PharmaNote®

Vol. 36, Issue 5 February 2021 Established 1985

Rukobia® (fostemsavir): Attempting to put the ART backing into antiretroviral therapy

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In 2019, 38 million people worldwide were living with human immunodeficiency virus (HIV), while in 2018, an estimated 1.2 million people in the United States (≥ 13 years old) had HIV.[1,2] Human immunodeficiency virus is a virus that attacks the body's immune system (CD4+ cells); if left untreated, it can lead to acquired immunodeficiency syndrome (AIDS).[3] Acquired immunodeficiency syndrome is defined as a profound immunologic deficit (CD4+ < 200 cells/mm3) coupled with opportunistic infections such as Pneumocystis carinii pneumonia (PCP), Kaposi's sarcoma, and others.[3,4] Human immunodeficiency virus type-1 (HIV-1) is one of the primary causes of AIDS.[4] Similarly, human immunodeficiency virus type-2 (HIV-2) can also cause AIDS, however it is less virulent, transmittable, and prevalent when compared to HIV-1 infections.[4] Both of these viruses are known as retroviruses which utilize the enzyme reverse transcriptase to translate RNA into DNA.[5] Major risk factors for contracting HIV include anorectal sexual intercourse (particularly in men who have sex with men (MSM)) and sharing of needles among various users (particularly in intravenous drug users (IVDU)).[4] It is also possible to contract HIV through vaginal sexual intercourse; however, the incidence of transmission is approximately 18 times lower in this patient population.[6]

The majority of patients (50-90%) that contract HIV typically present with an acute retroviral syndrome or mononucleosis-like illness in which the host body has an immune response to the virus.[4] The most common symptoms that present include fever, headache, sore throat, fatigue, GI upset, weight loss, myalgia, rash, and/or night sweats which typically last for approximately two weeks. At first the infection will present with a high viral load (106 viral copies/mL) and a rapid decline in the CD4+ cell count (normal values range from 500 to 1400 cells/mm3) then as the virus goes dormant CD4+ counts may increase slightly, and plasma viral RNA will decrease.[4]

Diagnosis of HIV relies on an enzyme-linked immunosorbent assay (ELISA) which will detect HIV-1 antibodies.[4] This assay detects immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies as well as p24 antigens; this is a highly sensitive (< 99%) and highly specific (> 99%) test. Positive tests require repeat testing to differentiate between HIV-1 and HIV-2 infections. HIV testing is recommended when symptoms are present or high-risk activities have occurred. The CDC recommends HIV screening at least once for anyone aged 13-64 years, and at least once per year for anyone with major risk factors as previously outlined.[4,7] After diagnosis, HIV is then continuously monitored by two biomarkers: CD4+ T-cell count and viral load.[4]

Current drug therapies on the market for HIV-1 infections include antiretroviral therapies (ARTs) such as reverse transcriptase inhibitors (NRTIs and NNRTIs), protease inhibitors (PIs), entry inhibitors (fusion inhibitors and CCR5 antagonists), and integrase strand transfer inhibitors (InSTIs).[4] In general, a combination of three antiretroviral therapies from two separate therapeutic classes are needed to suppress HIV viral loads to undetectable plasma levels and improve immune response with increases in CD4+ counts. Current guideline recommendations include an initial treatment with a three-drug regimen consisting of either two NRTIs or a tenofovir-based regimen with the addition of an InSTI, NNRTI, or a boosted PI.[8] New data now supports the use of a two-drug regimen consisting of dolutegravir (InSTI) and lamivudine (NRTI) as initial drug therapy for HIV infections.8 The goal of HIV pharmacotherapy is to suppress HIV viral load to undetectable plasma levels (usually HIV RNA < 50 copies/mL).[4] The guidelines also recommend drug-resistance testing during the initial acute phase of HIV infection where genotypic assays are preferred over phenotypic assays.[8] This testing, however, should not delay initial treatment.

While ARTs are highly effective, HIV drug resistance is still seen in virtually all countries.[9] One of the major contributors to antiretroviral therapy failure is HIV drug resistance. Nucleoside analogue reverse transcriptase inhibitors (NRTIs) and nonnucleoside analogue reverse transcriptase inhibitors (NNRTIs) have the highest rates of resistance among HIV drug therapies. On the contrary, protease inhibitors (PIs) and integrase strand transfer inhibitors (InSTIs) have some of the lowest rates of resistance among HIV drug therapies with InSTIs having the lowest risk of resistance.[9,10] Drug therapy resistance can be measured with a baseline genotype resistance test.10 Because of the growing re-

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sistance rates, there is a constant need for new drug therapies to be developed that can overcome these resistance patterns. Rukobia (fostemsavir) was approved on July 2nd, 2020 as a first-in-class attachment inhibitor to combat ART resistance in adults with HIV-1 infection.[11]

HIV Life cycle in brief

Understanding the life cycle of HIV is vital because many of the current available therapies target some point of its life cycle.4 Once HIV enters the host body, the protein (glycoprotein 160) on the surface of the virus will have a binding affinity for the host CD4+ receptors.[4] The glycoprotein 160 (gp160) is made up of two subunits known simply as glycoprotein 120 (gp120) and glycoprotein 41 (gp41). The subunit gp120 is responsible for the binding to CD4+ cells. After the virus binds to the host cells, a cascade of events occurs in which the virus will then further attach itself to chemokine coreceptors. Once the virus enters the host cell, viral replication can begin.[4]

Clinical Pharmacology

Mechanism of Action

Fostemsavir is a methyl phosphate prodrug of temsavir.[12] Temsavir is an attachment inhibitor that binds directly to the HIV -1 glycoprotein 120 (gp120) subunit within the HIV-1 envelope. By binding to the gp120 subunit, temsavir inhibits the HIV-1 virus from interacting and attaching to the cellular CD4+ T-cell receptors.[13] This mechanism of action differs from integrase inhibitors that act on and inhibit the action of the viral enzyme, integrase, which catalyzes the covalent insertion of viral DNA into host infected cells.[14] While fostemsavir is another attachment inhibitor, the proprietary mechanism of action makes it unique among other attachment inhibitors.

Pharmacokinetics

Fostemsavir is a water-soluble compound that increases the bioavailability, duration of action, and absorption of temsavir.[12] This favorable profile of fostemsavir allows for once to twice daily dosing. Temsavir C_{max} and AUC concentrations are 1,770 ng/mL and 12,900 ng*h/mL , respectively, with time to peak concentrations seen at two hours after administration.[15] Temsavir is 88.4% protein bound, primarily to albumin. Fostemsavir is primarily excreted in the urine (51%) and feces (33%).[15] A summary of pharmacokinetic parameters of temsavir can be found in **Table 1**.

Table 1 | Select Temsavir Pharmacokinetics[15]

	Temsavir
Absorption	
T_{max}[a] (hours)	2.0
Distribution	
Vd[b] (L)	29.5
Plasma Protein Binding	89.4% (Albumin
Metabolism	
Primary	Hydrolysis (esterases)
Secondary	Oxidation (CYP3A4)
Minor	UGT[c]
Elimination	
$T_{1/2}$[c](hours)	11
Urine	51%
Fecal	33%

[a]Time to maximum plasma concentration; [b]Voume of distribution; [c]Half-life

Clinical Trials

Fostemsavir was approved based off of a single phase III clinical trial commonly referred to as the BRIGHTE trial. One phase IIb trial was conducted to evaluate the safety and efficacy of fostemsavir prior to its full efficacy evaluation in the BRIGHTE trial. These two trials are reviewed below with the results of the BRIGHTE trial summarized in Table 2.

Phase IIb Trial: AI43801113[16]

The phase IIb trial AI438011 was conducted to determine the efficacy and safety of fostemsavir when compared to atazanavir boosted with ritonavir (ATV/r).[16] This study was a randomized, multinational, active-controlled, partially blinded trial conducted in treatment-experienced HIV-1 patients (defined as current or previous exposure to one antiretroviral drug for at least a week). It included patients who had a plasma HIV-1 RNA level of 1,000 copies/mL, CD4+ count > 50 cells/mm3, and HIV-1 genotype and phenotype indicating susceptibility to atazanavir (ATV), raltegravir (RAL), and tenofovir disoproxil fumarate (TDF). The study participants were randomized 1:1:1:1 to each fostemsavir dose (400 mg twice daily, 800 mg twice daily, 600 mg once daily, or 1200 mg once daily). After seven days of fostemsavir monotherapy versus ritonavir-boosted atazanavir (300 mg atazanavir with 100 mg ritonavir once daily), both study arms added a backbone of RAL (400 mg) and TDF (300 mg) once daily. The backbone regimen was maintained for the remainder of the study period (48 weeks). The baseline characteristics were well-balanced between the treatment arms. At week 24, 80% of patients on the 400 mg twice daily dose, 69% of patients on the 800 mg twice daily dose, 76% of patients on the 600 mg once daily dose, and 72% of patients on the 1200 mg once daily dose had HIV-1 RNA viral load < 50 copies/mL. At week 48, 82% of patients in the fostemsavir 400 mg group, 61% in the 800 mg group, 69% in the 600 mg group, and 68% in the 1200 mg group had HIV-1 RNA viral load < 50 copies/mL. The ATV/r group had 75% and 71% of patients, at weeks 24 and 48, respectively, achieve HIV-1 RNA viral load < 50 copies/mL. Thus, the study showed that fostemsavir had similar efficacy to ATV/r in achieving significant virologic suppression. In the 24-week analysis, 9% of patients in the fostemsavir group and 27% of patients in the ATV/r group experienced a mild-moderate adverse event. For the fostemsavir groups, the events were single instances with no dose relation. No patients experienced serious adverse events related to fostemsavir use. Most of the adverse events that did occur were related to gastrointestinal effects or elevated liver enzymes with hyperbilirubinemia being seen in the ATV/r group.

Phase III Trial: NCT02362503 (BRIGHTE)[11]

The BRIGHTE trial was a phase III, partially-randomized, international, double-blind, placebo-controlled trial.[11] [10]The trial enrolled 371 heavily treatment experienced patients with HIV-1 resistance. HIV-1 resistance was defined as having a viral load of 400 copies/mL and having two classes of antiretroviral (ARV) medications remaining at baseline (exhaustion of at least four to six ARV classes). The limited ARV medications remaining at

baseline were due to either resistance, intolerability, contraindication, or other safety concerns.

Patients were divided into randomized and nonrandomized cohorts. In the randomized cohort, the patients had between one or two antiretroviral classes remaining with at least one approved fully active agent per class. This group was randomized and blinded to either fostemsavir 600 mg by mouth twice daily and the addition of the current failing treatment or they were randomized to placebo and the current failing treatment for eight days. These patients were then switched to an open-label fostemsavir 600 mg by mouth twice daily regimen with the addition of an optimized regimen. In the nonrandomized cohort, the patients had to have between one or two antiretroviral classes remaining with zero fully active antiretrovirals remaining. These patients received fostemsavir 600 mg by mouth twice daily with the addition of an optimized regimen. The patients in this group started their regimen on day 1 and were followed throughout the 96-week study period with this regimen. The optimized regimen for both cohorts was individualized based on individual resistance patterns and prior treatment exposure. The optimized regimen included one fully active ARV in 52% of patients and two fully active ARVs in 42% of patients. The majority of patients received either dolutegravir (InSTI), darunavir (PI), or tenofovir (NRTI).

All of the endpoints measured in this study were evaluated in the randomized cohort. The primary endpoint was a decline in mean plasma viral load from day one of therapy until day 8. In the fostemsavir group, the mean HIV-1 RNA level was -0.79±0.05 $\log_{10}$ copies/mL. In the placebo group, the mean HIV-1 RNA level was -0.17±0.08 $\log^{10}$ copies/mL. The mean plasma HIV-1 RNA between-group difference was -0.625 $\log_{10}$ copies/mL in the fostemsavir group (95% CI: -0.810 to -0.441; p<0.0001). For patients with a baseline HIV-1 RNA level of ≥ 1000 log10 copies/mL, the mean HIV-1 RNA level in the fostemsavir group was -0.86 $\log_{10}$ copies/mL. In the placebo group, the mean HIV-1 RNA level was -0.20 $\log_{10}$ copies/mL. The mean plasma HIV-1 RNA between-group difference in this focused group was -0.665 $\log_{10}$ copies/mL in the fostemsavir group (95% CI: -0.867 to -0.463; p-value not reported).

The secondary endpoints were measured in, both, the randomized and nonrandomized cohort. They were a decrease in HIV-1 RNA in patients with > 0.5 $\log_{10}$ copies and > 1.0 $\log_{10}$ copies/mL, virologic response, the mean change in CD4+ T-cell count throughout the study period (96 weeks), the development of temsavir resistance, and the frequency of serious adverse events. These endpoints were measured in the fostemsavir group that also received the optimized regimen (all patients received this regimen after day 8). It was found that at weeks 24 and 48, 53% and 54% of patients in the randomized cohort had virologic response (HIV-1 RNA < 40 copies/mL), respectively. Conversely, at weeks 24 and 48 of the nonrandomized cohort, 37% and 38% of patients had virologic response, respectively. There was a steady increase of patients in the randomized cohort with HIV-1 RNA levels of < 40 copies/mL (62% vs 51%) or < 200 copies/mL (84% vs 75%) at week 48 when compared to week 12. CD4+ T-cell counts increased over time to a mean 139±135 cells/mm3. In the nonrandomized cohort, CD4+ T-cell counts also improved to a mean 63.5 cells/mm3. In this group, HIV-1 RNA levels of < 40 copies/mL (48%) or < 200 copies/mL (54%) at week 48 was similar to week 12 (38% and 54%, respectively). Virologic failure before week 24 was defined as 400 copies/mL after previously confirmed virologic suppression to < 400 copies/mL or an increase of at least 1.0 $\log_{10}$ copies/mL above nadir (40 copies/mL). At or after week 24, virologic failure was defined as 400 copies/mL. Virologic failure through week 48 was observed in 18% of patients in the randomized cohort and 46% of patients in the nonrandomized cohort. Of the 18% of patients in the randomized cohort who had virologic failure, 43% were found to have temsavir resistance. Of the 46% of patients in the nonrandomized cohort who had virologic failure, 70% were found to have temsavir resistance. Resistance was found to be associated with genotypic substitutions on the gp120 protein. More patients in the nonrandomized cohort reported having serious adverse events (44% vs 31%) which were related to complications of AIDS (including infections).

Adverse Effects and Precautions

Mild-moderate adverse reactions occurred in 21% of the subjects taking fostemsavir with only 3% reporting a serious adverse event.[15] A summary of these reactions and events can be found in **Table 3**. Fostemsavir is generally well-tolerated with 81% of reactions being mild-moderate in severity. The most common adverse reaction reported was nausea (6-10%) followed by diarrhea (4-6%). Other uncommon reactions include headache (4%), abdominal pain (3%), dyspepsia (3%), and fatigue (3%).

Precautions for fostemsavir include immune reconstitution

Table 2 | Primary and Select Secondary Outcomes of Fostemsavir Trials[11]

Primary Outcome	Intervention	Mean HIV-1 Log_{10} Levels (95% CI[a])	Difference (95% CI)
Change in HIV-1 viral load	Placebo	-0.166 (-0.326 to -0.007)	-0.625 (-0.810 to -0.441)
	Fostemsavir 600 mg BID[b]	-0.791 (-0.885 to -0.698)	
	Baseline HIV-1 RNA >1,000 copies/mL		
	Placebo	-0.198 (-0.373 to -0.023)	-0.665 (-0.867 to -0.463)
	Fostemsavir 600 mg BID	-0.863 (-0.963 to -0.762)	
Secondary Outcome	**Intervention**	**Percentage of Patients with HIV-1 RNA < 200 copies/mL**	**Percentage of Patients with HIV-1 RNA < 40 copies/mL**
Virologic response at week 48	Randomized cohort[c]	84%	62%
	Non-randomized cohort[d]	54%	48%

[a]Confidence Interval; [b]Twice daily; [c]Fostemsavir 600 mg BID + Optimized Regimen after Day 8; [d]Fostemsavir 600 mg BID + Optomized Regimen after Day 1

syndrome, QTc prolongation, and elevated liver enzymes in patients co-infected with hepatitis B (HBV) and/or hepatitis C (HCV).[15] Immune reconstitution syndrome occurs secondary to antiretroviral treatment, including fostemsavir, in which the patient develops an inflammatory response to indolent opportunistic infections. There have been three reported cases of Immune Reconstitution Inflammatory Syndrome (IRIS) in patients taking fostemsavir (<2%); this was the most common severe adverse event reported. Prolongation of the corrected QT interval (QTc) was rarely reported in patients taking fostemsavir (<2%), all of which were asymptomatic. When fostemsavir was studied at high doses (four times the recommended dose), the QTc interval increased by 11.2 ms. At therapeutic doses of fostemsavir, QTc prolongation was not observed. Which may indicate that this effect is dose-dependent. Caution, however, should be used in patients with a history of QTc prolongation, coadministration with QTc-prolonging medications, or in patients with significant pre-existing cardiac disease. Caution in elderly patients who may be more susceptible to QTc prolongation. Elevated alanine aminotransferases (ALTs) and aspartate transaminases (AST) were found to occur in 4-5% of patients taking fostemsavir. However, in patients who were also infected with HBV or HCV, this elevation was more frequently observed. Routine monitoring of liver function tests (LFTs) is recommended in patients who are co-infected with hepatitis B and/or C.[15]

Drug Interactions

Significant drug interactions can occur with the coadministration of several medications and fostemsavir.[15] Temsavir, the active moiety of fostemsavir, can increase plasma concentrations of grazoprevir or voxilaprevir due to the inhibition of the efflux transporter protein OATP1B1/3. Temsavir has been shown to increase concentrations of ethinyl estradiol when it is administered with oral contraceptives. When fostemsavir is given with rifampin, a strong CYP3A4 inducer, temsavir plasma concentrations are significantly reduced leading to a loss of virologic response, thus fostemsavir is contraindicated in coadministration with strong CYP3A inducers. Temsavir can also increase the concentration of statin medications leading to increased statin-associated adverse reactions/events. The risk of Torsade de Pointes is increased when fostemsavir is co-administered with other QTc prolonging medications.[15]

Dosage and Administration

Fostemsavir is currently only available as a 600 mg extended-release tablet.[15] The studied and recommended dose for HIV-1 multidrug-resistant infections was one, 600 mg, tablet taken twice daily (every 12 hours) with or without food. There are no known dose adjustments required for patients with renal or hepatic impairment. There is limited human data available on the use of fostemsavir in pregnant patients. In animal studies, no fetal abnormalities were observed in pregnant rats. The CDC recommends that all mothers who have HIV-1 infections to not breastfeed their infants as the virus can be transmitted through human breast milk. It is not known whether fostemsavir is present in or passes through human breast milk, however, in animal studies, fostemsavir was present in rat milk.[15]

Clinical Implications

The BRIGHTE trial was conducted to assess the efficacy and safety of fostemsavir. There was an additional phase IIb trial that assessed the efficacy and safety of fostemsavir, however BRIGHTE was the only trial that was used by the FDA to bring fostemsavir to the market. Efficacy of fostemsavir relied on the combination of other antiretroviral therapies termed "optimized background therapy (OBT)". Each patient received an appropriate OBT based on their individual resistance patterns and prior treatment exposure. This individualized treatment could introduce confounding into the study results and can be a major limitation to this study. The study investigators noted, however, that this regimen was needed and unavoidable for this study population due to the nature of multidrug-resistant HIV-1 infection.

The authors of the BRIGHTE trial designed their study to include a randomized and nonrandomized cohort. For the patient population enrolled in the study, this was an appropriate study design. This is because the patients who were enrolled in the nonrandomized cohort had no other therapy options available. It would be unethical to randomize these patients to placebo.

In the randomized cohort, 85% of patients were diagnosed with AIDS at baseline, while 90% of patients in the nonrandomized cohort were diagnosed with AIDS at baseline. This can limit the place in therapy for fostemsavir to patients who are disease-progressed. This would, however, be expected because BRIGHTE enrolled and studied patients who had already exhausted almost all other treatment options prior to the start of this medication. Without effective antiretroviral therapy on board, it would be expected that their disease would progress. The BRIGHTE trial showed a statistically and clinically significant improvement in reduction in viral load and increase in CD4+ cell count, both of which are clinical indicators for HIV/AIDS. When compared to placebo, fostemsavir was proven to be superior, and had demonstrated a viral load of < 200 copies/mL in the majority of patients in both studied cohorts. Both cohorts also had around 50% of patients achieve a viral load of < 40 copies/mL. This was particularly important because it was proven to be efficacious even after these patients had proven antiretroviral resistance and had failed multiple HIV medications. It is important to note, however, that temsavir resistance was also found in these patients. Both, the randomized and nonrandomized cohorts had temsavir resistance-associated virologic failure. The greatest percentage of patients failing treatment due to resistance was seen in the nonrandomized cohort after exhausting all other therapy options. This patient population may benefit from further studies evaluating sources of resistance as they are most likely to benefit from an additional therapy option.

Table 3 | Adverse Effects of Fostemsavir[11,15,16]

Adverse Effect	Incidence
Nausea	6-10%
Diarrhea	4-6%
Elevated Liver Enzymes	4-5%
Headache	4%
Abdominal Pain	3%
Dyspepsia	3%
Fatigue	3%
Immune Reconstitution Syndrome	<2%
QTc Prolongation	<2%

There are several limitations to the BRIGHTE trial. One limitation of the trial was the number of patients enrolled in the study. While this patient population is rare, the study population was still less than 400 enrolled patients. This small sample size can limit the generalizability and possibly limit the external validity of this trial. This sample size did, however, meet the study's predefined power of a 0.5 $\log_{10}$ difference between the groups in the randomized cohort (272 subjects) with 95% superiority (α=0.05) over placebo by enrolling at least 200 subjects. Another limitation was found in the demographics of the patients in the randomized and the nonrandomized cohorts. The nonrandomized cohort enrolled older patients (56% of patients were > 50 years old) when compared to the randomized cohort (40% of patients were > 50 years old). Younger patients tend to be healthier, are taking less medications, and have less comorbidities when compared to older patients, thus this is not a fair comparison. Additionally, the results of the trial could be inflated. The study showed that fostemsavir works against HIV-1 infections, however, it doesn't show if it's any more effective than other ARVs on the market because it was only compared to placebo. If fostemsavir was studied against placebo with the optimized regimen as a backbone for both treatment arms, it could prove to be more efficacious. It would also be beneficial to see if cross resistance would occur with fostemsavir if a patient were to experience virologic failure. For these reasons, additional studies need to be completed comparing fostemsavir to an active comparator. Another important limitation was that the primary endpoint was not assessed with the nonrandomized cohort. The authors claimed that this was necessary due to the nature of the study participants in that cohort. However, because the primary endpoint was measured in eight days, it's reasonable to allow for the more disease-progressed patients to be included in the primary endpoint if the goal was to have the patients switch to the optimized regimen regardless.

A 30-day supply of fostemsavir (60 tablets) is available for a cash price value of approximately $7,996. While fostemsavir is indicated for a unique patient population, integrase strand inhibitors are also some of the newer HIV agents on the market that have the fewest resistance rates. To compare, dolutegravir is available for a cash price value of approximately $4,462 for a 30-day supply (60 tablets – dose used in BRIGHTE trial) making fostemsavir approximately double the price of dolutegravir. From a patient/payer perspective, this can limit the use of fostemsavir and will likely be reserved as a last line option for patients who have known InSTI resistance.

Overall, fostemsavir is well-tolerated with the majority of reactions being related to gastrointestinal side effects. A minor set of patients who took fostemsavir reported having serious adverse reactions in which the major safety concern was the development of IRIS upon initiation of this therapy. This reaction is seen across the board among other antiretroviral therapies. While there are warnings for QTc prolongation, this is a rare outcome of this medication. Careful evaluation of other therapies that prolong the QTc interval in combination with fostemsavir can mitigate the concern for Torsades de Pointes. Liver function tests should be monitored regularly especially in patients who also have coinciding hepatitis infections.

Fostemsavir is not currently included in the treatment guidelines for HIV-1 infections. There could be a niche place in therapy for fostemsavir, however. As HIV-1 medications continue to grow in resistance rates across the globe, it's vital to continue to find novel treatment options for patients who have exhausted a myriad of medications. Due to the morbidity and mortality related to the progression of HIV to AIDS, allowing for new mechanisms of action that can overcome microbial resistance is direly needed. Fostemsavir can fit into this pocket of unique mechanisms of action and can foster innovative treatment options down the line.

Conclusion

RUKOBIA® (fostemsavir) is a first-in-class attachment inhibitor that was approved by the FDA in July 2020 in combination with other antiretrovirals for the treatment of multidrug resistant HIV-1 infections in heavily treatment experienced adults. According to current HIV-1 guidelines, fostemsavir does not have a place in therapy, but patients may benefit from fostemsavir as an add-on therapy when they have developed resistance to other antiretrovirals on the market. More studies need to be completed on efficacy and safety before a recommendation can be made on where fostemsavir can fit in the HIV drug arsenal.

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