2N(t)RTI in Antiretroviral-naive HIV-Infected Individua
644	NR	2012	Safety, Efficacy and Dose response study of BMS-986001 in subjects with HIV-1 Infection who are treatment-naive
645	NR	2012	A clinical trial to compare brain function and neurocognitive performance in antiretroviral treatments with different levels of penetration in the central nervous system

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
646	NR	2012	This open label trial will recruit patients with HIV who are already receiving anti-HIV treatment which includes a Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) and emtricitabine/tenofovir disoproxil fumurate (Truvada). Patients will be randomis
647	NR	2012	Safety and efficacy of switching a stable combined antiretroviral therapeutic regimen to atazanavir with ritonavir plus lamivudine in treatment experienced HIV positive patients with full and stable virological suppression
648	NR	2012	Study to test a new drug dolutegravir vs. darunavir+ritonavir for HIV patients who have never taken HIV medication
649	NR	2012	A Multicentre Trial of Second-line Antiretroviral Treatment Strategies in African Adults Using Atazanavir or Lopinavir/Ritonavir
650	NR	2012	A Clinical Trial Comparing the Efficacy of Darunavir/Ritonavir Monotherapy Versus a Triple Combination Therapy Containing Darunavir/Ritonavir and 2 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors in Patients With Undetectable Plasma HIV-1 RNA on Cu
651	NR	2012	MARCH Renal Substudy
652	NR	2012	Open-Label Study Comparing Efficacy and Safety of ATV/RTV+3TC With ATV/RTV+TDF/FTC in HIV-Infected, Treatment Naïve Subjects, Followed by Treatment With ATV/RTV+3TC
653	NR	2012	The Neurocognitive Sub-study of Encore1
654	NR	2012	Safety of Reduced Dose Zidovudine (AZT) Compared With Standard Dose AZT in Antiretroviral-naïve HIV-infected Patients
655	NR	2012	A Dose-Ranging Study to Compare Doravirine (MK-1439) Plus TRUVADA® Versus Efavirenz Plus TRUVADA® in Human Immunodeficiency Virus (HIV)-1 Infected Participants (MK-1439-007)
656	NR	2012	Differences Between Stavudine and Tenofovir Each Combined With Lamivudine and Efavirenz in SA HIV-infected Patients
657	NR	2012	Raltegravir-based Antiretroviral Therapy for Resistant HIV-1 Infection
658	NR	2012	Study Assessing Dolutegravir in HIV-1 Infected Subjects With Virus Resistant to Raltegravir and/or Elivitegravir
659	NR	2012	Safety and Efficacy of E/C/F/TDF Versus RTV-Boosted ATV Plus FTC/TDF in HIV-1 Infected, Antiretroviral Treatment-Naive Women
660	NR	2012	D/C/F/TAF Versus COBI-boosted DRV Plus FTC/TDF in HIV-1 Infected, Antiretroviral Treatment Naive Adults
661	NR	2012	A Clinical Trial Comparing the Efficacy of Tenofovir Disoproxil Fumarate/Emtricitabine/Rilpivirine (TDF/FTC/RPV) Versus TDF/FTC/Efavirenz (TDF/FTC/EFV) in Patients With Undetectable Plasma HIV-1 RNA on Current First-line Treatment
662	NR	2012	A Study to Compare Efficacy in Terms of Plasma HIV-1 RNA Between 2 Fixed Dose Combinations After a Switch in Fully Suppressed Patients
663	NR	2012	STALEO
664	NR	2012	A Safety and Efficacy Study of Amdoxovir in HIV-1 Treatment-experienced Subjects
665	Gupta	2013	Effects of switching from efavirenz to raltegravir on endothelial function, bone mineral metabolism, inflammation, and renal function: a randomized, controlled trial
666	Reynes	2013	Lopinavir/ritonavir combined with raltegravir or tenofovir/emtricitabine in antiretroviral-naive subjects: 96-week results of the PROGRESS study

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
667	Moyle	2013	96-Week results of abacavir/lamivudine versus tenofovir/emtricitabine, plus efavirenz, in antiretroviral-naive, HIV-1-infected adults: ASSERT study
668	Guaraldi	2013	Randomized trial to evaluate cardiometabolic and endothelial function in patients with plasma HIV-1 RNA suppression switching to darunavir/ritonavir with or without nucleoside analogues
669	Arathoon	2013	Effects of once-daily darunavir/ritonavir versus lopinavir/ritonavir on metabolic parameters in treatment-naive HIV-1-infected patients at week 96: ARTEMIS
670	Elion	2013	A randomized phase 3 study comparing once-daily elvitegravir with twice-daily raltegravir in treatment-experienced subjects with HIV-1 infection: 96-week results
671	Huang	2013	Bone mineral density effects of randomized regimen and nucleoside reverse transcriptase inhibitor selection from ACTG A5142
672	Hunt	2013	The immunologic effects of maraviroc intensification in treated HIV-infected individuals with incomplete CD4+ T-cell recovery: a randomized trial
673	Bernardino	2013	Switching to lopinavir/ritonavir with or without abacavir/lamivudine in lipoatrophic patients treated with zidovudine/abacavir/lamivudine
674	Bonjoch	2013	Switching the third drug of antiretroviral therapy to maraviroc in aviraemic subjects: a pilot, prospective, randomized clinical trial
675	Boyd	2013	Ritonavir-boosted lopinavir plus nucleoside or nucleotide reverse transcriptase inhibitors versus ritonavir-boosted lopinavir plus raltegravir for treatment of HIV-1 infection in adults with virological failure of a standard first-line ART regimen (SECOND-LINE): a randomised, open-label, non-inferiority study
676	Cahn	2013	Dolutegravir versus raltegravir in antiretroviral-experienced, integrase-inhibitor-naive adults with HIV: week 48 results from the randomised, double-blind, non-inferiority SAILING study
677	Campo	2013	SWIFT: prospective 48-week study to evaluate efficacy and safety of switching to emtricitabine/tenofovir from lamivudine/abacavir in virologically suppressed HIV-1 infected patients on a boosted protease inhibitor containing antiretroviral regimen
678	Cotter	2013	Impact of switching from zidovudine to tenofovir disoproxil fumarate on bone mineral density and markers of bone metabolism in virologically suppressed HIV-1 infected patients; a substudy of the PREPARE study
679	Walmsley	2013	Dolutegravir plus abacavir-lamivudine for the treatment of HIV-1 infection
680	Kumar	2013	Evaluation of cardiovascular biomarkers in a randomized trial of fosamprenavir/ritonavir vs. efavirenz with abacavir/lamivudine in underrepresented, antiretroviral-naïve, HIV-infected patients (SUPPORT): 96-week results
681	Martin	2013	Bone mineral density in HIV participants randomized to raltegravir and lopinavir/ritonavir compared with standard second line therapy
682	Rockstroh	2013	A randomized, double-blind comparison of coformulated elvitegravir/cobicistat/emtricitabine/tenofovir DF vs ritonavir-boosted atazanavir plus coformulated emtricitabine and tenofovir DF for initial treatment of HIV-1 infection: analysis of week 96 results
683	Rockstroh	2013	Durable efficacy and safety of raltegravir versus efavirenz when combined with tenofovir/emtricitabine in treatment-naive HIV-1-infected patients: final 5-year results from STARTMRK

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
684	Zolopa	2013	A randomized double-blind comparison of coformulated elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate for initial treatment of HIV-1 infection: analysis of week 96 results
685	Andersson	2013	Lopinavir/ritonavir, atazanavir/ritonavir, and efavirenz in antiretroviral-naïve HIV-1-infected individuals over 144 weeks: An open-label randomized controlled trial
686	Nishijima	2013	Switching tenofovir/emtricitabine plus lopinavir/r to raltegravir plus Darunavir/r in patients with suppressed viral load did not result in improvement of renal function but could sustain viral suppression: a randomized multicenter trial
687	Nishijima	2013	Abacavir/lamivudine versus tenofovir/emtricitabine with atazanavir/ritonavir for treatment-naive Japanese patients with HIV-1 infection: a randomized multicenter trial
688	Orkin	2013	Final 192-week efficacy and safety of once-daily darunavir/ritonavir compared with lopinavir/ritonavir in HIV-1-infected treatment-naïve patients in the ARTEMIS trial
689	Raffi	2013	Once-daily dolutegravir versus twice-daily raltegravir in antiretroviral-naive adults with HIV-1 infection (SPRING-2 study): 96 week results from a randomised, double-blind, non-inferiority trial
690	Raffi	2013	Once-daily dolutegravir versus raltegravir in antiretroviral-naive adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority SPRING-2 study
691	Ribera	2013	Impact of switching from zidovudine/lamivudine to tenofovir/emtricitabine on lipoatrophy: the RECOMB study
692	NR	2013	Pharmacokinetic Study of Albuvirtide and Lopinavir/Ritonavir in HIV-infected Patients
693	NR	2013	A Trial of Observed Long-acting, Anti-HIV Treatment With a Monoclonal CCR5 Antibody (PRO 140) as an Adjunct to a New, Optimized, Oral Antiretroviral Regimen in HIV-infected Injection Drug Users With Viral Rebound and Documented Poor Adherence
694	NR	2013	Antiretroviral treatment with maraviroc plus ritonavir-boosted darunavir for early salvage therapy
695	NR	2013	STUDY TO ASSESS CHANGES IN BONE DENSITY OF THE SWITCH FROM PROTEASE INHIBITORS TO DOLUTEGRAVIR IN HIV-1-INFECTED SUBJECTS WITH LOW BONE MINERAL DENSITY
696	NR	2013	Clinical research study involving an experimental combination medication called EVG/COBI/FTC/TDF. This is 1 pill containing 2 experimental medications, EVG and COBI, plus 2 medications already approved for the treatment of HIV-1 infection, FTC and TDF. I
697	NR	2013	PROBE TRIAL proof-of-concept study on the use of rilpivirine as substitutive agent for the HAART nucleosidic backbone in virologic suppressed patients
698	NR	2013	Study to compare a standard HIV regimen with dolutegravir/abacavir/lamivudine in women
699	NR	2013	Study investigating a new medicine - MK-1439 in patients diagnosed with HIV-1 without previous treatment for this disease. The study has 2 parts and neither the doctor or patient will know the treatment group. All the patients will be treated with Truvad
700	NR	2013	A study is to see if HIV-1 positive subjects currently taking an antiretroviral (ARV) regimen consisting of EVG/COBI/FTC/TDF (E/C/F/TDF) STR, Atripla® (also known as Sustiva®), cobicistat and atazanavir with Truvada® or ritonovir and atazanavir with Truv

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
701	NR	2013	Compare the Efficacy and Safety of Raltegravir Versus Efavirenz Combination Therapy in Treatment-naïve HIV-1 Patients
702	NR	2013	A Prospective, Open-label Trial of Two ABC/3TC Based Regimens in Late Presenter naïve Patients (CD4 <200 Cells/µL)
703	NR	2013	Virological and Immunological Safety of a Dose Reduction Strategy Antiretroviral Regimen With Efavirenz / Tenofovir / Emtricitabine
704	NR	2013	Evaluation of a Maintenance Strategy With Protease Inhibitors With or Without Lamivudine in Virologically Suppressed HIV Patients on Second Line Antiretroviral Treatment in Africa
705	NR	2013	Study to Evaluate the Safety and Efficacy of E/C/F/TAF (Genvoya®) Versus E/C/F/TDF (Stribild®) in HIV-1 Positive, Antiretroviral Treatment-Naive Adults
706	NR	2013	Multicentre Study To Assess Changes In Bone Mineral Density Of The Switch From Protease Inhibitors To Dolutegravir In HIV-1-Infected Subjects With Low Bone Mineral Density
707	NR	2013	Reduction of EArly mortaLITY in HIV-infected Adults and Children Starting Antiretroviral Therapy
708	NR	2013	Efficacy Study of Different Laboratory Management Strategies and Drug Regimens in HIV-infected Children in Africa
709	NR	2013	HAART study
710	NR	2013	Rilpivirine Food PK Study
711	NR	2013	A Study to Determine Safety and Efficacy of Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) in Human Immunodeficiency Virus (HIV)-1 Infected Antiretroviral Therapy (ART) Naïve Women (ARIA)
712	NR	2013	Study of Safety and Pharmacokinetics in Healthy Volunteers and Safety, Tolerability and Antiviral Activity of VM-1500 in Patients With Human Immunodeficiency Virus-1 Infection
713	Echeverría	2014	Randomised study to assess the efficacy and safety of once-daily etravirine-based regimen as a switching strategy in HIV-infected patients receiving a protease inhibitor-containing regimen. Etraswitch study
714	Fabbiani	2014	Safety and efficacy of treatment switch to raltegravir plus tenofovir/emtricitabine or abacavir/lamivudine in patients with optimal virological control: 48-week results from a randomized pilot study (Raltegravir Switch for Toxicity or Adverse Events, RASTA Study)
715	Gianotti	2014	Monotherapy with lopinavir/ritonavir versus standard of care in HIV-infected patients virologically suppressed while on treatment with protease inhibitor-based regimens: results from the MoLo study
716	Castagna	2014	Simplification to atazanavir/ritonavir monotherapy for HIV-1 treated individuals on virological suppression: 48-week efficacy and safety results
717	Cohen	2014	Week 48 results from a randomized clinical trial of rilpivirine/emtricitabine/tenofovir disoproxil fumarate vs. efavirenz/emtricitabine/tenofovir disoproxil fumarate in treatment-naive HIV-1-infected adults
718	Palella	2014	Simplification to rilpivirine/emtricitabine/tenofovir disoproxil fumarate from ritonavir-boosted protease inhibitor antiretroviral therapy in a randomized trial of HIV-1 RNA-suppressed participants
719	Landman	2014	Evaluation of four tenofovir-containing regimens as first-line treatments in Cameroon and Senegal: the ANRS 12115 DAYANA Trial
720	Moyle	2014	Changes in biomarkers in HIV-1-infected treatment-naive patients treated with tenofovir DF/emtricitabine plus atazanavir/ritonavir or lopinavir/ritonavir for 96 weeks: the CASTLE biomarker substudy

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
721	Sax	2014	Tenofovir alafenamide vs. tenofovir disoproxil fumarate in single tablet regimens for initial HIV-1 therapy: a randomized phase 2 study
722	Arribas	2014	Simplification to coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus continuation of ritonavir-boosted protease inhibitor with emtricitabine and tenofovir in adults with virologically suppressed HIV (STRATEGY-PI): 48 week results of a randomised, open-label, phase 3b, non-inferiority trial
723	Bedimo	2014	The RADAR study: week 48 safety and efficacy of RAltegravir combined with boosted DARunavir compared to tenofovir/emtricitabine combined with boosted darunavir in antiretroviral-naive patients. Impact on bone health
724	Cahn	2014	Dual therapy with lopinavir and ritonavir plus lamivudine versus triple therapy with lopinavir and ritonavir plus two nucleoside reverse transcriptase inhibitors in antiretroviral-therapy-naive adults with HIV-1 infection: 48 week results of the randomised, open label, non-inferiority GARDEL trial
725	Clotet	2014	Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naive adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study
726	Cooper	2014	Efficacy and safety of maraviroc vs. efavirenz in treatment-naive patients with HIV-1: 5-year findings
727	Sierra-Madero	2014	Effect of the CCR5 antagonist maraviroc on the occurrence of immune reconstitution inflammatory syndrome in HIV (CADIRIS): a double-blind, randomised, placebo-controlled trial
728	Wohl	2014	Simplification to abacavir/lamivudine + atazanavir maintains viral suppression and improves bone and renal biomarkers in ASSURE, a randomized, open label, non-inferiority trial
729	Lennox	2014	Efficacy and tolerability of 3 nonnucleoside reverse transcriptase inhibitor-sparing antiretroviral regimens for treatment-naive volunteers infected with HIV-1: a randomized, controlled equivalence trial
730	Martinez	2014	Early lipid changes with atazanavir/ritonavir or darunavir/ritonavir
731	Menezes	2014	A randomized clinical trial comparing metabolic parameters after 48 weeks of standard- and low-dose stavudine therapy and tenofovir disoproxil fumarate therapy in HIV-infected South African patients
732	Negredo	2014	Improvement in bone mineral density after switching from tenofovir to abacavir in HIV-1-infected patients with low bone mineral density: two-centre randomized pilot study (OsteoTDF study)
733	Paton	2014	Assessment of second-line antiretroviral regimens for HIV therapy in Africa
734	Pozniak	2014	Switching to coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus continuation of non-nucleoside reverse transcriptase inhibitor with emtricitabine and tenofovir in virologically suppressed adults with HIV (STRATEGY-NNRTI): 48 week results of a randomised, open-label, phase 3b non-inferiority trial
735	Raffi	2014	Ritonavir-boosted darunavir combined with raltegravir or tenofovir-emtricitabine in antiretroviral-naive adults infected with HIV-1: 96 week results from the NEAT001/ANRS143 randomised non-inferiority trial
736	NR	2014	Efficacy and safety of Albuvirtide plus Lopinavir-ritonavir in HIV-1-infected adults failed standard first-line ART regimen
737	NR	2014	A study of Chinese-Western-Combined Therapy for AIDS to improve effect and decrease toxicity
738	NR	2014	Safety Sudy of Atazanavir Capsules in the Treatment of HIV in Patients Ages 6 - 18 Years

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
739	NR	2014	A clinical research study to see how six medications that are approved for the treatment of HIV-1 infection affect the kidneys. The six approved medications are Stribild, Truvada, Atripla, Reyataz, Norvir, and Kivexa. Both the patient and the investigato
740	NR	2014	Randomized study in patients with chronic HIV infection
741	NR	2014	Clinical trial to determinate viral load in seminal fluid in HIV-positive patients without previous treatment
742	NR	2014	Reformulated raltegravir (1200 mg) once a day versus raltegravir (400 mg) twice a day in treatment-naïve patients
743	NR	2014	Immune reconstitution in severely immunosuppressed antiretroviral-naive HIV-1?infected patients (<100 CD4+ T cells/?L) taking antiretroviral regimens based on dolutegravir or ritonavir-boosted darunavir (the AdvanZ-4 Trial)
744	NR	2014	Study to Evaluate the Pharmacodynamics, Safety and Pharmacokinetics of BMS-955176 and BMS-955176 with Atazanavir +/- Ritonavir in HIV-1 Infected Subjects
745	NR	2014	Study to Evaluate Efficacy, Safety and Tolerability of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Regimen Versus Boosted Protease Inhibitor (bPI) Along With Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) Regimen in Virolo
746	NR	2014	ODYSSEY: once daily Dolutegravir in Young people vS Standard thErapY
747	NR	2014	First-Line Treatment for HIV-2
748	NR	2014	Safety, Pharmacokinetics, and Antiviral Activity of GS-9883 in HIV-1 Infected Subjects
749	NR	2014	Safety and Efficacy of Doravirine (MK-1439) in Participants With Human Immunodeficiency Virus 1 (HIV-1) (MK-1439-018)
750	NR	2014	Tipranavir and Ritonavir vs. Saquinavir and Ritonavir Used With Two Nucleoside Reverse Transcriptase Inhibitors in Single Protease Inhibitor-experienced HIV-1 Patients
751	NR	2014	Evaluation of the Safety and Efficacy of Reformulated Raltegravir (MK-0518) 1200 mg Once Daily in Combination With TRUVADA™ in Human Immunodeficiency Virus (HIV)-1 Infected, Treatment-Naive Participants (MK-0518-292)
752	NR	2014	Safety & Efficacy of Dual Therapy With Raltegravir/Lamivudine
753	NR	2014	Exploratory Study of Tipranavir and Ritonavir in Multiple Protease Inhibitor-experienced HIV Patients
754	NR	2014	Evaluation of Renal Function, Efficacy, and Safety When Switching From Tenofovir/Emtricitabine Plus a Protease Inhibitor/Ritonavir, to a Combination of Raltegravir (MK-0518) Plus Nevirapine Plus Lamivudine in HIV-1 Participants With Suppressed Viremia an
755	NR	2014	Efficacy and Safety Study of Darunavir for the Treatment of HIV/AIDS
756	NR	2014	A Randomised Trial of Dolutegravir (DTG)-Based Antiretroviral Therapy vs. Standard of Care (SOC) in Children With HIV Infection Starting First-line or Switching to Second-line ART
757	NR	2014	Efavirenz to Dolutegravir Switch in Patients With CNS Toxicity
758	NR	2014	Comparative Efficacy and Safety Study of Dolutegravir and Lopinavir/Ritonavir in Second-line Treatment
759	NR	2014	Study to Evaluate Efficacy and Safety of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Regimen Versus Boosted Protease Inhibitor (bPI) Along With Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) Regimen in Virologically-Suppre

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
760	NR	2014	Efficacy and Safety Study of Darunavir for the Treatment of HIV/AIDS
761	NR	2014	PROJECT AHORA-L
762	NR	2014	A Phase III Multicenter, Double-Blind, Randomized, Active Comparator-Controlled Clinical Trial to Evaluate the Safety and Efficacy of Reformulated Raltegravir 1200 mg Once Daily Versus Raltegravir 400 mg Twice Daily, Each in Combination With TRUVADA™, in
763	NR	2014	A PHASE 3B, RANDOMISED, OPEN-LABEL STUDY OF THE ANTIVIRAL ACTIVITY AND SAFETY OF DOLUTEGRAVIR COMPARED TO LOPINAVIR/RITONAVIR BOTH ADMINISTERED WITH DUAL NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR THERAPY IN HIV-1 INFECTED ADULT SUBJECTS WITH TREATMENT F
764	NR	2014	DRV/r + RPV QD: Efficacy and Toxicity Reduction
765	NR	2014	Effect of switching efavirenz to rilpivirine in treatment of HIV- infected patients with dyslipidemia
766	NR	2014	A Phase IIIb Study of the Safety, Efficacy, and Tolerability of Switching to a Fixed-dose Combination of Abacavir/Dolutegravir/ Lamivudine From Current Antiretroviral Regimen
767	Gallant	2015	Brief Report: Cobicistat Compared With Ritonavir as a Pharmacoenhancer for Atazanavir in Combination With Emtricitabine/Tenofovir Disoproxil Fumarate: Week 144 Results
768	Gathe	2015	Patient-Reported Symptoms over 48 Weeks in a Randomized, Open-Label, Phase 3b Non-inferiority Trial of Adults with HIV Switching to Coformulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir DF Versus Continuation of Ritonavir-Boosted Protease Inhibitor with Emtricitabine and Tenofovir DF
769	Gallant	2015	Cobicistat Compared With Ritonavir as a Pharmacoenhancer for Atazanavir in Combination With Emtricitabine/Tenofovir Disoproxil Fumarate: week 144 Results
770	Mills	2015	Switching from a tenofovir disoproxil fumarate (TDF)-based regimen to a tenofovir alafenamide (TAF)-based regimen: data in virologically suppressed adults through 48 weeks of treatment
771	Walmsley	2015	Dolutegravir plus abacavir/lamivudine for the treatment of HIV-1 infection in antiretroviral therapy-naive patients: week 96 and week 144 results from the SINGLE randomized clinical trial
772	Goodal	2015	Once vs. twice-daily lopinavir/ritonavir in HIV-1-infected children: paediatric European Network for Treatment of AIDS (PENTA)
773	Akil	2015	Dolutegravir versus placebo in subjects harbouring HIV-1 with integrase inhibitor resistance associated substitutions: 48-week results from VIKING-4, a randomized study
774	Mills	2015	Tenofovir Alafenamide Versus Tenofovir Disoproxil Fumarate in the First Protease Inhibitor-Based Single-Tablet Regimen for Initial HIV-1 Therapy: A Randomized Phase 2 Study
775	Miro	2015	Immune Reconstitution in Severely Immunosuppressed Antiretroviral-Naive HIV-1-Infected Patients Starting Efavirenz, Lopinavir-Ritonavir, or Atazanavir-Ritonavir Plus Tenofovir/Emtricitabine: Final 48-Week Results (The Advanz-3 Trial)
776	Antinori	2015	Week 48 efficacy and central nervous system analysis of darunavir/ritonavir monotherapy versus darunavir/ritonavir with two nucleoside analogues

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
777	Arribas	2015	Dual treatment with lopinavir-ritonavir plus lamivudine versus triple treatment with lopinavir-ritonavir plus lamivudine or emtricitabine and a second nucleos(t)ide reverse transcriptase inhibitor for maintenance of HIV-1 viral suppression (OLE): a randomised, open-label, non-inferiority trial
778	Chéret	2015	Intensive five-drug antiretroviral therapy regimen versus standard triple-drug therapy during primary HIV-1 infection (OPTIPRIM-ANRS 147): a randomised, open-label, phase 3 trial
779	Coovadia	2015	Efavirenz-Based Antiretroviral Therapy Among Nevirapine-Exposed HIV-Infected Children in South Africa: A Randomized Clinical Trial
780	Stein	2015	A prospective, randomized clinical trial of antiretroviral therapies on carotid wall thickness
781	Taiwo	2015	Less Bone Loss With Maraviroc- Versus Tenofovir-Containing Antiretroviral Therapy in the AIDS Clinical Trials Group A5303 Study
782	Tashima	2015	HIV Salvage Therapy Does Not Require Nucleoside Reverse Transcriptase Inhibitors: A Randomized, Controlled Trial
783	Tebas	2015	Greater change in bone turnover markers for efavirenz/emtricitabine/tenofovir disoproxil fumarate versus dolutegravir + abacavir/lamivudine in antiretroviral therapy-naive adults over 144 weeks
784	Walmsley	2015	Brief Report: Dolutegravir Plus Abacavir/Lamivudine for the Treatment of HIV-1 Infection in Antiretroviral Therapy-Naive Patients: Week 96 and Week 144 Results From the SINGLE Randomized Clinical Trial
785	Lalezari	2015	Safety and efficacy of the HIV-1 attachment inhibitor prodrug BMS-663068 in treatment-experienced individuals: 24 week results of AI438011, a phase 2b, randomised controlled trial
786	Margolis	2015	Cabotegravir plus rilpivirine, once a day, after induction with cabotegravir plus nucleoside reverse transcriptase inhibitors in antiretroviral-naive adults with HIV-1 infection (LATTE): a randomised, phase 2b, dose-ranging trial
787	Martinez	2015	Differential body composition effects of protease inhibitors recommended for initial treatment of HIV infection: a randomized clinical trial
788	Molina	2015	Once-daily dolutegravir versus darunavir plus ritonavir for treatment-naive adults with HIV-1 infection (FLAMINGO): 96 week results from a randomised, open-label, phase 3b study
789	Moyle	2015	A randomized comparative trial of continued abacavir/lamivudine plus efavirenz or replacement with efavirenz/emtricitabine/tenofovir DF in hypercholesterolemic HIV-1 infected individuals
790	Paton	2015	Protease inhibitor monotherapy for long-term management of HIV infection: a randomised, controlled, open-label, non-inferiority trial
791	NR	2015	Safety and efficacy study of Different Interval Dose Administration Sifuvirtide for Injection
792	NR	2015	The Dolutegravir Antiretroviral Mono-Therapy for HIV Trial
793	NR	2015	A study to test the safety, tolerability and ability to maintain HIV suppression of switching from a tenofovir disoproxil fumarate (TDF) containing regimen to elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide (E/C/F/TAF) fixed-dose combination
794	NR	2015	This study will test an experimental drug called GS-9883/F/TAF (GS-9883/emtricitabine/tenofovir alafenamide) fixed dose combination (FDC) for the treatment of HIV-1 infection. The purpose of this study is to test the effectiveness of switching to GS-9883

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
795	NR	2015	This study will test an experimental drug called GS-9883/emtricitabine/tenofovir alafenamide (GS-9883/F/TAF) for the treatment of HIV-1 infection. The purpose of this study is to evaluate safety, and to determine whether GS-9883/F/TAF as a fixed dose com
796	NR	2015	The purpose of this study is to evaluate if F/R/TAF works as well as Eviplera. It is also to see if F/R/TAF will maintain the control of your HIV-1 infection when compared to Eviplera. Safety, how well your body accepts the drug, will be evaluated
797	NR	2015	A study to test the safety, tolerability and ability to maintain HIV suppression of of switching from a current regimen consisting of abacavir/lamivudine (ABC/3TC) plus a third antiretroviral agent to the elvitegravir/cobicistat/emtricitabine/tenofovir a
798	NR	2015	The purpose of this study is to evaluate if F/R/TAF works as well as Atripla. It is also to see if F/R/TAF will maintain the control of your HIV-1 infection when compared to Atripla. Safety, how well your body accepts the drug, will be evaluated
799	NR	2015	Outcome of plasma lipid profile in patients switching from Atripla® to Eviplera® compared to continuing on Atripla® (EfaRiLipidomics)
800	NR	2015	A pilot 24-week open-label, randomized, controlled clinical trial to assess the safety, tolerability and efficacy of dual therapy with Raltegravir/Lamivudine combination when replacing standard combination therapy in HIV-infected patients with prolonged
801	NR	2015	clinical trial to assess the safety, tolerability and efficacy of two dolutegravir-based simplification strategies in HIV-infected patients with prolonged virological suppression
802	NR	2015	The role of Home packs of HIV PEPSE in High Risk Individuals
803	NR	2015	MK-1439A once a day versus ATRIPLA once a day in treatment-naïve HIV-1 infected subjects
804	NR	2015	A Study to Evaluate Efficacy and Safety of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Fixed Dose Combination (FDC) Versus a Regimen Consisting of Darunavir/Cobicistat FDC with Emtricitabine/Tenofovir Disoproxil Fumarate FDC in T
805	NR	2015	Switch from Efavirenz/Atripla to Rilpivirine
806	NR	2015	A Phase III, randomized, multicenter, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current integrase inhibitor, NNRTI, or PI-based antiretroviral regimen in HIV
807	NR	2015	De Dolutegravir Antiretroviral Mono-Therapy for HIV Trial
808	NR	2015	Study investigating a new medicine - Doravirine in patients diagnosed with HIV-1 without previous treatment for this disease. Neither the doctor or patient will know the treatment group. All the patients will be treated with Truvada or Epzicom/Kivexa, so
809	NR	2015	SMILE: strategy for Maintenance of HIV suppression with elvitegravir + darunavir/ritonavir in children (PENTA 17)
810	NR	2015	A Study of Islatravir (MK-8591) in Anti-Retroviral Therapy-Naive, Human Immunodeficiency Virus-1 Infected Participants (MK-8591-003)
811	NR	2015	Safety and Efficacy of a Switch to MK-1439A in Human Immunodeficiency Virus (HIV-1)-Infected Participants Virologically Suppressed on an Anti-retroviral Regimen in Combination With Two Nucleoside Reverse Transcriptase Inhibitors (MK-1439A-024)
812	NR	2015	Switch Study to Evaluate F/TAF in HIV-1 Infected Adults Who Are Virologically Suppressed on Regimens Containing ABC/3TC

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
813	NR	2015	Darunavir/Ritonavir + Lamivudine Versus Darunavir/Ritonavir +Emtricitabine/Tenofovir in Naïve HIV-1 Infected Subjects
814	NR	2015	Test Albuvirtide in Experienced Patients
815	NR	2015	Strategy for Maintenance of HIV Suppression With Once Daily Integrate Inhibitor+Darunavir/Ritonavir in Children
816	NR	2015	Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Adults Who Are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fum
817	NR	2015	Efficacy, Safety and Optimal Dose Selection VM-1500 in Comparison to Efavirenz When Added to Standard-of-care Antiretroviral Therapy
818	NR	2015	Study to Evaluate the Efficacy of MONotherapy of TiviCAY® Versus a Triple Therapy in HIV-1-infected Patients
819	NR	2015	Strategy-confirming Study of BMS-955176 to Treat HIV-1 Infected Treatment-experienced Adults
820	NR	2015	Switching From a Tenofovir Disoproxil Fumarate (TDF) Containing Regimen to Elvitegravir/Cobicistat/Emtricitabine/ Tenofovir Alafenamide (E/C/F/TAF) Fixed-Dose Combination (FDC) in Virologically-Suppressed, HIV-1 Infected Adults Aged ≥ 60 Years
821	NR	2015	Safety and Efficacy of Switching From Regimens of ABC/3TC + a 3rd Agent to E/C/F/TAF Fixed-Dose Combination (FDC) in Virologically-Suppressed HIV 1 Infected Adults
822	NR	2015	Renal Integrase Study
823	NR	2015	Darunavir/Cobicistat and Dolutegravir to Maintain Virologic Suppression and Reduce NRTI-associated Toxicity
824	NR	2015	Safety and Efficacy of Switching From Regimens Consisting of Boosted Atazanavir or Darunavir Plus Either Emtricitabine/Tenofovir or Abacavir/Lamivudine to Bictegravir/Emtricitabine/Tenofovir Alafenamide in Virologically Suppressed HIV-1 Infected Adults
825	NR	2015	Safety and Efficacy of Switching From Dolutegravir and ABC/3TC or ABC/DTG/3TC to B/F/TAF in HIV-1 Infected Adults Who Are Virologically Suppressed
826	NR	2015	Dual Therapy With Boosted Darunavir + Dolutegravir
827	NR	2015	Safety, PK and PD Study of ABX464 in Untreated HIV Patients
828	NR	2015	Immune Recovery in Advanced , ARV-naïve, HIV-1-infected Individuals Taking Dolutegravir or Ritonavir-boosted Darunavir
829	NR	2015	Safety and Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide Versus Abacavir/Dolutegravir/Lamivudine in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults
830	NR	2015	Safety and Efficacy of Bictegravir + Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naive Adults
831	NR	2015	MK-1439A VERSUS ATRIPLA™ IN TREATMENT-NAÏVE HIV-INFECTED SUBJECTS
832	NR	2015	A PHASE 2B RANDOMIZED, ACTIVE-CONTROLLED, STAGED, OPEN-LABEL TRIAL TO INVESTIGATE SAFETY AND EFFICACY OF BMS-955176 IN COMBINATION WITH DOLUTEGRAVIR AND ATAZANAVIR (WITH OR WITHOUT RITONAVIR) IN TREATMENT-EXPERIENCED HIV-1 INFECTED ADULTS
833	NR	2015	Bone Mineral Density in Human Immunodeficiency Virus Type 1 (HIV-1)-Infected Adult Subjects Switching From a Tenofovir Regimen to a Dolutegravir Plus Rilpivirine Regimen

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
834	Gallant	2016	Efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate given as fixed-dose combinations containing emtricitabine as backbones for treatment of HIV-1 infection in virologically suppressed adults: a randomised, double-blind, active-controlled phase 3 trial
835	Ripa	2016	Maraviroc in addition to cART during primary HIV infection: results from MAIN randomized clinical trial and 96-weeks follow-up
836	Van Lunzen	2016	Switch to ritonavir-boosted atazanavir plus raltegravir in virologically suppressed patients with HIV-1 infection: a randomized pilot study
837	van Lunzen	2016	Rilpivirine vs. efavirenz-based single-tablet regimens in treatment-naive adults: week 96 efficacy and safety from a randomized phase 3b study
838	Wilkins	2016	Patient-reported outcomes in the single-tablet regimen (STaR) trial of rilpivirine/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate in antiretroviral treatment-naive adults infected with HIV-1 through 48 weeks of treatment
839	Hamzah	2016	Effects on vitamin D, bone and the kidney of switching from fixed-dose tenofovir disoproxil fumarate/emtricitabine/efavirenz to darunavir/ritonavir monotherapy: a randomized, controlled trial (MIDAS)
840	Maggiolo	2016	NRTI Sparing Therapy in Virologically Controlled HIV-1 Infected Subjects: Results of a Controlled, Randomized Trial (Probe)
841	Cook	2016	Bone Mineral Density and Vitamin D Levels in HIV Treatment-Naïve African American Individuals Randomized to Receive HIV Drug Regimens
842	Collins	2016	A Randomized Switch From Nevirapine-Based Antiretroviral Therapy to Single Tablet Rilpivirine/Emtricitabine/Tenofovir Disoproxil Fumarate in Virologically Suppressed Human Immunodeficiency Virus-1-Infected Rwandans
843	Cooper	2016	Tipranavir/Ritonavir (500/200 mg and 500/100 mg) Was Virologically Non-Inferior to Lopinavir/Ritonavir (400/100 mg) at Week 48 in Treatment-Naïve HIV-1-Infected Patients: A Randomized, Multinational, Multicenter Trial
844	Rougemont	2016	Safety of zidovudine dose reduction in treatment-naïve HIV infected patients. A randomized controlled study (MiniZID)
845	Slama	2016	Efficacy and safety of once-daily ritonavir-boosted atazanavir or darunavir in combination with a dual nucleos(t)ide analogue backbone in HIV-1-infected combined ART (cART)-naive patients with severe immunosuppression: a 48 week, non-comparative, randomized, multicentre trial (IMEA 040 DATA trial)
846	Stellbrink	2016	Once-daily maraviroc versus tenofovir/emtricitabine each combined with darunavir/ritonavir for initial HIV-1 treatment
847	The BREATHER (PENTA 16) Trial Group	2016	Weekends-off efavirenz-based antiretroviral therapy in HIV-infected children, adolescents, and young adults (BREATHER): a randomised, open-label, non-inferiority, phase 2/3 trial
848	Wohl	2016	The ASSURE study: HIV-1 suppression is maintained with bone and renal biomarker improvement 48 weeks after ritonavir discontinuation and randomized switch to abacavir/lamivudine + atazanavir
849	Wu	2016	Efficacy and safety of long-acting HIV fusion inhibitor albuvirtide in antiretroviral-experienced adults with HIV-1: interim 48-week results from the randomized, controlled, phase 3, non-inferiority TALENT study
850	La Rosa	2016	Raltegravir in second-line antiretroviral therapy in resource-limited settings (SELECT): a randomised, phase 3, non-inferiority study

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
851	Llamoso	2016	HIV-1 attachment inhibitor prodrug BMS-663068 in antiretroviral-experienced subjects: week 96 safety analysis
852	McComsey	2016	Body Composition Changes After Initiation of Raltegravir or Protease Inhibitors: ACTG A5260s
853	Mills	2016	Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study
854	Mulenga	2016	Abacavir, zidovudine, or stavudine as paediatric tablets for African HIV-infected children (CHAPAS-3): an open-label, parallel-group, randomised controlled trial
855	Musiime	2016	Once vs twice-daily abacavir and lamivudine in African children
856	Pett	2016	Maraviroc, as a Switch Option, in HIV-1–infected Individuals With Stable, Well-controlled HIV Replication and R5-tropic Virus on Their First Nucleoside/Nucleotide Reverse Transcriptase Inhibitor Plus Ritonavir-boosted Protease Inhibitor Regimen: Week 48 Results of the Randomized, Multicenter MARCH Study
857	Rojas	2016	Improvement of lipoatrophy by switching from efavirenz to lopinavir/ritonavir
858	Santos	2016	Short Communication: Efficacy and Safety of Treatment Simplification to Lopinavir/Ritonavir or Darunavir/Ritonavir Monotherapy: A Randomized Clinical Trial
859	Overton	2016	Effects of once-daily darunavir/ritonavir versus atazanavir/ritonavir on insulin sensitivity in HIV-infected persons over 48 weeks: results of an exploratory substudy of METABOLIK, a phase 4, randomized trial
860	NR	2016	Safety study of ABX464 in HIV controlled patients treated with boosted protease inhibitor treatment
861	NR	2016	A study to evaluate the efficacy, safety, and tolerability of dolutegravir plus lamivudine compared to dolutegravir plus tenofovir/emtricitabine in HIV-1-infected patients that have not been treated yet
862	NR	2016	Assess the effect of switching HIV-1 infected subjects with CNS toxicity (= Grade 2) from ATRIPLA™ or its components to MK-1439A
863	NR	2016	Switching to tenofovir alafenamide fumarate or abacavir in patients with renal impairment due to tenofovir disoproxil fumarate
864	NR	2016	A Phase III study to compare two drugs (called Cabotegravir and Rilpivirine, as oral tablets followed by long-acting injections) to current HIV regimens containing three drugs
865	NR	2016	Single and Repeated Dose Escalation Study of GSK2838232
866	NR	2016	Comparative efficacy and safety study of dolutegravir and lopinavir/ritonavir in second-line treatment
867	NR	2016	Safety and Biological Activity of Vesatolimod in HIV-1 Infected, Virologically Suppressed Adults
868	NR	2016	Effects of Switching From ATRIPLA^TM (Efavirenz, Tenofovir, Emtricitabine) to MK-1439A (Doravirine, Tenofovir, Lamivudine) in Virologically-Suppressed Participants (MK-1439A-028)
869	NR	2016	Evaluation of Low-dose Darunavir in a Switch Study
870	NR	2016	Impact of CCR5 Blockade in HIV+ Kidney Transplant Recipients
871	NR	2016	Efficacy, and Safety Study of Optimized Background Antiretroviral Regimen (OB) in Combination With Enfuvirtide in the Treatment-Experienced Participants With Human Immunodeficiency Virus-1 (HIV-1) Infection
872	NR	2016	Switching From Tenofovir Disoproxil Fumarate to Abacavir or Tenofovir Alafenamide
873	NR	2016	Bone Health in Aging HIV Infected Women

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
874	NR	2016	Protease Inhibitor vs. Raltegravir-based ART and Inflammation in HIV Infection
875	NR	2016	Safety and Efficacy of Switching to a FDC of B/F/TAF From E/C/F/TAF, E/C/F/TDF, or ATV+RTV+FTC/TDF in Virologically Suppressed HIV-1 Infected Women
876	NR	2016	Efficacy and Safety of a Dolutegravir-based Regimen for the Initial Management of HIV Infected Adults in Resource-limited Settings
877	NR	2016	Dose Optimisation of Stavudine for the Treatment of HIV Infection
878	NR	2016	Study Evaluating the Efficacy, Safety, and Tolerability of Switching to Long-acting Cabotegravir Plus Long-acting Rilpivirine From Current Antiretroviral Regimen in Virologically Suppressed HIV-1-infected Adults
879	NR	2016	An Efficacy, Safety, and Tolerability Study Comparing Dolutegravir Plus Lamivudine With Dolutegravir Plus Tenofovir/Emtricitabine in Treatment naïve HIV Infected Subjects (Gemini 1)
880	NR	2016	An Efficacy, Safety, and Tolerability Study Comparing Dolutegravir (DTG) Plus Lamivudine (3TC) With Dolutegravir Plus Tenofovir/Emtricitabine in Treatment naïve HIV Infected Subjects (Gemini 2)
881	NR	2016	Study to Evaluate the Efficacy, Safety, and Tolerability of Long-acting Intramuscular Cabotegravir and Rilpivirine for Maintenance of Virologic Suppression Following Switch From an Integrase Inhibitor in HIV-1 Infected Therapy Naive Participants
882	NR	2016	Study to evaluate and compare anti retroviral tablet formulations for oral fixed dose and solutions in children
883	NR	2016	Malnutrition and Antiretroviral Timing in Children with HIV (MATCH)
884	NR	2016	toxicity, and the drug dosing parameters evaluations comparing dispersible tablets of efavirenz and oral liquid in children
885	DeJesus	2017	Switching from efavirenz, emtricitabine, and tenofovir disoproxil fumarate to tenofovir alafenamide coformulated with rilpivirine and emtricitabine in virally suppressed adults with HIV-1 infection: a randomised, double-blind, multicentre, phase 3b, non-inferiority study
886	Di Giambenedetto	2017	Treatment simplification to atazanavir/ritonavir + lamivudine versus maintenance of atazanavir/ritonavir + two NRTIs in virologically suppressed HIV-1-infected patients: 48 week results from a randomized trial (ATLAS-M)
887	Gallant	2017	Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial
888	Gatell	2017	Switching from a ritonavir-boosted protease inhibitor to a dolutegravir-based regimen for maintenance of HIV viral suppression in patients with high cardiovascular risk
889	Girard	2017	Week 96 efficacy and safety of darunavir/ritonavir monotherapy vs. darunavir/ritonavir with two nucleoside reverse transcriptase inhibitors in the PROTEA trial
890	Van Der Heijden	2017	A switch to raltegravir does not lower platelet reactivity in HIV-infected adults
891	Cournil	2017	Evolution of renal function in African patients initiating second-line antiretroviral treatment: findings from the ANRS 12169 2LADY trial
892	Trottier	2017	Dolutegravir/abacavir/lamivudine versus current ART in virally suppressed patients (STRIIVING): a 48-week, randomized, non-inferiority, open-label, Phase IIIb study

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
893	Arribas	2017	Simplification to single-tablet regimen of elvitegravir, cobicistat, emtricitabine, tenofovir DF from multi-tablet ritonavir-boosted protease inhibitor plus coformulated emtricitabine and tenofovir DF regimens: week 96 results of STRATEGY-PI
894	Harris	2017	Efficacy and safety of "unboosting" atazanavir in a randomized controlled trial among HIV-infected patients receiving tenofovir DF
895	Pozniak	2017	Switching to the single-tablet regimen of elvitegravir, cobicistat, emtricitabine, and tenofovir DF from non-nucleoside reverse transcriptase inhibitor plus coformulated emtricitabine and tenofovir DF regimens: Week 96 results of STRATEGY-NNRTI
896	Huhn	2017	A Randomized, Open-Label Trial to Evaluate Switching to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Plus Darunavir in Treatment-Experienced HIV-1-Infected Adults
897	Agwu	2017	Decline in CD4 T lymphocytes with monotherapy bridging strategy for non-adherent adolescents living with HIV infection: Results of the IMPAACT P1094 randomized trial
898	Boyd	2017	Body composition and metabolic outcomes after 96 weeks of treatment with ritonavir-boosted lopinavir plus either nucleoside or nucleotide reverse transcriptase inhibitors or raltegravir in patients with HIV with virological failure of a standard first-line antiretroviral therapy regimen: a substudy of the randomised, open-label, non-inferiority SECOND-LINE study
899	Ciaffi	2017	Boosted protease inhibitor monotherapy versus boosted protease inhibitor plus lamivudine dual therapy as second-line maintenance treatment for HIV-1-infected patients in sub-Saharan Africa (ANRS12 286/MOBIDIP): a multicentre, randomised, parallel, open-label, superiority trial
900	Dahourou	2017	Efavirenz-based simplification after successful early lopinavir-boosted-ritonavir-based therapy in HIV-infected children in Burkina Faso and Côte d'Ivoire: the MONOD ANRS 12206 non-inferiority randomised trial
901	Kroidl	2017	Virological efficacy of 24-week fozivudine-based regimen in ART-naive patients from Tanzania and Côte d'Ivoire
902	Margolis	2017	Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial
903	Negredo	2017	Switching from a ritonavir-boosted PI to dolutegravir as an alternative strategy in virologically suppressed HIV-infected individuals
904	Orkin	2017	Switching from tenofovir disoproxil fumarate to tenofovir alafenamide coformulated with rilpivirine and emtricitabine in virally suppressed adults with HIV-1 infection: a randomised, double-blind, multicentre, phase 3b, non-inferiority study
905	Perez-Molina	2017	Simplification to dual therapy (atazanavir/ritonavir+lamivudine) versus standard triple therapy [atazanavir/ritonavir+two nucleos(t)ides] in virologically stable patients on antiretroviral therapy: 96 week results from an open-label, non-inferiority, randomized clinical trial (SALT study)
906	Pulido	2017	Dual Therapy With Darunavir and Ritonavir Plus Lamivudine vs Triple Therapy With Darunavir and Ritonavir Plus Tenofovir Disoproxil Fumarate and Emtricitabine or Abacavir and Lamivudine for Maintenance of Human Immunodeficiency Virus Type 1 Viral Suppression: Randomized, Open-Label, Noninferiority DUAL-GESIDA 8014-RIS-EST45 Trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
907	Raffi	2017	Brief Report: Long-Term (96-Week) Efficacy and Safety After Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in HIV-Infected, Virologically Suppressed Adults
908	NR	2017	A Clinical Trial to Study the Safety and Efficacy of TLE-400mg Vs TLE-600mg in Indian Patients with HIV-1 Infection
909	NR	2017	DREAM study
910	NR	2017	A study to evaluate the effect of changing HIV medication (from a protease inhibitor or efavirenz to raltegravir) on liver fat, fat tissue and metabolic parameters (blood sugar and cholesterol, etc) in overweight or obese patients with metabolic problems
911	NR	2017	This study will test an experimental drug called B/F/TAF (bictegravir/emtricitabine/tenofovir alafenamide) fixed dose combination (FDC) for the treatment of HIV-1 infection. The purpose of this study is to test the effectiveness of switching to B/F/TAF F
912	NR	2017	Children with HIV in Africa – pharmacokinetics and acceptability of simple second-line antiretroviral regimens
913	NR	2017	Activity of MK-8504 in Anti-retroviral-naïve, Human Immunodeficiency Virus 1 (HIV-1) Infected Participants (MK-8504-002)
914	NR	2017	MK-8591 With Doravirine and Lamivudine in Participants Infected With Human Immunodeficiency Virus Type 1 (MK-8591-011)
915	NR	2017	UB-421 Combine With Optimized Background Therapy Regimen in Multi-Drug Resistant HIV-1 Infection Patients
916	NR	2017	ADVANCE Study of DTG + TAF + FTC vs DTG + TDF + FTC and EFV + TDF+FTC in First-line Antiretroviral Therapy
917	NR	2017	Efficacy, Safety and Tolerability Study of Long-acting Cabotegravir Plus Long-acting Rilpivirine (CAB LA + RPV LA) in Human-immunodeficiency Virus-1 (HIV-1) Infected Adults
918	NR	2017	Switching TDF/FTC/EFV to TDF/FTC/RPV VS Continuing TDF/FTC/EFV in HIV Patients With Complete Virological Suppression
919	NR	2017	Effect on Liver Fat and Metabolic Parameters When Switching a Protease Inhibitor or Efavirenz to Raltegravir
920	NR	2017	A Phase IV, Open-label, Randomised, Pilot Clinical Trial Designed to Evaluate the Potential Neurotoxicity of Dolutegravir/Lamivudine/Abacavir in Neurosymptomatic HIV Patients and Its Reversibility After Switching to Elvitegravir/Cobicistat/Emtricitabine
921	NR	2017	(mo)BETTA Trial in Transwomen for Optimization of ART
922	Fabbiani	2018	Atazanavir/ritonavir with lamivudine as maintenance therapy in virologically suppressed HIV-infected patients: 96 week outcomes of a randomized trial
923	Hakim	2018	Lopinavir plus nucleoside reverse-transcriptase inhibitors, lopinavir plus raltegravir, or lopinavir monotherapy for second-line treatment of HIV (EARNEST): 144-week follow-up results from a randomised controlled trial
924	Li	2018	Dual therapy with lopinavir/ritonavir plus lamivudine could be a viable alternative for antiretroviral-therapy-naive adults with HIV-1 infection regardless of HIV viral load or subgenotype in resource-limited settings: A randomised, open-label and non-inferiority study from China
925	Jespersen	2018	Protease Inhibitors or NNRTIs as First-Line HIV-1 Treatment in West Africa (PIONA): A Randomized Controlled Trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
926	Amstutz	2018	SESOTHO trial ("Switch Either near Suppression Or THOusand") - switch to second-line versus WHO-guided standard of care for unsuppressed patients on first-line ART with viremia below 1000 copies/mL: protocol of a multicenter, parallel-group, open-label, randomized clinical trial in Lesotho, Southern Africa
927	Daar	2018	Efficacy and safety of switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from boosted protease inhibitor-based regimens in virologically suppressed adults with HIV-1: 48 week results of a randomised, open-label, multicentre, phase 3, non-inferiority trial
928	Winston	2018	Tenofovir alafenamide plus emtricitabine versus abacavir plus lamivudine for treatment of virologically suppressed HIV-1-infected adults: a randomised, double-blind, active-controlled, non-inferiority phase 3 trial
929	Kityo	2018	Raltegravir-intensified initial antiretroviral therapy in advanced HIV disease in Africa: A randomised controlled trial
930	Kumar	2018	Switch to doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) maintains virologic suppression trough 48 weeks: results of the DRIVE-SHIFT trial
931	Margolis	2018	Safety, efficacy and durability of long-acting CAB and RPV as two-drug im maintenance therapy for HIV-1 infection: lATTE-2 Week 160 results
932	McComsey	2018	Switch from tenofovir disoproxil fumarate combination to dolutegravir with rilpivirine improves parameters of bone health
933	Molina	2018	Doravirine versus ritonavir-boosted darunavir in antiretroviral-naive adults with HIV-1 (DRIVE-FORWARD): 48-week results of a randomised, double-blind, phase 3, non-inferiority trial
934	Molina	2018	Switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from dolutegravir plus abacavir and lamivudine in virologically suppressed adults with HIV-1: 48 week results of a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial
935	Pasquau	2018	High quality of life, treatment tolerability, safety and efficacy in HIV patients switching from triple therapy to lopinavir/ritonavir monotherapy: A randomized clinical trial
936	Pett	2018	Week 96 results of the randomized, multicentre Maraviroc Switch (MARCH) study
937	Rasmussen	2018	The effect of antiretroviral intensification with dolutegravir on residual virus replication in HIV-infected individuals: a randomised, placebo-controlled, double-blind trial
938	DeJesus	2018	Superior Efficacy and Improved Renal and Bone Safety After Switching from a Tenofovir Disoproxil Fumarate- to a Tenofovir Alafenamide-Based Regimen Through 96 Weeks of Treatment
939	NR	2018	Evaluation of the efficacy and safety of integrase inhibitor in the treatment of acute HIV infection
940	NR	2018	A clinical trial to study the effects of newly marketed antiretroviral drug, Tab. Dolutegravir 50 mg, when given along with other Antiretroviral drugs in HIV1 positive individuals
941	NR	2018	To determine the efficacy, safety and tolerability of two approved medicines, dolutegravir (DTG) plus lamivudine (3TC) taken together as a single tablet, compared with subjects taking their current tenofovir alafenamide (TAF)-based regimen (TBR) for the
942	NR	2018	An open-label, multi-centre, randomised, switch study to evaluate the virological efficacy over 96 weeks of 2-drug therapy with DTG/RPV FDC in antiretroviral treatment-experienced HIV-1 infected subjects virologically suppressed with NNRTIs resistance mu

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
943	NR	2018	Raltegravir One Thousand two hundred vs Darunavir-cb in Immnunosupressed Patients: ROTDIP Study
944	NR	2018	DETOX Study
945	NR	2018	EFFICACY AND SAFETY OF A SIMPLIFICATION TREATMENT BASED ON DOLUTEGRAVIR AND DARUNAVIR / COBICISTAT VS USUAL TREATMENT IN SUPPRESSED HIV-1-INFECTED PATIENTS WITH MULTIDRUG RESISTANCE
946	NR	2018	Dose Ranging Trial of MK-8591 Given in Combination with Doravirine (DOR) and Lamivudine (3TC)
947	NR	2018	A phase IV, open-label pilot study investigating non-invasive markers of hepatic fibrosis in people living with HIV-1 and non-alcoholic fatty liver disease randomised to receiving optimised background therapy (OBT) plus maraviroc or OBT
948	NR	2018	Single-Dose Study of MK-4250 Monotherapy in Anti-Retroviral Therapy-Naive, Human Immunodeficiency Virus (HIV)-1 Infected Participants (MK-4250-002)
949	NR	2018	Same-Day Treatment With Genvoya vs. EFV/TDF/3TC
950	NR	2018	Safety, Pharmacokinetics, and Antiviral Activity of GS-6207 Administered Subcutaneously in HIV-1 Infected Adults
951	NR	2018	The HIV Functional Cure Potential of UB-421 in ART Stabilized HIV-1 Patients
952	NR	2018	A Proof of Concept Study of GSK3640254 in Human Immunodeficiency Virus-1 (HIV-1) Infected Treatment-naive Adults
953	NR	2018	Albuvirtide and 3BNC117 as Long-Acting Maintenance Therapy in Virologically Suppressed Subjects
954	NR	2018	Evaluating Long-Acting Antiretroviral Therapy in Non-Adherent HIV-Infected Individuals
955	NR	2018	A Clinical Trial to Evaluate the Reversibility of Abacavir/Lamivudine/Dolutegravir CNS-Related Neurotoxicity After Switching to Tenofovir/Alafenamide/Emtricitabine/Darunavir/Cobicistat (TAF/FTC/DRV/c)
956	NR	2018	Switch From Dual Regimens Based on Dolutegravir Plus a Reverse Transcriptase Inhibitor to E/C/F/TAF in Virologically Suppressed, HIV-1 Infected Patients (Be-OnE)
957	NR	2018	Switch Study to Evaluate Dolutegravir Plus Lamivudine in Virologically Suppressed Human Immunodeficiency Virus Type 1 Positive Adults (TANGO)
958	Maggiolo	2019	Bone mineral density in virologically suppressed people aged 60 years or older with HIV-1 switching from a regimen containing tenofovir disoproxil fumarate to an elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide single-tablet regimen: a multicentre, open-label, phase 3b, randomised trial
959	Hocqueloux	2019	Dolutegravir Monotherapy Versus Dolutegravir/Abacavir/Lamivudine for Virologically Suppressed People Living With Chronic Human Immunodeficiency Virus Infection: The Randomized Noninferiority MONotherapy of TiviCAY Trial
960	Rizzardini	2019	Randomized study evaluating the efficacy and safety of switching from an an abacavir/lamivudine-based regimen to an elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide single-tablet regimen
961	Gatell	2019	Doravirine dose selection and 96-week safety and efficacy versus efavirenz in antiretroviral therapy-naive adults with HIV-1 infection in a Phase lIb trial

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
962	Aboud	2019	Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (DAWNING): an open-label, non-inferiority, phase 3b trial
963	Braun	2019	Noninferiority of Simplified Dolutegravir Monotherapy Compared to Continued Combination Antiretroviral Therapy That Was Initiated During Primary Human Immunodeficiency Virus Infection: a Randomized, Controlled, Multisite, Open-label, Noninferiority Trial
964	Venter	2019	Efficacy and Safety of Tenofovir Disoproxil Fumarate Versus Low-Dose Stavudine Over 96 Weeks: A Multicountry Randomized, Noninferiority Trial
965	Venter	2019	The ADVANCE trial: phase 3, randomized comparison of TAF/FTC/DTG, TDF/FTC/DTG or TDF/FTC/EFV for firstline treatment of HIV-1 infection
966	Wiriyatanakorn	2019	Switching Tenofovir/Emtricitabine/Efavirenz (TDF/FTC/EFV) to TDF/FTC/Rilpivirine vs Continuing TDF/FTC/EFV in HIV-Infected Patients With Virological Suppression: A Randomized Controlled Trial
967	Johnson	2019	Switching to Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF) Maintains HIV-1 Virologic Suppression Through 48 Weeks: Results of the DRIVE-SHIFT Trial
968	Maggiolo	2019	RPV+DRV/cobi as 2DR option in HIV-infected subjects on virologic suppression
969	Munderi	2019	Switching at low HIV-1 RNA into fixed dose combinations: TDF/FTC/RPV is non-inferior to TDF/FTC/ EFV in first-line suppressed patients living with HIV
970	Murray	2019	Patient-reported tolerability and acceptability of cabotegravir + rilpivirine long-acting injections for the treatment of HIV-1 infection: 96-week results from the randomized LATTE-2 study
971	Mussini	2019	A prospective randomized trial on abacavir/lamivudine plus darunavir/ritonavir or raltegravir in HIV-positive drug-naïve patients with CD4<200 cells/uL (the PRADAR study)
972	Orkin	2019	Doravirine/Lamivudine/Tenofovir disoproxil fumarate is non-inferior to efavirenz/emtricitabine/tenofovir disoproxil fumarate in treatment-naive adults with human immunodeficiency virus-1 infection: Week 48 results of the DRIVE-AHEAD Trial
973	Kouanfack	2019	Dolutegravir-Based or Low-Dose Efavirenz-Based Regimen for the Treatment of HIV-1
974	NR	2019	Dual therapy with lopinavir/ritonavir plus lamivudine could be an effective alternative for antiretroviral-therapy-naive adults with HIV-1 infection in resource-limited settings: planned 144 week, a randomized, open-label and non-inferiority study from C
975	NR	2019	A Study to Assess the Acceptability of Scored Film-coated darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) Fixed-dose Combination (FDC) Tablets in HIV-1 Infected Pediatric Participants (Aged =6 to <12 years), Using Matching Placebo Ta
976	NR	2019	Randomized, double blind, safety, efficacy Doravirine/Islatravir in Treatment naÃ¯ve
977	NR	2019	ANRS 173 ALTAR (ALlÃ©gement du Traitement AntiRÃ©troviral)
978	NR	2019	The RIO Trial: a randomised placebo controlled trial of ART plus dual long-acting HIV-specific broadly neutralising antibodies (bNAbs) vs ART plus placebo in treated Primary HIV Infection on viral control off ART
979	NR	2019	Will switching HIV-1-infected patients who have drug resistant HIV and stable on a regimen based on a protease inhibitor to another regimen based on the integrase inhibitor bictegravir be as equally effective?

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
980	NR	2019	To determine the efficacy, safety and tolerability of two approved medicines, dolutegravir (DTG) plus lamivudine (3TC) taken together as a single tablet, compared with subjects taking their current antiretroviral therapy regimen (CAR) for the treatment o
981	NR	2019	Dolutegravir plus tenofovir alafenamide as a double-drug regimen in HIV positive patients
982	NR	2019	Combining TLR9 Agonist With bNAbs for Reservoir Reduction and Immunological Control of HIV
983	NR	2019	A Drug Safety and Dose-exploratory Clinical Study of Azvudine Tablets in Patients Who Have Not Received Anti-HIV Treatment
984	NR	2019	RPV+DRV/Cobi Dual Therapy in Subjects With HIV Controlled Infection
985	NR	2019	Study to Evaluate the Safety and Efficacy of GS-6207 in Combination With Other Antiretroviral Agents in People Living With HIV
986	NR	2019	Regimen Switch to Dolutegravir/Lamivudine Fixed Dose Combination From Current Antiretroviral Regimen in HIV-1 Infected and Virologically Suppressed Adults (SALSA)
987	NR	2019	Tenofovir/Lamivudine/Dolutegravir Combination as Second Line ART: a Randomised Controlled Trial (ARTIST)
988	NR	2019	VISEND
989	NR	2019	Lopinavir/r/ Lamivudine/ Abacavir as an Easy to Use Paediatric Formulation (LOLIPOP)
990	Guo	2020	Antiretroviral Long-Term Efficacy and Resistance of Lopinavir/Ritonavir Plus Lamivudine in HIV-1-Infected Treatment-Naïve Patients (ALTERLL): 144-Week Results of a Randomized, Open-Label, Non-Inferiority Study From Guangdong, China
991	Lévy	2020	Addition of Maraviroc Versus Placebo to Standard Antiretroviral Therapy for Initial Treatment of Advanced HIV Infection: A Randomized Trial
992	Di Cristo	2020	96-week results of a dual therapy with darunavir/ritonavir plus rilpivirine once a day vs triple therapy in patients with suppressed viraemia: virological success and non-HIV related morbidity evaluation
993	Iwuji	2020	A phase IV randomised, open-label pilot study to evaluate switching from protease-inhibitor based regimen to Bictegravir/Emtricitabine/Tenofovir Alafenamide single tablet regimen in Integrase inhibitor-naïve, virologically suppressed HIV-1 infected adults harbouring drug resistance mutations (PIBIK study): study protocol for a randomised trial
994	Amstutz	2020	Switch to second-line versus continued first-line antiretroviral therapy for patients with low-level HIV-1 viremia: An open-label randomized controlled trial in Lesotho
995	Schürmann	2020	Safety, pharmacokinetics, and antiretroviral activity of islatravir (ISL, MK-8591), a novel nucleoside reverse transcriptase translocation inhibitor, following single-dose administration to treatment-naive adults infected with HIV-1: an open-label, phase 1b, consecutive-panel trial
996	Sculier	2020	Efficacy and safety of dolutegravir plus emtricitabine versus standard ART for the maintenance of HIV-1 suppression: 48-week results of the factorial, randomized, non-inferiority SIMPL'HIV trial
997	Spinner	2020	Efficacy and Safety of Switching to Dolutegravir With Boosted Darunavir in Virologically Suppressed Adults With HIV-1: A Randomized, Open-Label, Multicenter, Phase 3, Noninferiority Trial: The DUALIS Study
998	Swindells	2020	Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
999	Swindells	2020	Cabotegravir + rilpivirine long-acting as HIV-1 maintenance therapy: ATLAS Week 96 results
1000	van Wyk	2020	Efficacy and Safety of Switching to Dolutegravir/Lamivudine Fixed-Dose 2-Drug Regimen vs Continuing a Tenofovir Alafenamide-Based 3- or 4-Drug Regimen for Maintenance of Virologic Suppression in Adults Living With Human Immunodeficiency Virus Type 1: Phase 3, Randomized, Noninferiority TANGO Study
1001	Van Wyk	2020	Switching to DTG/3TC fixed-dose combination (FDC) is non-inferior to continuing a TAF-based regimen (TBR) in maintaining virologic suppression through 96 weeks (TANGO study)
1002	Venter	2020	Dolutegravir with emtricitabine and tenofovir alafenamide or tenofovir disoproxil fumarate versus efavirenz, emtricitabine, and tenofovir disoproxil fumarate for initial treatment of HIV-1 infection (ADVANCE): week 96 results from a randomised, phase 3, non-inferiority trial
1003	Wyk	2020	Efficacy and Safety of Switching to Dolutegravir/ Lamivudine Fixed-Dose 2-Drug Regimen vs Continuing a Tenofovir Alafenamide–Based 3- or 4-Drug Regimen for Maintenance of Virologic Suppression in Adults Living With Human Immunodeficiency Virus Type 1: Phase 3, Randomized, Noninferiority TANGO Study
1004	Molina	2020	Doravirine versus ritonavir-boosted darunavir in antiretroviral-naive adults with HIV-1 (DRIVE-FORWARD): 96-week results of a randomised, double-blind, non-inferiority, phase 3 trial
1005	Orkin	2020	Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection
1006	Orkin	2020	Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (TDF) Versus Efavirenz/Emtricitabine/TDF in Treatment-naive Adults With Human Immunodeficiency Virus Type 1 Infection: Week 96 Results of the Randomized, Double-blind, Phase 3 DRIVE-AHEAD Noninferiority Trial
1007	Palanuphap	2020	Switching protease inhibitors to rilpivirine in HIV-positive individuals with complete viral suppression and without prior HIV drug resistance in a resource-limited setting: a randomized controlled trial
1008	Raffi	2020	Five-year follow-up of patients enrolled in the NEAT 001/ANRS 143 randomized clinical trial: NEAT 001/ANRS 143 LONG TERM study
1009	Calmy	2020	Dolutegravir-based and low-dose efavirenz-based regimen for the initial treatment of HIV-1 infection (NAMSAL): week 96 results from a two-group, multicentre, randomised, open label, phase 3 non-inferiority trial in Cameroon
1010	NR	2020	A Drug Safety and Dose-exploratory Clinical Study of Azvudine Tablets in Patients Who Have Not Received Anti-HIV Treatment (FNC)
1011	NR	2020	Clinical Study to evaluate a switch to Doravirine/Islatravir in Participants with HIV-1 Virologically Suppressed on treatment with Bictegravir/Emtricitabine/Tenofovir Alafenamide
1012	NR	2020	Study to see the changes in body weight and body composition of a darunavir/cobicistat based treatment in HIV-infected people who have gained weight during a dolutegravir-based treatment
1013	NR	2020	Doravirine/Islatravir in heavily treatment-experienced participants
1014	NR	2020	A study looking at the effects of switching anti-HIV therapy in people with HIV who have difficulty sleeping
1015	NR	2020	A clinical trial that evaluates safety, tolerability, pharmacokinetics, and pharmacodynamic characteristics after oral administration of investigational product(AVI-CO-004Tab) 10 days to male volunteers with AIDS

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (continuação)

Estudos excluídos por não descreverem eventos adversos especificamente em mulheres			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1016	NR	2020	Randomized, Double-blind, Efficacy, and Safety Study of Doravirine/Islatravir (DOR/ISL) in Treatment-naïve Participants With Human Immunodeficiency Virus Type 1 (HIV-1) Infection (MK-8591A-020)
1017	NR	2020	Phase III Clinical Study of Azvudine in Hiv-infected Treatment Naive Patients
1018	NR	2020	Safety and Efficacy of a Switch to Doravirine/Islatravir in Participants With HIV-1 (MK-8591A-017))
1019	NR	2020	A Study of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) Evaluated as a Fixed Dose Combination Regimen in Participants Switching From an Integrase Inhibitor Who Have Experienced Rapid Weight Gain
1020	NR	2020	The HIV Functional Cure Potential of UB-421 in ART Stabilized HIV-1 Patients
1021	NR	2020	A Study to Evaluate Efficacy and Safety of Cabotegravir (CAB) Long Acting (LA) Plus (+) Rilpivirine (RPV) LA Versus BIKTARVY® (BIK) in Participants With Human Immunodeficiency Virus (HIV)-1 Who Are Virologically Suppressed
1022	NR	2020	Efficacy of Efavirenz 400mg vs. 600mg Combined With Lamivudine and Tenofovir in Treatment Naive HIV Infection
1023	NR	2020	DTG/3TC Fixed Dose Formulations for the Maintenance of Virological Suppression in Children With HIV Infection Aged 2 to <15 Years Old
1024	NR	2020	Continuation of Protease-Inhibitor Based Second-Line Therapy vs. Switch to B/F/TAF in Virologically Suppressed Adults
1025	NR	2020	Rapid Start vs. Standard Start Antiretroviral Therapy (ART) in HIV
1026	NR	2020	Doravirine for Persons With Excessive Weight Gain on Integrase Inhibitors and Tenofovir Alafenamide
1027	NR	2020	Study to Assess Adverse Events and How Intravenous (IV) or Subcutaneous (SC) ABBV-382 Moves Through the Body of Adult Participants With Human Immuno-Deficiency Virus (HIV-1)
1028	Molina	2021	Islatravir in combination with doravirine for treatment-naive adults with HIV-1 infection receiving initial treatment with islatravir, doravirine, and lamivudine: a phase 2b, randomised, double-blind, dose-ranging trial
1029	Orkin	2021	Long-acting cabotegravir plus rilpivirine for treatment in adults with HIV-1 infection: 96-week results of the randomised, open-label, phase 3 FLAIR study
Estudos excluídos pelo texto na íntegra não estar disponível, mesmo depois de contato com pesquisadores			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
1	NR	1989	Antiviral trial conducted
2	Vesterdal	1989	AIDS. Trial with Retrovir for HIV-positive subjects
3	Demonty	1993	[Antiretroviral therapy]
4	NR	1995	[The safety and efficacy of saquinavir in the therapy of HIV infection]
5	Staszewski	1996	Evaluation of the efficacy and tolerance of R 018893, R 089439 (loviride) and placebo in asymptomatic HIV-1-infected patients. Loviride Collaborative Study Group
6	Vella	1996	A randomized controlled trial of a protease inhibitor (saquinavir) in combination with zidovudine in previously untreated patients with advanced HIV infection
7	Pollard	1997	Randomized double-blind study of combination therapy with didanosine and stavudine in HIV-infected individuals

Quadro 6 – Lista de estudos excluídos segundo motivo de exclusão (conclusão)

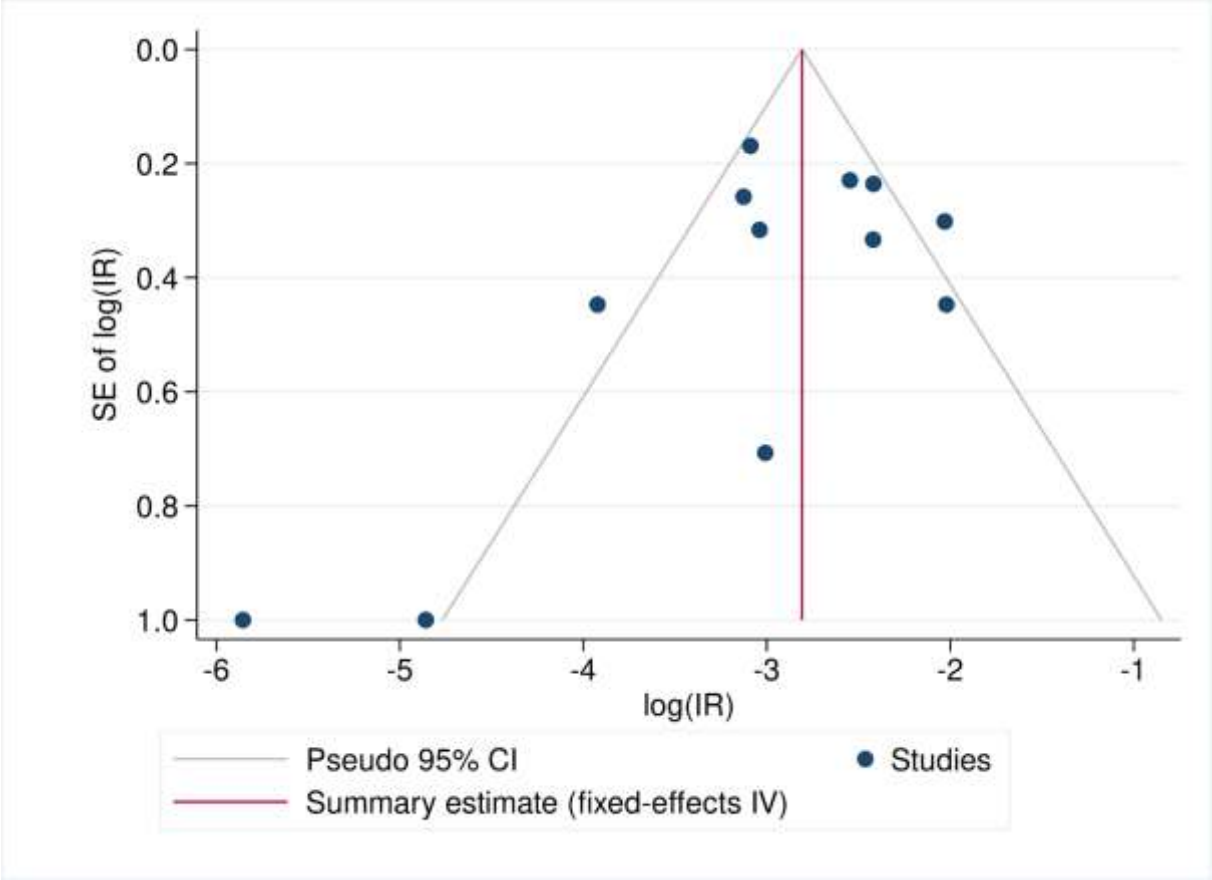
Estudos excluídos pelo texto na íntegra não estar disponível, mesmo depois de contato com pesquisadores			
Quanti-dade	Primeiro autor ou grupo de pesquisa	Ano	Título
8	Moyle	1997	Zidovudine monotherapy versus zidovudine plus zalcitabine combination therapy in HIV-positive persons with CD4 cell counts 300-500 cells/mm3: a double-blind controlled trial. The M50003 Study Group Coordinating and Writing Committee
9	Saimot	1997	Ritonavir, stavudine and didanosine as first-line tritherapy in HIV-1-infected individuals: Results of an ongoing open-label trial
10	Angarano	1997	A randomized double-blind study of virological, clinical and safety effects of a combination of stavudine and didanosine versus zidovudine and didanosine in treatment-naive HIV-infected individuals
11	Raffi	1998	Stavudine plus didanosine and nevirapine in antiretroviral-naive HIV-infected adults: Preliminary safety and efficacy results
12	Molina	1999	Results of the ALBI trial: A randomized comparison of stavudine/didanosine, zidovudine/lamivudine and alternating treatment in antiretroviral-naive patients
13	Murphy	1999	Stavudine, lamivudine plus novel protease inhibitor therapy in antiretroviral-naive HIV-infected individuals treated for 24 weeks
14	Staszewski	1999	Update on study 006--EFV + AZT + 3TC versus the current 'standard of care' IDV + AZT + 3TC
15	Saez-Llorens	2000	Ziagen (Abacavir, ABC) combined with 3TC & ZDV is safe and effective through 48 weeks in HIV-1 infected antiretroviral therapy-experienced children (CNA3006)
16	NR	2001	No adverse effects in infants following short-course zidovudine
17	Wagner	2001	Rand Corp. study seeks participants
18	Dobkin	2002	Tenofovir: the first nucleotide for HIV infection
19	NR	2003	[96-week treatment outcome confirms long term efficacy of tenofovir DF]
20	Blasko	2003	[HIV-1 fusion inhibitor improves treatment in HIV-1-resistant patients]
21	Moyle	2005	The role of zidovudine in development of lipoatrophy
22	Smith	2006	The long-term consequences of antiretroviral therapy
23	Coleman	2007	A comparison of different protease inhibitors on coronary heart disease risk

NR = não reportado; TARV = terapia antirretroviral; ARV = antirretroviral

Fonte: Elaboração própria

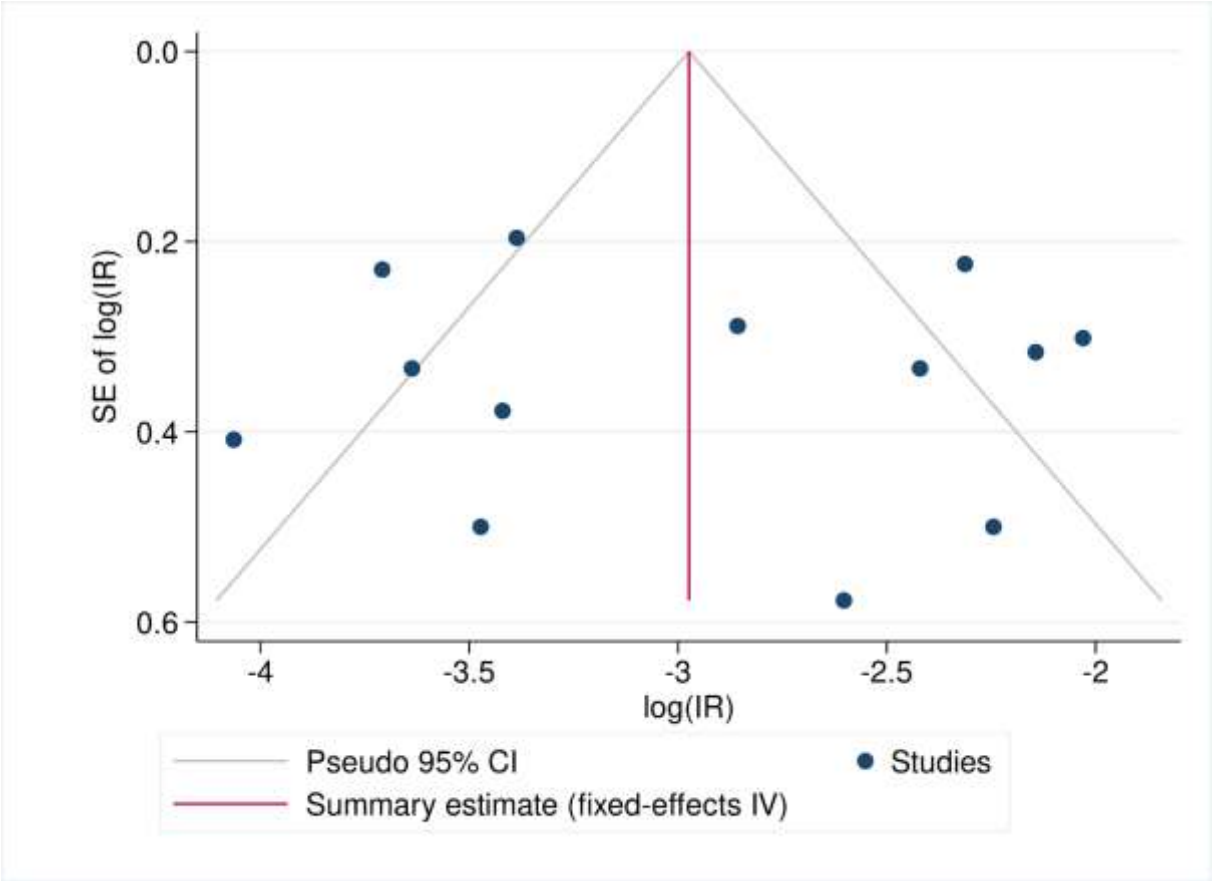
APÊNDICE E – AVALIAÇÃO DO VIÉS DE PUBLICAÇÃO

Figura 3 – Gráfico de funil para descontinuação por eventos adversos



Fonte: Elaboração própria. IR = incidence rate (taxa de incidência)

Figura 4 – Gráfico de funil para eventos adversos sérios clínicos e laboratoriais



Fonte: Elaboração própria. IR = incidence rate (taxa de incidência)

APÊNDICE F – RESULTADOS POR ESQUEMA ARV

Tabela 2 - Eventos adversos por esquema antirretroviral (continua)

Atazanavir 300 mg/dia + Ritonavir 100 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	2	533	81,97	4,16 - 1611,00
Eventos adversos clínicos e/ou laboratoriais	1	247	972,10	1,82 - 511395,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	1	247	594,80	1,10 - 318800,00
Eventos adversos clínicos relacionados a TARV	1	286	570,60	1,07 - 315895,00
Eventos adversos graves clínicos graus 3 e/ou 4	1	286	117,60	0,22 - 62379,00
Eventos adversos graves laboratoriais graus 3 e/ou 4	1	286	703,70	1,32 - 364000,00
Eventos adversos graves clínicos e/ou laboratoriais grau 3	1	247	181,00	0,34 - 98849,50
Eventos adversos graves clínicos e/ou laboratoriais grau 4	1	247	42,49	0,08 - 23669,50
Eventos adversos sérios clínicos e/ou laboratoriais	1	247	96,95	0,18 - 51859,50
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV	1	247	12,70	0,02 - 7228,85
Eventos adversos sérios clínicos relacionados a TARV	1	286	18,85	0,03 - 10450,00
Morte por todas as causas	2	533	0,73	0,00 - 60,56
Morte por eventos adversos relacionados a TARV	2	533	0,00	0,00 - 0,03
Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	1	234	0,00	0,00 - 0,20
Descontinuação por eventos adversos relacionados a TARV	1	234	0,00	0,00 - 0,20
Eventos adversos clínicos e/ou laboratoriais	1	234	718,40	1,35 - 375995,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	1	234	91,31	0,17 - 49459,50
Eventos adversos graves laboratoriais graus 3 e/ou 4	1	234	188,80	0,35 - 100900,00
Eventos adversos sérios clínicos e/ou laboratoriais	1	234	30,64	0,06 - 17229,50
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV	1	234	0,00	0,00 - 0,20
Eventos adversos sérios clínicos relacionados a TARV	1	234	0,00	0,00 - 0,20

Tabela 2 - Eventos adversos por esquema antirretroviral (continuação)

Bictegravir/Entricitabina/Tenofovir alafenamida 50/200/25 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Morte por todas as causas	1	234	0,00	0,00 - 0,20
Morte por eventos adversos relacionados a TARV	1	234	0,00	0,00 - 0,20
Darunavir/Cobicistate 800/150 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	1	41	121,30	0,21 - 67219,50
Descontinuação por eventos adversos relacionados a TARV	1	41	121,30	0,21 - 67219,50
Eventos adversos clínicos e/ou laboratoriais	1	41	913,40	1,67 - 482400,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	1	41	545,80	0,99 - 304395,00
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4	1	41	95,23	0,17 - 53989,50
Eventos adversos sérios clínicos e/ou laboratoriais	1	41	95,23	0,17 - 53989,50
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 relacionados a TARV	1	41	42,17	0,06 - 24359,50
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV	1	41	68,36	0,11 - 39559,00
Morte por todas as causas	1	41	0,00	0,00 - 1,07
Morte por eventos adversos relacionados a TARV	1	41	0,00	0,00 - 1,07
Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	2	184	15,41	0,21 - 876,59
Descontinuação por eventos adversos relacionados a TARV	2	184	15,41	0,21 - 876,59
Eventos adversos clínicos e/ou laboratoriais	2	184	922,90	56,88 - 15170,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	2	184	357,80	8,25 - 15370,00
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4	2	184	80,75	3,16 - 2072,00
Eventos adversos sérios clínicos e/ou laboratoriais	2	184	40,91	1,16 - 1488,95

Tabela 2 - Eventos adversos por esquema antirretroviral (continuação)

Darunavir/Cobicistate/Entricitabina/Tenofovir alafenamida 800/150/200/10 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 relacionados a TARV	2	184	21,91	0,47 - 943,60
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV	2	184	0,00	0,00 - 0,12
Eventos adversos sérios clínicos relacionados a TARV	1	140	0,00	0,00 - 0,35
Morte por todas as causas	2	184	0,00	0,00 - 0,09
Morte por eventos adversos relacionados a TARV	2	184	0,00	0,00 - 0,12
Dolutegravir/Abacavir/Lamivudina 50/600/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Osteoporose por eventos adversos	1	59	6,15	0,01 - 4037,00
Descontinuação por eventos adversos	2	307	61,58	2,14 - 1797,00
Eventos adversos clínicos e/ou laboratoriais	1	248	933,00	1,69 - 498690,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	1	248	395,20	0,73 - 211000,00
Eventos adversos graves clínicos e/ou laboratoriais grau 3	1	248	83,97	0,16 - 45879,50
Eventos adversos graves clínicos e/ou laboratoriais grau 4	1	248	12,36	0,02 - 7240,75
Eventos adversos sérios clínicos e/ou laboratoriais	2	307	67,41	2,66 - 1763,95
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV	1	248	0,00	0,00 - 0,21
Eventos adversos sérios clínicos relacionados a TARV	1	248	0,00	0,00 - 0,21
Morte por todas as causas	2	307	1,04	0,00 - 72,82
Morte por eventos adversos relacionados a TARV	2	307	0,00	0,00 - 0,05
Efavirenz 600 mg/dia + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Eventos adversos laboratoriais	1	242	40,55	0,08 - 21369,50

Tabela 2 - Eventos adversos por esquema antirretroviral (continuação)

Efavirenz 600 mg/dia + Fumarato de tenofovir desoproxila 300 mg/dia + Lamivudina 300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	1	29	0,00	0,00 - 0,48
Descontinuação por eventos adversos relacionados a TARV	1	29	0,00	0,00 - 0,48
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4	1	29	77,39	0,14 - 42889,50
Eventos adversos sérios clínicos e/ou laboratoriais	1	29	112,10	0,21 - 61089,00
Morte por todas as causas	1	29	7,30	0,01 - 4814,00
Morte por eventos adversos relacionados a TARV	1	29	0,00	0,00 - 0,48
Efavirenz 600 mg/dia + Lamivudina/Zidovudina 150/300 mg 12/12h				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	1	30	126,40	0,23 - 69389,00
Eventos adversos laboratoriais	1	241	65,60	0,12 - 36399,50
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4	1	30	137,80	0,25 - 74109,50
Eventos adversos sérios clínicos e/ou laboratoriais	1	30	126,40	0,23 - 69389,00
Morte por todas as causas	1	30	7,42	0,01 - 4967,95
Morte por eventos adversos relacionados a TARV	1	30	0,00	0,00 - 0,49
Elvitegravir/Cobicistate/Entricitabina/Fumarato de tenofovir desoproxila 150/150/200/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	1	289	18,05	0,03 - 9868,95
Eventos adversos clínicos relacionados a TARV	1	289	322,40	0,60 - 174800,00
Eventos adversos graves clínicos graus 3 e/ou 4	1	289	93,37	0,17 - 50589,50
Eventos adversos graves laboratoriais graus 3 e/ou 4	1	289	251,40	0,46 - 136000,00
Eventos adversos sérios clínicos relacionados a TARV	1	289	10,21	0,02 - 5968,00
Morte por todas as causas	1	289	0,00	0,00 - 0,17
Morte por eventos adversos relacionados a TARV	1	289	0,00	0,00 - 0,17

Tabela 2 - Eventos adversos por esquema antirretroviral (continuação)

Lopinavir/Ritonavir 400/100 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	2	371	0,31	0,00 - 29,70
Descontinuação por eventos adversos relacionados a TARV	1	251	0,00	0,00 - 0,06
Eventos adversos graves clínicos graus 3 e/ou 4	2	371	45,40	1,90 - 1001,00
Eventos adversos graves laboratoriais graus 3 e/ou 4	2	371	71,04	4,07 - 1235,00
Eventos adversos graves clínicos grau 4	1	251	9,79	0,02 - 5430,00
Eventos adversos sérios clínicos e/ou laboratoriais	2	371	20,74	0,78 - 491,70
Morte por todas as causas	2	371	5,75	0,08 - 226,10
Morte por eventos adversos relacionados a TARV	2	371	0,94	0,00 - 60,39
Nevirapina 200 mg 12/12h + Entricitabina/Fumarato de tenofovir desoproxila 200/300 mg/dia				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	2	370	44,25	2,38 - 838,60
Descontinuação por eventos adversos relacionados a TARV	1	249	44,89	0,09 - 24219,50
Eventos adversos graves clínicos graus 3 e/ou 4	2	370	45,83	2,46 - 876,20
Eventos adversos graves laboratoriais graus 3 e/ou 4	2	370	86,76	5,09 - 1528,00
Eventos adversos graves clínicos grau 4	1	249	8,60	0,02 - 4567,85
Eventos adversos sérios clínicos e/ou laboratoriais	2	370	30,05	1,33 - 637,10
Morte por todas as causas	2	370	7,87	0,26 - 238,40
Morte por eventos adversos relacionados a TARV	2	370	0,29	0,00 - 20,77
Todos os tratamentos				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Descontinuação por eventos adversos	15	2388	20,78	5,58 - 57,31
Descontinuação por eventos adversos relacionados a TARV	7	988	4,31	0,13 - 54,72
Eventos adversos clínicos e/ou laboratoriais	6	954	888,20	759,90 - 1045,00
Eventos adversos laboratoriais	2	483	52,02	1,89 - 1388,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	6	954	341,60	133,60 - 862,70

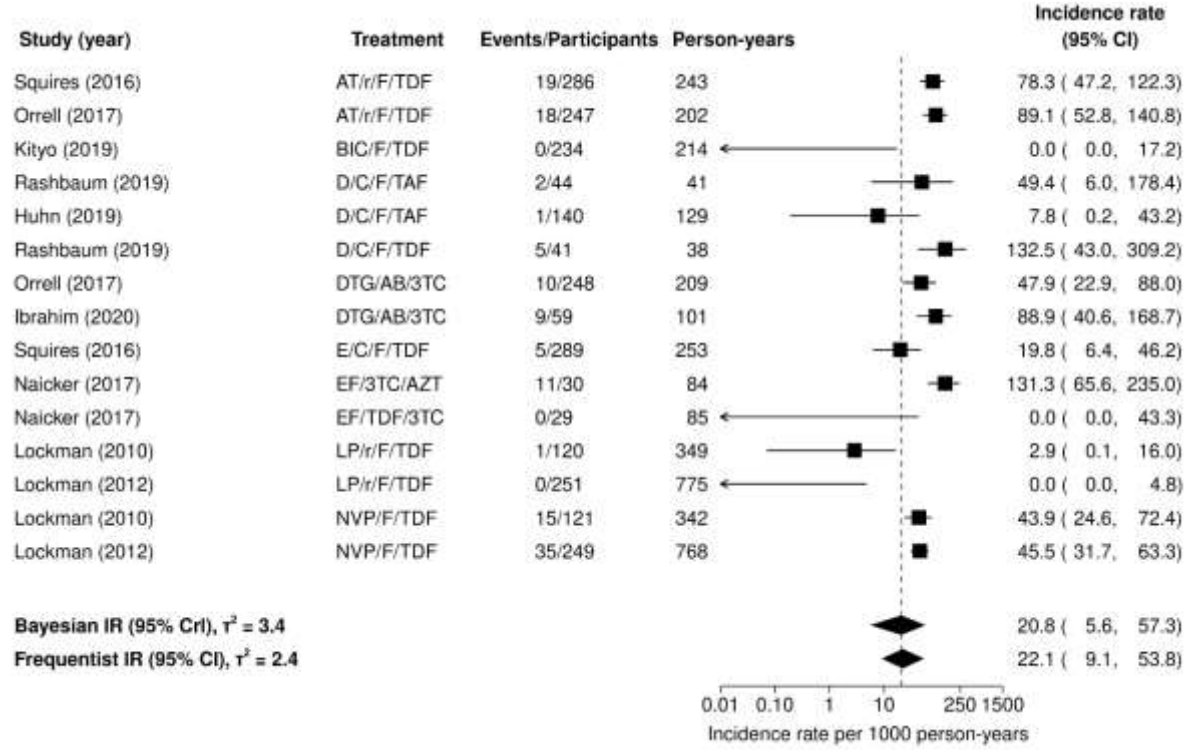
Tabela 2 - Eventos adversos por esquema antirretroviral (conclusão)

Todos os tratamentos				
Desfecho	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)
Eventos adversos clínicos relacionados a TARV	2	575	431,50	13,84 - 13630,00
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4	5	284	96,34	55,04 - 158,90
Eventos adversos graves clínicos graus 3 e/ou 4	6	1316	59,93	33,74 - 104,60
Eventos adversos graves laboratoriais graus 3 e/ou 4	7	1550	145,10	57,71 - 359,90
Eventos adversos graves clínicos e/ou laboratoriais grau 3	2	495	125,50	3,51 - 4295,00
Eventos adversos graves clínicos e/ou laboratoriais grau 4	2	495	25,05	0,50 - 1017,00
Eventos adversos graves clínicos grau 4	2	500	9,31	0,39 - 216,30
Eventos adversos sérios clínicos e/ou laboratoriais	13	1813	49,34	31,60 - 77,10
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 relacionados a TARV	3	225	27,75	2,56 - 272,90
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV	6	954	1,09	0,01 - 21,47
Eventos adversos sérios clínicos relacionados a TARV	5	1197	1,53	0,01 - 21,29
Morte por todas as causas	15	2388	4,47	1,42 - 7,91
Morte por eventos adversos relacionados a TARV	15	2388	0,18	0,00 - 1,56

Fonte: Elaboração própria

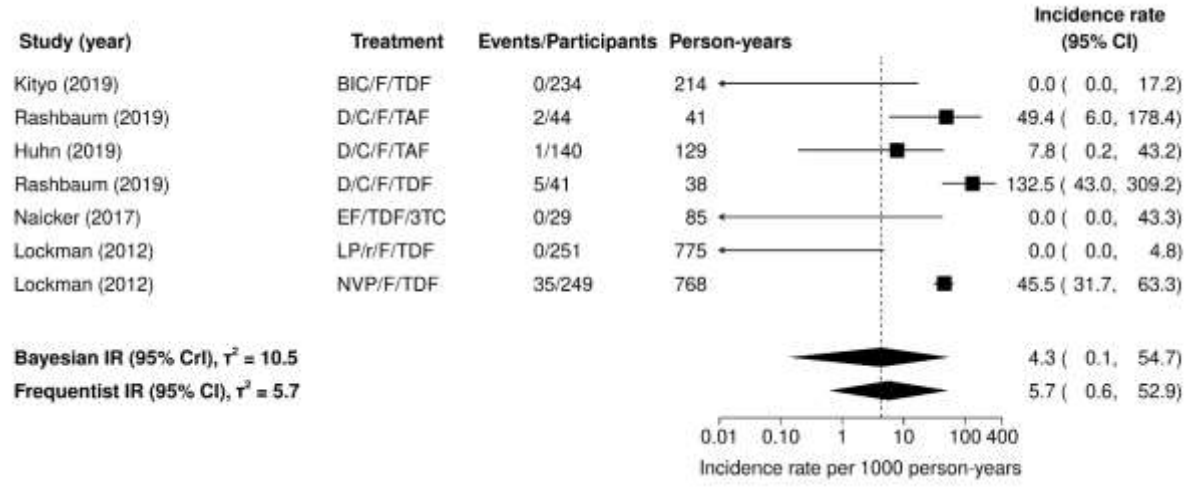
APÊNDICE G – GRÁFICOS COM AS ANÁLISES DAS TAXAS DE INCIDÊNCIA

Figura 5 – Análises das taxas de incidência de descontinuação por eventos adversos



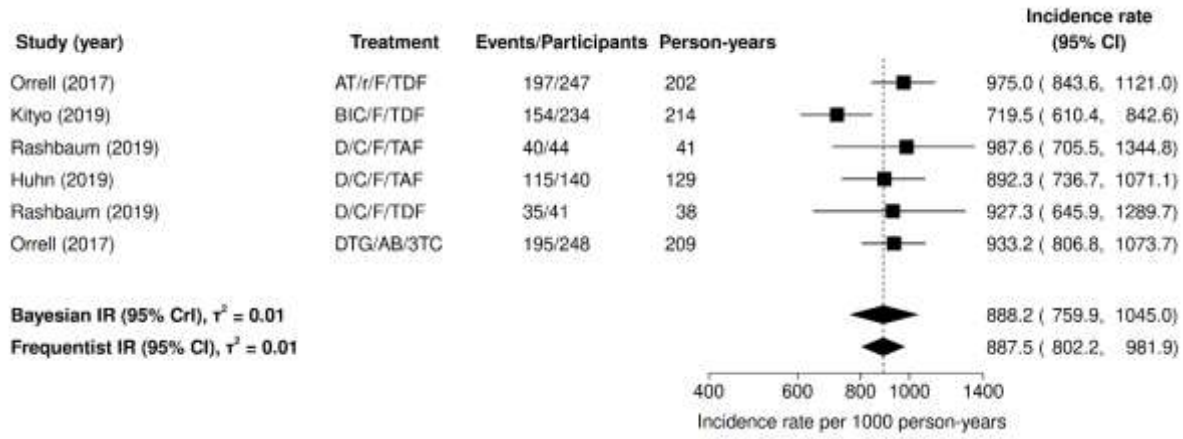
Fonte: Elaboração própria.

Figura 6 – Análises das taxas de incidência de descontinuação por eventos adversos relacionados a TARV



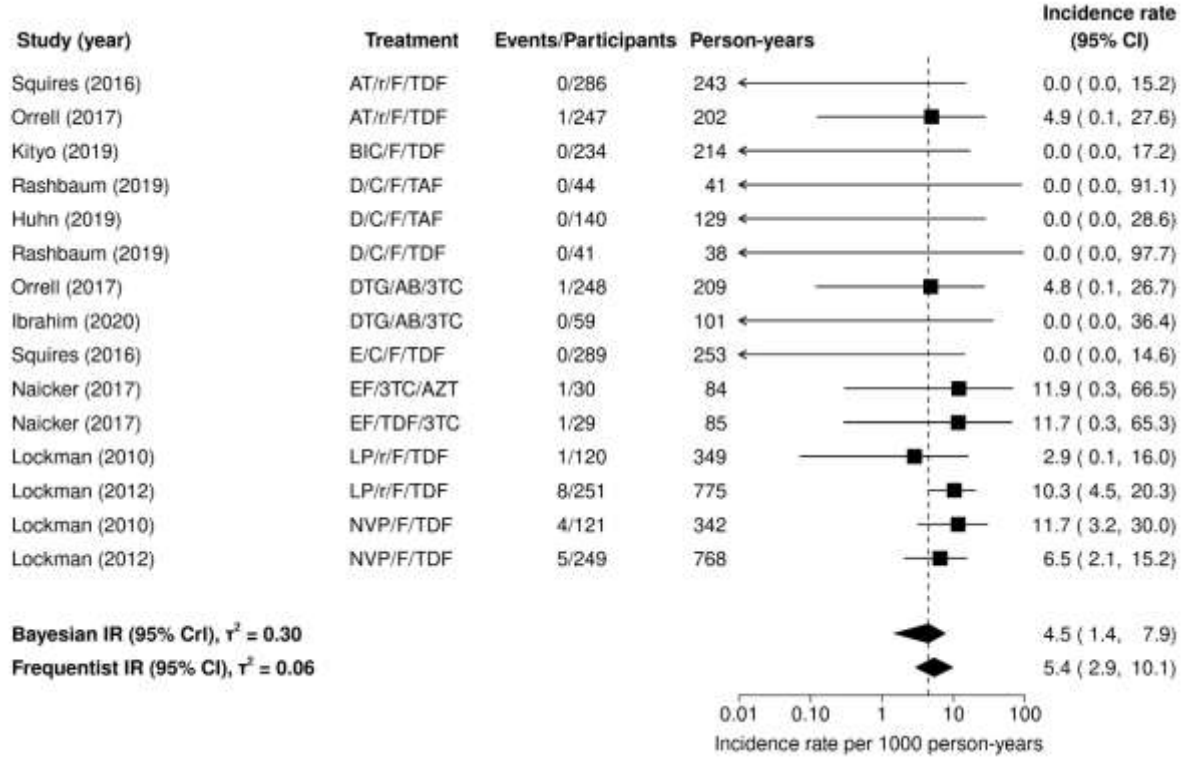
Fonte: Elaboração própria.

Figura 7 – Análises das taxas de incidência de qualquer evento adverso clínico e/ou laboratorial



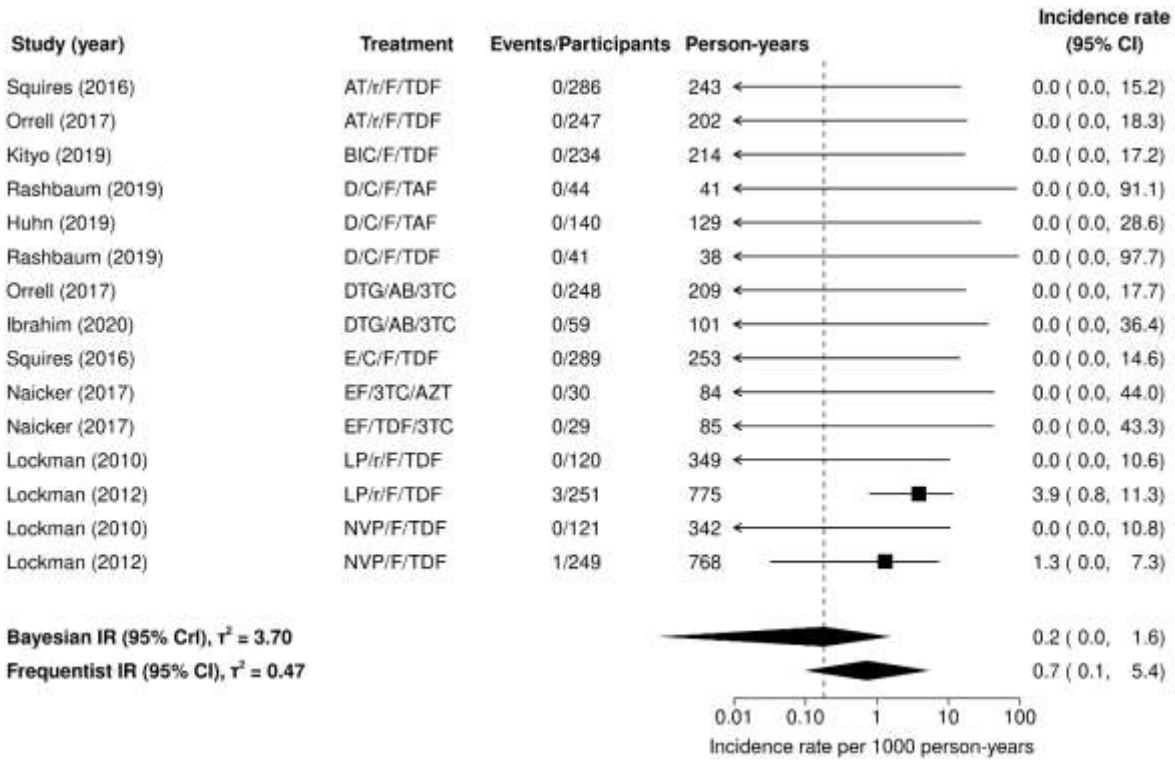
Fonte: Elaboração própria.

Figura 8 – Análises das taxas de incidência de morte por todas as causas



Fonte: Elaboração própria.

Figura 9 – Análises das taxas de incidência de morte por eventos adversos relacionados a TARV



Fonte: Elaboração própria.

APÊNDICE H – ANÁLISES DE SUBGRUPO

Tabela 3 – Análises de subgrupo (continua)

Análise por cegamento (duplo-cego *vs* aberto)							
Desfecho	Subgrupo	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)		
Descontinuação por eventos adversos	Duplo-cego	4		52,77	8,89	-	285,10
	Aberto	11		12,04	1,43	-	57,06
Descontinuação por eventos adversos relacionados a TARV	Duplo-cego	2		76,47	1,65	-	2755,00
	Aberto	5		0,82	0,01	-	22,93
Eventos adversos clínicos e/ou laboratoriais	Duplo-cego	2		950,80	55,35	-	16180,00
	Aberto	4		874,20	629,30	-	1213,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	Duplo-cego	2		578,70	30,71	-	10720,00
	Aberto	4		264,90	46,68	-	1457,00
Análise por intenção de tratar (protocolo *vs* intenção de tratar)							
Desfecho	Subgrupo	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)		
Descontinuação por eventos adversos	Protocolo	10		13,09	1,90	-	55,53
	Intenção de tratar	5		53,61	3,90	-	316,20
Descontinuação por eventos adversos relacionados a TARV	Protocolo	4		1,34	0,01	-	49,34
	Intenção de tratar	3		20,77	0,18	-	691,30
Eventos adversos clínicos e/ou laboratoriais	Protocolo	4		874,20	628,00	-	1213,00
	Intenção de tratar	2		950,80	55,35	-	16180,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	Protocolo	4		264,70	46,89	-	1468,00
	Intenção de tratar	2		579,00	30,71	-	10710,00
Análise por nível de CD4 (média >250 células/mm^3 *vs* média <250 células/mm^3)							
Desfecho	Subgrupo	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)		
Descontinuação por eventos adversos	>250	11		33,45	8,98	-	87,29
	<250	4		5,44	0,10	-	142,70
Descontinuação por eventos adversos relacionados a TARV	>250	5		6,26	0,12	-	106,40
	<250	2		1,98	0,00	-	413,39

Tabela 3 – Análises de subgrupo (conclusão)

Análise por exposição prévia a TARV (virgens de tratamento *vs* experenciadas)							
Desfecho	Subgrupo	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)		
Descontinuação por eventos adversos	Virgens de tratamento	12		25,53	6,36	-	77,30
	Experenciadas	3		5,95	0,04	-	282,49
Descontinuação por eventos adversos relacionados a TARV	Virgens de tratamento	5		7,53	0,14	-	161,60
	Experenciadas	2		0,97	0,00	-	85,97
Eventos adversos clínicos e/ou laboratoriais	Virgens de tratamento	4		952,90	781,20	-	1153,00
	Experenciadas	2		794,40	42,10	-	15130,00
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV	Virgens de tratamento	4		520,00	305,40	-	909,49
	Experenciadas	2		140,10	3,73	-	5242,95
Análise por financiamento (indústria *vs* misto[1] *vs* governamental)							
Desfecho	Subgrupo	Nº de braços dos estudos	Nº de mulheres	Taxa de incidência (nº eventos/1000 pessoas-ano)	Intervalo de credibilidade (95%)		
Descontinuação por eventos adversos	Indústria	9		36,10	9,99	-	98,27
	Misto[1]	4		5,49	0,10	-	142,60
	Governamental	2		10,22	0,01	-	1559,95
Descontinuação por eventos adversos relacionados a TARV	Indústria	4		11,74	0,24	-	256,50
	Misto[1]	2		1,98	0,00	-	417,50
	Governamental	1		0,00	0,00	-	0,48

Fonte: Elaboração própria

1. Misto: estudo financiado pela indústria e por órgãos governamentais

APÊNDICE I – AVALIAÇÃO DA CERTEZA DA EVIDÊNCIA

Tabela 4 – Sumário dos resultados (continua)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Descontinuação por eventos adversos (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
9[1,2,3,4,5,6,7,8,9]	ensaios clínicos randomizados	muito grave[a]	muito grave[b]	não grave	muito grave[c]	nenhum	131	2388	taxa de eventos 20.78 por 1000 pessoas-ano (5.58 para 57.31)	⨁◯◯◯ Muito baixa	IMPORTANTE
Descontinuação por eventos adversos relacionados a TARV (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
5[2,3,4,5,6]	ensaios clínicos randomizados	muito grave[d]	muito grave[b]	não grave	muito grave[c]	nenhum	43	988	taxa de eventos 4.31 por 1000 pessoas-ano (0.13 para 54.72)	⨁◯◯◯ Muito baixa	IMPORTANTE

Tabela 4 – Sumário dos resultados (continuação)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Eventos adversos clínicos e/ou laboratoriais (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
4[3,4,5,8]	ensaios clínicos randomizados	muito grave[e]	muito grave[b]	não grave	muito grave[c]	nenhum	736	954	taxa de eventos 888.20 por 1000 pessoas-ano (759.9 para 1045)	⨁◯◯◯ Muito baixa	IMPORTANTE
Eventos adversos laboratoriais (seguimento: variação 184 semanas para 184 semanas; avaliado com: taxa de incidência)											
1[10]	ensaios clínicos randomizados	muito grave[f]	não grave	não grave	muito grave[c]	nenhum	91	483	taxa de eventos 52.02 por 1000 pessoas-ano (1.89 para 1388)	⨁◯◯◯ Muito baixa	NÃO IMPORTANTE
Eventos adversos clínicos e/ou laboratoriais relacionados a TARV (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
4[3,4,6,8]	ensaios clínicos randomizados	muito grave[e]	muito grave[b]	não grave	muito grave[c]	nenhum	298	954	taxa de eventos 341.60 por 1000 pessoas-ano (133.6 para 862.7)	⨁◯◯◯ Muito baixa	IMPORTANTE

Tabela 4 – Sumário dos resultados (continuação)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Eventos adversos clínicos relacionados a TARV (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
1[9]	ensaios clínicos randomizados	muito grave[f]	não grave	não grave	muito grave[c]	nenhum	221	575	taxa de eventos 431.50 por 1000 pessoas-ano (13.84 para 13630)	⨁◯◯◯ Muito baixa	IMPORTANTE
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 (seguimento: variação 48 semanas para 156 semanas; avaliado com: taxa de incidência)											
3[3,5,6]	ensaios clínicos randomizados	muito grave[g]	muito grave[b]	não grave	muito grave[c]	nenhum	37	284	taxa de eventos 96.34 por 1000 pessoas-ano (55.04 para 158.9)	⨁◯◯◯ Muito baixa	CRÍTICO
Eventos adversos graves clínicos graus 3 e/ou 4 (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
3[1,2,9]	ensaios clínicos randomizados	muito grave[h]	muito grave[b]	não grave	muito grave[c]	nenhum	158	1316	taxa de eventos 59.93 por 1000 pessoas-ano (33.74 para 104.6)	⨁◯◯◯ Muito baixa	CRÍTICO

Tabela 4 – Sumário dos resultados (continuação)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Eventos adversos graves laboratoriais graus 3 e/ou 4 (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
4[1,2,4,9]	ensaios clínicos randomizados	muito grave[i]	muito grave[b]	não grave	muito grave[c]	nenhum	452	1550	taxa de eventos 145.10 por 1000 pessoas-ano (57.71 para 359.9)	⊕◯◯◯ Muito baixa	CRÍTICO
Eventos adversos graves clínicos e/ou laboratoriais grau 3 (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
1[8]	ensaios clínicos randomizados	muito grave[f]	não grave	não grave	muito grave[c]	nenhum	55	495	taxa de eventos 125.50 por 1000 pessoas-ano (3.51 para 4295)	⊕◯◯◯ Muito baixa	IMPORTANTE
Eventos adversos graves clínicos e/ou laboratoriais grau 4 (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
1[8]	ensaios clínicos randomizados	muito grave[f]	não grave	não grave	muito grave[c]	nenhum	12	495	taxa de eventos 25.05 por 1000 pessoas-ano (0.5 para 1017)	⊕◯◯◯ Muito baixa	CRÍTICO

Tabela 4 – Sumário dos resultados (continuação)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Eventos adversos graves clínicos grau 4 (seguimento: variação 168 semanas para 168 semanas; avaliado com: taxa de incidência)											
1[2]	ensaios clínicos randomizados	muito grave[f]	não grave	não grave	muito grave[c]	nenhum	15	500	taxa de eventos 9.31 por 1000 pessoas-ano (0.39 para 216.3)	⊕◯◯◯ Muito baixa	CRÍTICO
Eventos adversos sérios clínicos e/ou laboratoriais (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
8[1,2,3,4,5,6,7,8]	ensaios clínicos randomizados	muito grave[j]	muito grave[b]	não grave	muito grave[c]	nenhum	140	1813	taxa de eventos 49.34 por 1000 pessoas-ano (31.6 para 77.1)	⊕◯◯◯ Muito baixa	CRÍTICO
Eventos adversos graves clínicos e/ou laboratoriais graus 3 e/ou 4 relacionados a TARV (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
2[3,6]	ensaios clínicos randomizados	muito grave[k]	muito grave[b]	não grave	muito grave[c]	nenhum	6	225	taxa de eventos 27.75 por 1000 pessoas-ano (2.56 para 272.9)	⊕◯◯◯ Muito baixa	CRÍTICO

Tabela 4 – Sumário dos resultados (continuação)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Eventos adversos sérios clínicos e/ou laboratoriais relacionados a TARV (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
4[3,4,6,8]	ensaios clínicos randomizados	muito grave[e]	muito grave[b]	não grave	muito grave[c]	nenhum	6	954	taxa de eventos 1.09 por 1000 pessoas-ano (0.01 para 21.47)	⨁◯◯◯ Muito baixa	CRÍTICO
Eventos adversos sérios clínicos relacionados a TARV (seguimento: variação 48 semanas para 48 semanas; avaliado com: taxa de incidência)											
4[4,6,8,9]	ensaios clínicos randomizados	muito grave[i]	muito grave[b]	não grave	muito grave[c]	nenhum	8	1197	taxa de eventos 1.53 por 1000 pessoas-ano (0.01 para 21.29)	⨁◯◯◯ Muito baixa	CRÍTICO
Morte por todas as causas (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
9[1,2,3,4,5,6,7,8,9]	ensaios clínicos randomizados	muito grave[a]	muito grave[b]	não grave	muito grave[c]	nenhum	22	2388	taxa de eventos 4.47 por 1000 pessoas-ano (1.42 para 7.91)	⨁◯◯◯ Muito baixa	CRÍTICO

Tabela 4 – Sumário dos resultados (conclusão)

№ dos estudos	Avaliação da certeza da evidência						Efeito			Certeza	Importância
	Delineamento do estudo	Risco de viés	Inconsistência	Evidência indireta	Imprecisão	Outras considerações	№ de eventos	№ de indivíduos	Taxa (95% CrI)		
Morte por eventos adversos relacionados a TARV (seguimento: variação 48 semanas para 168 semanas; avaliado com: taxa de incidência)											
9[1,2,3,4,5,6,7,8,9]	ensaios clínicos randomizados	muito grave[a]	muito grave[b]	não grave	muito grave[c]	nenhum	4	2388	taxa de eventos 0.18 por 1000 pessoas-ano (0 para 1.56)	⨁◯◯◯ Muito baixa	CRÍTICO

Fonte: Elaboração própria

Explicações

a. Oito estudos com alto risco de viés e um com alguma preocupação com risco de viés segundo RoB2 da Cochrane.

b. No tipo de análise estatística utilizado nessa revisão, os intervalos de credibilidade muito amplos sugerem alta heterogeneidade. Ademais, há heterogeneidade decorrente de diferenças clínicas (principalmente pela presença de diferentes esquemas ARV, em que um mesmo esquema se repete em no máximo dois braços dos estudos incluídos), no cegamento e no financiamento.

c. Os intervalos de credibilidade são bastante amplos.

d. Quatro estudos com alto risco de viés e um com alguma preocupação com risco de viés segundo RoB2 da Cochrane.

e. Três estudos com alto risco de viés e um com alguma preocupação com risco de viés segundo RoB2 da Cochrane.

f. Um estudo com alto risco de viés segundo RoB2 da Cochrane.

g. Dois estudos com alto risco de viés e um com alguma preocupação com risco de viés segundo RoB2 da Cochrane.

h. Três estudos com alto risco de viés segundo RoB2 da Cochrane.

i. Quatro estudos com alto risco de viés segundo RoB2 da Cochrane.

j. Sete estudos com alto risco de viés e um com alguma preocupação com risco de viés segundo RoB2 da Cochrane.

k. Um estudo com alto risco de viés e um com alguma preocupação com risco de viés segundo RoB2 da Cochrane.

Referências

1.LOCKMAN, S. *et al*. Antiretroviral Therapies in Women after Single-Dose Nevirapine Exposure. New England Journal of Medicine; 2010.

2.LOCKMAN, S. *et al*. Nevirapine- versus lopinavir/ritonavir-based initial therapy for HIV-1 infection among women in Africa: a randomized trial. PLoS medicine; 2012.

3.RASHBAUM, B. *et al*. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naïve patients with HIV-1: subgroup analyses of the phase 3 AMBER study. HIV Research & Clinical Practice; 2019.

4.KITYO, C. *et al*. Switching to Fixed-Dose Bictegravir, Emtricitabine, and Tenofovir Alafenamide (B/F/TAF) in Virologically Suppressed HIV-1 Infected Women: A Randomized, Open-Label, Multicenter, Active-Controlled, Phase 3, Noninferiority Trial. JAIDS Journal of Acquired Immune Deficiency Syndromes; 2019.

5.NAICKER, N. *et al*. Efficacy and Safety of Tenofovir-Containing Antiretroviral Therapy in Women who Acquired HIV while Enrolled in Tenofovir Gel Prophylaxis Trials. Antiviral Therapy; 2017.

6.HUHN, G. D. *et al*. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-experienced, virologically suppressed patients with HIV-1: subgroup analyses of the phase 3 EMERALD study. AIDS Research and Therapy; 2019.

7.IBRAHIM, F. *et al*. Bone mineral density, kidney function, weight gain and insulin resistance in women who switch from TDF/FTC/NNRTI to ABC/3TC/DTG. HIV Medicine; 2020.

8.ORRELL, C. *et al*. Fixed-dose combination dolutegravir, abacavir, and lamivudine versus ritonavir-boosted atazanavir plus tenofovir disoproxil fumarate and emtricitabine in previously untreated women with HIV-1 infection (ARIA): week 48 results from a randomised, open-label, non-inferiority, phase 3b study. The Lancet HIV; 2017.

9.SQUIRES, K. *et al*. Integrase inhibitor versus protease inhibitor based regimen for HIV-1 infected women (WAVES): a randomised, controlled, double-blind, phase 3 study. The Lancet HIV; 2016.

10.FIRNHABER, C. *et al*. Differences in antiretroviral safety and efficacy by sex in a multinational randomized clinical trial. HIV Clinical Trials; 2015.