Lopinavir-Ritonavir (Kaletra)

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Drug Summary

Lopinavir-ritonavir is a fixed-dose combination of a protease inhibitor (lopinavir) and a pharmacokinetic booster (ritonavir). Lopinavir-ritonavir was used for years as an anchor drug in regimens for treatment-naïve individuals and as part of salvage antiretroviral therapy. In addition, lopinavir-ritonavir was widely used for pregnant women with HIV and for postexposure prophylaxis (PEP). With the availability of newer anchor drugs that offer lower pill burden and lower risk of adverse effects, lopinavir-ritonavir is now rarely used in the United States. Lopinavir-ritonavir may be dosed once daily for treatment-naïve individuals and for some treatment-experienced individuals; for those with three or more lopinavir-associated resistance mutations, those taking certain other antiretroviral medications that interact with lopinavir, and for pregnant women, only twice-daily dosing is recommended. Even with once-daily dosing, pill burden is higher than with newer options and many individuals taking this combination have switched to other medications for convenience or to reduce side effects. Other limitations of lopinavir-ritonavir include drug interactions, gastrointestinal side effects, and metabolic adverse effects such as hyperlipidemia.

Key Clinical Trials

For treatment-naïve individuals, lopinavir-ritonavir has been compared to a number of other anchor agents (in combination with two NRTIs). In various trials, rates of HIV suppression in lopinavir-ritonavir groups were comparable to those in groups who received ritonavir-boosted fosamprenavir [KLEAN] or ritonavir-boosted atazanavir [CASTLE] and were higher than with nelfinavir [M98-863]. In one trial of treatment-naïve individuals, virologic efficacy rates were similar between groups that received lopinavir-ritonavir versus efavirenz (LAKE), but in another trial, virologic suppression rates were significantly higher with efavirenz as compared to lopinavir-ritonavir [ACTG 5142]. Lopinavir-ritonavir and ritonavir-boosted darunavir resulted in statistically equivalent virologic suppression rates in an overall study population of treatment-naïve persons, but in the subset of participants with baseline viral load above 100,000 copies/mL, failure to achieve virologic suppression was significantly more common in the lopinavir-ritonavir arm [ARTEMIS]. For antiretroviral-naïve individuals, once-daily lopinavir-ritonavir was found to be non-inferior to twice-daily lopinavir-ritonavir when each was combined with tenofovir DF-emtricitabine [M02-418]. In individuals who had previously experienced
virologic failure on a protease inhibitor-based regimen, lopinavir-ritonavir plus two NRTIs performed as well as unboosted atazanavir plus two NRTIs in terms of virologic suppression, though lipid changes were worse in the lopinavir-ritonavir arm [Study 043]. Similarly, individuals with multiple prior ART failures were enrolled in a trial that compared lopinavir-ritonavir to ritonavir-boosted atazanavir (each with tenofovir DF and another NRTI), and virologic suppression rates were similar, but atazanavir led to less lipid changes [Study 045]. In ART-experienced, lopinavir-naïve individuals, lopinavir-ritonavir was compared to ritonavir-boosted darunavir (each with optimized background regimen) and virologic efficacy rates were similar, but less resistance mutations occurred in participants who failed boosted darunavir [TITAN]. Lopinavir-ritonavir has also been studied as part of dual antiretroviral treatment for initial therapy or simplification, either combined with efavirenz [ACTG 5142], raltegravir [PROGRESS], lamivudine [GARDEL], or emtricitabine or lamivudine [OLE].

Adverse Effects

Side effects of lopinavir-ritonavir may include nausea, diarrhea, or elevation of hepatic transaminases. Lopinavir-ritonavir may raise serum lipid parameters and blood sugar, and has been associated with lipoaccumulation and prolonged PR and QT cardiac intervals.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), lopinavir-ritonavir plus a preferred two NRTI backbone is designated as an Alternative Protease Inhibitor Regimen in the category Alternative Initial Regimens in Pregnancy. The guidelines specify that although lopinavir-ritonavir has been used extensively in pregnancy and pharmacokinetic parameters exist, it causes more nausea than the preferred agents, requires twice-daily administration during pregnancy, and the dose should be increased during the third trimester (which may add risk of side effects).

- For additional information regarding the safety and toxicity of lopinavir-ritonavir in pregnancy see the HHS Perinatal Guidelines summary on Lopinavir-Ritonavir.

Resistance

For a listing of the most common clinically significant mutations associated with lopinavir-ritonavir (LPV-RTV) resistance, see the PI Resistance Notes on the Stanford University HIV Drug Resistance Database.

Key Drug Interactions
For complete information on lopinavir-ritonavir-related drug interactions, see the Drug Interactions section in the Lopinavir-Ritonavir (Kaletra) Prescribing Information.