



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 9/13/2019

Visit the *AIDSinfo* website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression (Last updated October 25, 2018; last reviewed October 25, 2018)

Panel's Recommendations

- Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance make it possible to consider switching an effective regimen to an alternative regimen in some situations.
- The fundamental principle of regimen switching is to maintain viral suppression without jeopardizing future treatment options **(AI)**.
- It is critical to review a patient's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results, before selecting a new antiretroviral therapy regimen **(AI)**.
- Adverse events, drug-drug or drug-food interactions, pill burden, pregnancy, cost, or the desire to simplify a regimen may prompt a regimen switch. Within-class and between-class switches can usually maintain viral suppression, provided that there is no viral resistance to the ARV agents in the new regimen **(AI)**.
- Monotherapy with either a boosted protease inhibitor or an integrase strand transfer inhibitor has been associated with unacceptable rates of virologic failure and the development of resistance; therefore, monotherapy as a switching strategy **is not recommended (AI)**.
- When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, ARV drugs that are active against HBV infection should be continued. Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage.
- Consultation with an HIV specialist should be considered when planning a regimen switch for a patient with a history of resistance to one or more drug classes **(BIII)**.
- Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

With currently available antiretroviral therapy (ART), most patients living with HIV can achieve and maintain HIV viral suppression. Furthermore, advances in treatment and a better understanding of drug resistance make it possible to consider switching from an effective regimen to another regimen in some situations (see below). When considering such a switch, clinicians must keep several key principles in mind in order to maintain viral suppression while addressing the concerns with the current regimen.

Reasons to Consider Regimen Switching in the Setting of Viral Suppression

- To simplify a regimen by reducing pill burden and/or dosing frequency
- To enhance tolerability and/or decrease short- or long-term toxicity (see [Adverse Effects of Antiretroviral Agents](#) and [Table 18](#) for a more in-depth discussion of possible toxicities)
- To prevent or mitigate drug-drug interactions (see [Drug-Drug Interactions](#))
- To eliminate food or fluid requirements
- To allow for optimal use of ART during pregnancy or in cases where pregnancy may occur (see the [Perinatal Guidelines](#))
- To reduce costs (see [Cost Considerations and Antiretroviral Therapy](#))

General Principles of Regimen Switching

Maintain Viral Suppression

The fundamental principle of regimen switching is to maintain viral suppression without jeopardizing future treatment options **(AI)**. If a regimen switch results in virologic failure with the emergence of new resistance

mutations, the patient may require more complex or expensive regimens.

Careful Review of Antiretroviral History Before Switch

The review of a patient's full antiretroviral (ARV) history—including virologic responses, past ARV-associated toxicities, and cumulative resistance test results—is warranted before any treatment switch (AI). If a patient with pre-ART wild-type HIV achieves and maintains viral suppression after ART initiation, one can assume that no new resistance mutation emerged while the patient was on the suppressive regimen.

Assess Prior Resistance Before Switch

Review of cumulative resistance test results is essential when designing a new regimen. Cumulative resistance test results refer to all previous and currently available results from standard genotype, proviral DNA genotype, phenotype, and tropism assays that can be used to guide the selection of a new regimen. Once selected, a resistance mutation is generally archived in the HIV reservoir and is likely to re-emerge under the appropriate selective drug pressure, even if it is not detected in the patient's most recent resistance test. When resistance data are not available, resistance may often be inferred from a patient's treatment history. For example, a patient who experienced virologic failure on a lamivudine (3TC)-containing regimen or an emtricitabine (FTC)-containing regimen in the past is likely to have the M184V substitution, even if it is not documented. For patients with documented failure on a regimen that contains elvitegravir (EVG), raltegravir (RAL), or a non-nucleoside reverse transcriptase inhibitor (NNRTI), resistance to these drugs should be assumed because these drugs generally have a lower barrier to resistance than other ARV drugs. If there is uncertainty about prior resistance, it is generally not advisable to switch a suppressive ARV regimen unless the new regimen is likely to be at least as active against potential resistant virus as the suppressive regimen. This is particularly applicable when switching ARV-experienced individuals from a regimen with a high barrier to resistance to one with a lower barrier to resistance.¹ Consulting an HIV specialist is recommended when contemplating a regimen switch for a patient with a history of resistance to one or more drug classes (BIII).

If switching is considered in patients with suppressed viral loads who do not have prior resistance data, next-generation proviral DNA genotypic resistance testing can be considered. For patients who have no prior virologic failures and who are on their first or second regimen, or those who have genotypic test results from prior virologic failures, the use of the proviral DNA genotypic test is unlikely to provide useful information. In individuals with multiple prior failures or a history of multiple prior ARV regimens, the use of proviral DNA genotypic testing may be useful. However, the results must be interpreted with caution, as these assays may not detect all of a patient's drug resistance mutations, especially those that were selected by a previous ART regimen. In addition, these assays may identify mutations that appear to be inconsistent with a patient's response to treatment, making the clinical relevance of the assay results questionable. Overall, the clinical utility of these assays remains an area of active investigation (see [Drug-Resistance Testing](#)).

Switching in a Person with Hepatitis B Virus Coinfection

When switching an ARV regimen in a patient with hepatitis B virus (HBV)/HIV coinfection, tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) should be continued as part of the new regimen, unless these drugs are contraindicated. Both TDF and TAF are active against HBV infection.² Discontinuation of these drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage. Using 3TC or FTC as the only active drug for HBV infection **is not recommended**, as HBV resistance to these drugs can emerge rapidly. If TDF or TAF cannot be used as part of the ARV regimen, refer to [Hepatitis B Virus/HIV Coinfection](#) for recommendations.

Assess for Potential Drug Interactions

Before switching a regimen, it is important to review the ARV drugs in the new regimen and concomitant medications to assess whether there are any potential drug-drug interactions. For example, rilpivirine (RPV) may interact with acid-lowering agents, and TAF and bictegravir (BIC) may interact with rifamycins (see

[Drug-Drug Interactions](#)). In addition to new drug interactions, the discontinuation of some ARV drugs may also necessitate adjusting the dosage of concomitant medications. For example, discontinuation of pharmacokinetic boosters (ritonavir or cobicistat) may reduce the concentrations of some concomitant medications. Concomitant medications which may have previously been managed with dose adjustments will need to be re-evaluated in the context of the new ART regimen.

Assess for Potential for Pregnancy

A pregnancy test should be performed for those of childbearing potential prior to switching ART. If a person with HIV is found to be pregnant, clinicians should refer to the [Perinatal Guidelines](#) for recommendations on the safety and efficacy of ARV use in pregnancy. Preliminary data from Botswana suggest there may be an increased risk of neural tube defects (NTDs) in infants born to women who were receiving dolutegravir (DTG) at the time of conception.^{3,4}

Until more information is available:

- Clinicians should discuss the possible association between NTDs and DTG use during conception and the benefits of DTG for HIV treatment with individuals of childbearing potential; clinicians should also provide appropriate counseling so that the individual can make an informed decision about the use of DTG (**AIII**).
- DTG is **not recommended** for those:
 - Who are pregnant and within 12 weeks post-conception;
 - Who are of childbearing potential, sexually active, and not using effective contraception; *or*
 - Who are contemplating pregnancy.
- It is unknown whether the possible risk of NTDs associated with DTG use at the time of conception is shared by other integrase strand transfer inhibitors (INSTIs) (i.e., a class effect).
- BIC is structurally similar to DTG, but there are no safety data on the use of BIC around the time of conception. For those who are of childbearing potential, but who are not pregnant, an approach similar to that outlined for DTG should be taken before considering BIC-containing ART.

Monitoring after Switch

Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch (see below).

Specific Regimen Switching Considerations (also see [Adverse Effects of Antiretroviral Agents](#))

As with ART-naïve patients, the use of a three-drug combination regimen is generally recommended when switching patients with suppressed viral loads to a new regimen. Patients with no resistance mutations can likely switch to any regimen that has been shown to be highly effective in ART-naïve patients. In addition, there is growing evidence that certain two-drug regimens can maintain virologic suppression, as discussed below. Monotherapy with either a boosted protease inhibitor (PI) or an INSTI has been explored in several trials or cohort studies. Monotherapy has been associated with a higher rate of virologic failure than other regimens and has been associated with the development of resistance, especially INSTI monotherapy; therefore, monotherapy as a switching strategy is **not recommended (AI)**.

Strategies with Good Supporting Evidence

Three-Drug Regimens

Within-Class Switches

Within-class switches that are prompted by adverse events or the availability of ARVs within the same class

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

H-24

that offer a better safety profile, reduced dosing frequency, higher barrier to resistance, or lower pill burden usually maintain viral suppression, provided there is no drug resistance to the new ARV. Some examples of within-class switch strategies are switching from:

- TDF^{5,6} or abacavir (ABC)⁷ to TAF
- RAL to elvitegravir/cobicistat (EVG/c)⁸ or DTG
- DTG^{9,10}, EVG/c, or RAL to BIC
- Efavirenz (EFV) to RPV^{6,11}
- A ritonavir-boosted PI (PI/r) to a PI coformulated with cobicistat (PI/c)
- Boosted atazanavir (ATV/c or ATV/r) to unboosted ATV (when used with ABC/3TC)¹²⁻¹⁴

Between-Class Switches

Between-class switches generally maintain viral suppression, provided there is no resistance to the other components of the regimen. Such switches should be avoided if there is any doubt about the activity of the other agents in the regimen. As noted earlier, prior resistance test results will be very informative in guiding this switch.

Some examples of between-class switch strategies are:

- Replacing a boosted PI with an INST (e.g., DTG,¹⁵ BIC,¹⁶ or EVG^{17,18})
- Replacing a boosted PI with RPV¹⁹
- Replacing an NNRTI with an INSTI^{20,21}
- Replacing a boosted PI with maraviroc (MVC).²² When switching to MVC, co-receptor usage in patients with virologic suppression can be determined from proviral DNA (see [Co-receptor Tropism Assays](#)) obtained from peripheral blood mononuclear cells.²²⁻²⁴

Two-Drug Regimens

There is growing evidence that some two-drug regimens are effective in maintaining virologic control in patients who initiated therapy and achieved virologic suppression with three-drug regimens. However, caution should be taken in patients with HBV coinfection, as these simplified regimens may not have adequate anti-HBV activity. Below are examples of successful strategies for switching from three- to two-drug regimens in persons with suppressed HIV.

Dolutegravir plus Rilpivirine

Two Phase 3 trials enrolled 1,024 participants with viral suppression for ≥ 1 year and no history of virologic failure.²⁵ Participants were randomized to stay on their combination ART regimen or to switch to a regimen of once-daily DTG plus RPV. Viral suppression was maintained in 95% to 96% of the participants in both arms at 48 weeks. DTG plus RPV is available as a coformulated single-tablet regimen. This regimen is a reasonable option when the use of nucleoside reverse transcriptase inhibitors (NRTIs) is neither desirable nor necessary. It should only be given to patients who do not have chronic HBV infection, have no evidence of resistance to either DTG or RPV, and have no significant drug-drug interaction that might reduce either drug's concentration (**AI**).

Ritonavir-Boosted Protease Inhibitor plus Lamivudine or Emtricitabine

There is growing evidence that a PI/r-based regimen plus 3TC can maintain viral suppression in patients who initiated triple-drug therapy, who achieved sustained viral suppression for ≥ 1 year, and who have no evidence of, or risk of resistance to, either the PI/r or 3TC. A PI/r plus 3TC/FTC may be a reasonable option when the

continued use of TDF, TAF, or ABC is contraindicated or not desirable. Examples of boosted PI plus 3TC regimens which have been studied in clinical trials include the following:

- ATV/r plus 3TC **(CI)**,^{26,27}
- Darunavir/ritonavir (DRV/r) plus 3TC **(BI)**,²⁸ *or*
- Lopinavir/ritonavir (LPV/r) plus 3TC **(CI)**.²⁹

Strategies for Patients with Viral Suppression and a History of Treatment Failure

Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine plus Darunavir

The combination of EVG/c/TAF/FTC plus DRV has been shown to be a potential simplification strategy in patients with complicated salvage regimens.³⁰ A randomized controlled trial enrolled 135 virologically suppressed patients who were receiving DRV-containing ART and had resistance to at least two ARV drug classes, but no INSTI resistance. Eligible participants could have up to three thymidine analog resistance mutations and/or the K65R mutation, but no history of either the Q151M mutation or T69 insertion mutations. The patients were randomized 2:1 to either switch to a regimen of EVG/c/TAF/FTC plus DRV or remain on their original regimen. At 24 weeks, 97% of the patients in the EVG/c/TAF/FTC plus DRV arm maintained virologic suppression. The pill burden was reduced from an average of five tablets per day to two tablets per day. This regimen would be an appropriate option for individuals with similar treatment and drug resistance histories as those included in this study **(AI)**.

Strategies with Some Supporting Evidence

Other switching strategies in patients with viral suppression have some evidence to support their use. These strategies cannot be recommended until further evidence is available. If used, patients should be closely monitored to assure that viral suppression is maintained. Some of these strategies are listed below.

Boosted Protease Inhibitor plus Integrase Strand Transfer Inhibitor

In two small observational studies (which included 13 participants and 56 participants) in which participants were switched from their current ART regimens to DRV/r plus DTG, viral suppression was maintained in over 97% of the patients for a mean of 12.8 months in the first cohort and at 48 weeks in the second cohort.^{31,32}

Dolutegravir plus Lamivudine

A switch to DTG plus 3TC as maintenance strategy in patients with viral suppression has been examined in two small clinical trials and in two observational studies.

Clinical Trials

The LAMIDOL trial evaluated a regimen of DTG and 3TC as a maintenance strategy in patients with virologic suppression who had no evidence of NRTI, INSTI, or PI resistance.³³ At 24 weeks, 103 of the 104 participants remained virologically suppressed.

The ASPIRE study included 90 participants with viral suppression on three-drug ART and no history of virologic failure. These participants were randomized to remain on their current regimen or to switch to DTG plus 3TC. The DTG plus 3TC regimen was noninferior to continuing the three-drug ART regimens (91% vs. 89% of participants remained virologically suppressed by Week 48, respectively).³⁴

Observational Studies

A prospective observational study included 94 patients with viral suppression who were switched to DTG plus 3TC and who maintained viral suppression for 24 weeks following the switch.³⁵ Another study evaluated the safety and efficacy of this regimen in 206 patients who switched due to either drug toxicity or a desire to simplify their regimens. At Week 48, the estimated probability of maintaining viral suppression was 98.2%; at Week 96, the estimated probability was 95.1%.³⁶

Strategies Not Recommended

Boosted Protease Inhibitor Monotherapy

The strategy of switching patients with virologic suppression without PI resistance from one ART regimen to PI/r monotherapy has been evaluated in several studies. The rationale for this strategy is to avoid NRTI toxicities and decrease costs while taking advantage of the high barrier to resistance of PIs. PI/r monotherapy maintains virologic suppression in most patients, but at lower rates than regimens that include one or two NRTIs.³⁷⁻

³⁹ Low-level viremia, generally without the emergence of PI resistance, appears to be more common with monotherapy than with regimens that include one or two NRTIs. In most studies, resuming NRTIs in patients who are experiencing low-level viral rebound has led to re-suppression.⁴⁰⁻⁴³ No clinical trials evaluating the use of coformulated PI/c regimens as monotherapy or comparing different PI/r monotherapy regimens have been conducted. On the basis of the results from these studies, boosted PI monotherapy **is not recommended (AI)**.

Dolutegravir Monotherapy

The strategy of switching virologically suppressed patients to DTG monotherapy has been evaluated in cohort studies and in clinical practice,^{44,45} as well as in a randomized controlled trial.⁴⁶ This strategy has been associated with an unacceptable risk of virologic failure and subsequent development of INSTI resistance; therefore, it **is not recommended (AI)**.

Boosted Atazanavir plus Raltegravir

In a randomized study, virologically suppressed patients switched to a regimen consisting of ATV/r plus RAL or ATV/r plus TDF/FTC. The ATV/r plus RAL regimen switch was associated with higher rates of virologic failure and treatment discontinuations than switching to ATV/r plus TDF/FTC.⁴⁷ A regimen consisting of ATV/r plus RAL cannot currently be recommended **(AI)**.

Maraviroc plus Boosted Protease Inhibitor

In a randomized controlled trial, virologically suppressed patients who were on a regimen of two NRTIs plus a boosted PI and who had only CCR5-tropic HIV (as detected by proviral DNA testing) were randomized to continue their present regimen or to switch to MVC plus two NRTIs or to MVC plus a boosted PI. The boosted PI plus MVC regimen switch was associated with higher rates of virologic failure and treatment discontinuations than the other two regimens. Based on these results, a regimen consisting of a boosted PI and MVC cannot be recommended **(AI)**.⁴⁸

Maraviroc plus Raltegravir

In a nonrandomized pilot study, virologically suppressed patients were switched from their prescribed regimen to MVC plus RAL. This combination led to virologic relapse in five out of 44 patients.⁴⁹ On the basis of these study results, use of a combination of MVC and RAL **is not recommended (AII)**.

Monitoring after Treatment Changes

After a treatment switch, patients should be evaluated closely for 3 months (e.g., a clinic visit or phone call 1 to 2 weeks after the change and a viral load test to check for rebound viremia 4 to 8 weeks after the switch) **(AIII)**. The purpose of this close monitoring is to assess medication tolerance and conduct targeted laboratory testing if the patient had pre-existing laboratory abnormalities or if there are potential concerns with the new regimen. For example, if lipid abnormalities were present and were a reason for the ARV change, or if lipid abnormalities are a concern with the new regimen, fasting cholesterol subsets and triglycerides should be assessed within 3 months after the change in therapy. In the absence of any new complaints, laboratory abnormalities, or evidence of viral rebound at this 3-month visit, clinical and laboratory monitoring of the patient may resume on a regularly scheduled basis (see [Laboratory Testing for Initial Assessment and Monitoring](#)).

References

1. Eron JJ, Young B, Cooper DA, et al. 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. *Lancet*. 2010;375(9712):396-407. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20074791>.
2. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29405329>.
3. Zash R, Makhema J, Shapiro RL. Neural-Tube Defects with Dolutegravir Treatment from the Time of Conception. *N Engl J Med*. 2018;379(10):979-981. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30037297>.
4. Zash R, Holmes L, Makhema J, et al. Surveillance for neural tube defects following antiretroviral exposure from conception. Presented at: 22nd International AIDS Conference. 2018. Amsterdam.
5. Gallant JE, Daar ES, Raffi F, et al. 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. *Lancet HIV*. 2016;3(4):e158-165. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/27036991>.
6. Hagins D, Orkin C, Daar ES, et al. 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. *HIV Med*. 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30101539>.
7. Winston A, Post FA, DeJesus E, et al. 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. *Lancet HIV*. 2018;5(4):e162-e171. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29475804>.
8. Mills A, Crofoot G, Ortiz R, et al. Switching from twice-daily raltegravir plus tenofovir disoproxil fumarate/emtricitabine to once-daily elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate in virologically suppressed, HIV-1-infected subjects: 48 weeks data. *HIV Clin Trials*. 2014;15(2):51-56. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24710918>.
9. Molina JM, Ward D, Brar I, et al. 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. *Lancet HIV*. 2018;5(7):e357-e365. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29925489>.
10. Bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) [package insert]. Gilead Sciences. 2018. Available at: http://www.gilead.com/~media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.pdf.
11. Mills AM, Cohen C, DeJesus E, et al. Efficacy and safety 48 weeks after switching from efavirenz to rilpivirine using emtricitabine/tenofovir disoproxil fumarate-based single-tablet regimens. *HIV Clin Trials*. 2013;14(5):216-223. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24144898>.
12. Squires KE, Young B, DeJesus E, et al. ARIES 144 week results: durable virologic suppression in HIV-infected patients simplified to unboosted atazanavir/abacavir/lamivudine. *HIV Clin Trials*. 2012;13(5):233-244. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23134624>.
13. Ghosn J, Carosi G, Moreno S, et al. Unboosted atazanavir-based therapy maintains control of HIV type-1 replication as effectively as a ritonavir-boosted regimen. *Antivir Ther*. 2010;15(7):993-1002. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21041914>.
14. Wohl DA, Bhatti L, Small CB, et al. 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. *HIV Med*. 2016;17(2):106-117. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26176344>.
15. Gatell JM, Assoumou L, Moyle G, et al. Switching from a ritonavir-boosted protease inhibitor to a dolutegravir-based regimen for maintenance of HIV viral suppression in patients with high cardiovascular risk. *AIDS*. 2017;31(18):2503-2514. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29112070>.
16. Daar ES, DeJesus E, Ruane P, et al. 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. *Lancet HIV*. 2018;5(7):e347-e356. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29925490>.
17. Arribas JR, DeJesus E, van Lunzen J, et al. 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. *HIV Clin Trials*. 2017;18(3):118-125. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28555519>.

18. Hodder S, Squires K, Kityo C, et al. Brief report: efficacy and safety of switching to coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide (E/C/F/TAF) in virologically suppressed women. *J Acquir Immune Defic Syndr*. 2018;78(2):209-213. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29481486>.
19. Palella FJ Jr, Fisher M, Tebas P, et al. Simplification to rilpivirine/emtricitabine/tenofovir disoproxil fumarate from ritonavir-boosted protease inhibitor antiretroviral therapy in a randomized trial of HIV-1 RNA-suppressed participants. *AIDS*. 2014;28(3):335-344. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24670520>.
20. Pozniak A, Markowitz M, Mills A, et al. 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. *Lancet Infect Dis*. 2014;14(7):590-599. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24908550>.
21. Arribas JR, Pialoux G, Gathe J, et al. 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. *Lancet Infect Dis*. 2014;14(7):581-589. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24908551>.
22. Pett SL, Amin J, Horban A, et al. Week 96 results of the randomized, multicentre Maraviroc Switch (MARCH) study. *HIV Med*. 2018;19(1):65-71. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28703491>.
23. Vitiello P, Brudney D, MacCartney M, et al. Responses to switching to maraviroc-based antiretroviral therapy in treated patients with suppressed plasma HIV-1-RNA load. *Intervirology*. 2012;55(2):172-178. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22286889>.
24. Bonjoch A, Pou C, Perez-Alvarez N, et al. Switching the third drug of antiretroviral therapy to maraviroc in aviraemic subjects: a pilot, prospective, randomized clinical trial. *J Antimicrob Chemother*. 2013;68(6):1382-1387. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23354282>.
25. Llibre JM, Hung CC, Brinson C, et al. 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. *Lancet*. 2018;391(10123):839-849. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29310899>.
26. Perez-Molina JA, Rubio R, Rivero A, et al. Dual treatment with atazanavir-ritonavir plus lamivudine versus triple treatment with atazanavir-ritonavir plus two nucleos(t)ides in virologically stable patients with HIV-1 (SALT): 48 week results from a randomised, open-label, non-inferiority trial. *Lancet Infect Dis*. 2015;15(7):775-784. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26062881>.
27. Fabbiani M, Gagliardini R, Ciccarelli N, et al. Atazanavir/ritonavir with lamivudine as maintenance therapy in virologically suppressed HIV-infected patients: 96 week outcomes of a randomized trial. *J Antimicrob Chemother*. 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29668978>.
28. Pulido F, Ribera E, Lagarde M, et al. Dual therapy with darunavir and ritonavir plus lamivudine versus triple therapy with darunavir and ritonavir plus tenofovir disoproxil fumarate and emtricitabine or abacavir and lamivudine for maintenance of HIV-1 viral suppression: randomised, open label, non-inferiority DUAL-GESIDA 8014-RIS-EST45 trial. *Clin Infect Dis*. 2017. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/29020293>.
29. Arribas JR, Girard PM, Landman R, et al. 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. *Lancet Infect Dis*. 2015;15(7):785-792. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26062880>.
30. Huhn GD, Tebas P, Gallant J, et al. A randomized, open-label trial to evaluate switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide plus darunavir in treatment-experienced HIV-1-infected adults. *J Acquir Immune Defic Syndr*. 2017;74(2):193-200. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27753684>.
31. Capetti AF, Cossu MV, Orofino G, et al. A dual regimen of ritonavir/darunavir plus dolutegravir for rescue or simplification of rescue therapy: 48 weeks' observational data. *BMC Infect Dis*. 2017;17(1):658. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28964268>.
32. Wheeler J, Chan S, Harrigan PR, Becker M, Kasper K, Keynan Y. Dolutegravir with boosted darunavir treatment simplification for the transmitted HIV thymidine analog resistance in Manitoba, Canada. *Int J STD AIDS*. 2018;29(5):520-522. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29513131>.
33. Joly V, Burdet C, Landman R, et al. Promising results of dolutegravir + lamivudine maintenance in ANRS 167 LAMIDOL

Trial. Presented at: Conference on Retroviruses and Opportunistic Infections. 2017. Seattle, WA. Available at: <http://www.croiconference.org/sessions/promising-results-dolutegravir-lamivudine-maintenance-anrs-167-lamidol-trial>.

34. Taiwo BO, Marconi VC, Berzins B, et al. Dolutegravir Plus Lamivudine Maintains Human Immunodeficiency Virus-1 Suppression Through Week 48 in a Pilot Randomized Trial. *Clin Infect Dis*. 2018;66(11):1794-1797. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29293895>.
35. Maggiolo F, Gulminetti R, Pagnucco L, et al. Lamivudine/dolutegravir dual therapy in HIV-infected, virologically suppressed patients. *BMC Infect Dis*. 2017;17(1):215. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28302065>.
36. Borghetti A, Baldin G, Lombardi F, et al. Efficacy and tolerability of lamivudine plus dolutegravir as a switch strategy in a multicentre cohort of patients with suppressed HIV-1 replication. *HIV Med*. 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29573320>.
37. Bierman WF, van Agtmael MA, Nijhuis M, Danner SA, Boucher CA. HIV monotherapy with ritonavir-boosted protease inhibitors: a systematic review. *AIDS*. 2009;23(3):279-291. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19114854>.
38. Arribas JR, Clumeck N, Nelson M, Hill A, van Delft Y, Moecklinghoff C. 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. *HIV Med*. 2012;13(7):398-405. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22413874>.
39. Ciaffi L, Koulla-Shiro S, Sawadogo AB, et al. 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. *Lancet HIV*. 2017. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28566227>.
40. Guiguet M, Ghosn J, Duvivier C, et al. Boosted protease inhibitor monotherapy as a maintenance strategy: an observational study. *AIDS*. 2012;26(18):2345-2350. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22695301>.
41. Karlstrom O, Josephson F, Sonnerborg A. Early virologic rebound in a pilot trial of ritonavir-boosted atazanavir as maintenance monotherapy. *J Acquir Immune Defic Syndr*. 2007;44(4):417-422. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17159658>.
42. Katlama C, Valantin MA, Algarte-Genin M, et al. Efficacy of darunavir/ritonavir maintenance monotherapy in patients with HIV-1 viral suppression: a randomized open-label, noninferiority trial, MONOI-ANRS 136. *AIDS*. 2010;24(15):2365-2374. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20802297>.
43. Vernazza P, Daneel S, Schiffer V, et al. The role of compartment penetration in PI-monotherapy: the Atazanavir-Ritonavir Monomaintenance (ATARITMO) Trial. *AIDS*. 2007;21(10):1309-1315. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17545707>.
44. Blanco JL, Rojas J, Paredes R, et al. Dolutegravir-based maintenance monotherapy versus dual therapy with lamivudine: a planned 24 week analysis of the DOLAM randomized clinical trial. *J Antimicrob Chemother*. 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29608685>.
45. Oldenbuettel C, Wolf E, Ritter A, et al. Dolutegravir monotherapy as treatment de-escalation in HIV-infected adults with virological control: DoluMono cohort results. *Antivir Ther*. 2017;22(2):169-172. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27588613>.
46. Wijting I, Roxk C, Boucher C, et al. Dolutegravir as maintenance monotherapy for HIV (DOMONO): a phase 2, randomised non-inferiority trial. *Lancet HIV*. 2017;4(12):e547-e554. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29107562>.
47. van Lunzen J, Pozniak A, Gatell JM, et al. Brief report: switch to ritonavir-boosted atazanavir plus raltegravir in virologically suppressed patients with HIV-1 infection: a randomized pilot study. *J Acquir Immune Defic Syndr*. 2016;71(5):538-543. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26605505>.
48. Pett SL, Amin J, Horban A, et al. 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. *Clin Infect Dis*. 2016;63(1):122-132. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27048747>.
49. Katlama C, Assoumou L, Valantin MA, et al. Maraviroc plus raltegravir failed to maintain virological suppression in HIV-infected patients with lipohypertrophy: results from the ROCnRAL ANRS 157 study. *J Antimicrob Chemother*. 2014;69(6):1648-1652. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24535278>.