Darunavir (Prezista)

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Drug Summary

Darunavir is a potent, later-generation protease inhibitor that must be combined with a pharmacokinetic booster, either cobicistat or ritonavir. Boosted darunavir is an option for initial antiretroviral therapy and it is also a common component of salvage regimens for treatment-experienced individuals. Darunavir has a unique resistance pathway and retains activity following the development of drug resistance with most other protease inhibitors, with a notable exception that virologic failure on fosamprenavir can result in cross resistance with darunavir. In addition, darunavir has a high barrier to drug resistance, and when patients taking darunavir develop virologic failure, darunavir-associated resistance mutations usually are not present. For treatment-naive patients, ritonavir-boosted darunavir is dosed once daily; for treatment-experienced patients, the dosing of darunavir is determined by whether or not darunavir-associated mutations are present. If they are absent, ritonavir-boosted darunavir can be dosed once daily, but if darunavir-associated mutations are present, the dosing should be twice daily. The fixed-dose combination of darunavir-cobicistat should only be used when once daily darunavir dosing is appropriate. The primary disadvantages of darunavir include moderate gastrointestinal side effects, potential for drug interactions, and possible adverse reactions in individuals with history of severe sulfa allergy (darunavir contains a sulfonamide moiety).

Key Clinical Trials

Darunavir has been extensively studied in treatment-naïve and treatment-experienced individuals. In antiretroviral-naïve adults, a comparison of once-daily ritonavir-boosted darunavir with lopinavir-ritonavir (given once or twice-daily), each with tenofovir DF-emtricitabine, showed similar virologic efficacy between the two arms, except for the subset of participants with pre-treatment HIV RNA levels above 100,000 copies/mL, who achieved higher rates of virologic suppression with ritonavir-boosted darunavir [ARTEMIS]. In treatment-naïve individuals, a randomized comparison of once-daily ritonavir-boosted darunavir and once-daily dolutegravir, each with two NRTIs, showed that the darunavir arm was inferior, largely due to more side effects and treatment discontinuations [FLAMINGO]. In a trial of treatment-naïve individuals randomized to ritonavir-boosted darunavir, ritonavir-boosted atazanavir, or raltegravir, each with tenofovir DF-emtricitabine, raltegravir achieved the best virologic outcomes, followed by boosted darunavir, and then boosted atazanavir.
Outcome differences in that trial were largely driven by tolerability. In
[ARDENT (ACTG 5257)]. A noncomparative trial that included individuals
with virologic failure and multiclass drug resistance found high rates of virologic success with a
salvage regimen that included ritonavir-boosted darunavir (given twice daily) plus raltegravir plus
etravirine [TRIO]. In treatment-experienced patients with no darunavir-associated mutations but
detectable HIV RNA while taking stable antiretroviral therapy, a randomized switch to either once-
daily or twice-daily ritonavir-boosted darunavir plus NRTIs resulted in no statistically significant
difference in rates of HIV RNA suppression at week 48 [ODIN]. Several studies demonstrated the
efficacy of monotherapy with ritonavir-boosted darunavir as a simplification strategy in patients
with previously suppressed HIV RNA levels on a standard three-drug regimen [MONOI] and [MONET].

Adverse Effects

Common adverse effects with darunavir (given in conjunction with one of the pharmacologic
boosters, ritonavir or cobicistat) include nausea, diarrhea, and other gastrointestinal upset.
Darunavir may also cause headache, rash, elevation of hepatic transaminases, or increases in serum
lipid parameters. Darunavir contains a sulfonamide moiety and thus should be used cautiously in
individuals with a known sulfonamide allergy. Although the rates of allergic reaction with darunavir
are higher in individuals with a history of sulfonamide allergy when compared with individuals with
no history of sulfonamide allergy, clinically significant reactions occur infrequently. Nonetheless,
most experts would avoid use of darunavir in patients with a history of severe sulfonamide allergy,
such as a prior incidence of Stevens-Johnson syndrome.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During
Pregnancy (last updated October 19, 2017), ritonavir-boosted darunavir plus a preferred two-NRTI
backbone is designated as one of the Preferred Protease Inhibitor Regimens in the category
Preferred Initial Regimens in Pregnancy. The guidelines recommend that boosted darunavir must be
dosed twice daily during pregnancy.

- For additional information regarding the safety and toxicity of darunavir in pregnancy see the
  HHS Perinatal Guidelines summaries on Darunavir and Ritonavir.

Resistance

For a listing of the most common clinically significant mutations associated with darunavir (DRV)
resistance, see the PI Resistance Notes on the Stanford University HIV Drug Resistance Database.
Key Drug Interactions

For complete information on darunavir-related drug interactions, see the Drug Interactions section in the Darunavir (Prezista) Prescribing Information.
Figures

Figure 1 darunavir-prezista_800mg-tablet

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The most up to date version of this content may be obtained from: https://www.hiv.uw.edu/page/treatment/drugs/darunavir