Doravirine-Tenofovir DF-Lamivudine *(Delstrigo)*

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Drug Summary

Doravirine-tenofovir DF-lamivudine is a single-tablet regimen dosed once daily with or without food that is indicated for adults with no prior antiretroviral treatment history or to replace the current antiretroviral regimen in those who have HIV-1 RNA levels less than 50 copies per mL on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine, lamivudine, or tenofovir. The non-nucleoside reverse transcriptase inhibitor (NNRTI) anchor drug in this regimen—doravirine—retains activity in the presence of several common NNRTI drug-resistant mutations (e.g. K103N and G190A). Several key reverse transcriptase mutations cause more than 100-fold reduced susceptibility of HIV to doravirine: (1) Y188L alone or in combination with K103N or V106I, (2) V106A in combination with G190A and F227L, or (3) E138K in combination with Y181C and M230L. In addition, treatment failure with a doravirine-containing regimen can result in emergence of resistance-associated substitutions that may confer cross-resistance to efavirenz, etravirine, nevirapine, and rilpivirine.

Unlike the NNRTI rilpivirine, there are no CD4 count or HIV RNA level criteria for the use of doravirine. In addition, doravirine does not have restrictions for use in combination with proton pump inhibitors. The single-tablet regimen doravirine-tenofovir DF-lamivudine is a potent and well-tolerated NNRTI single-tablet regimen, but its use may be somewhat limited by the since current recommendations to use integrase strand transfer inhibitors as the anchor drug when initiating antiretroviral therapy.

Key Clinical Trials

The phase 3, randomized-controlled trial [DRIVE AHEAD] compared doravirine-tenofovir DF-lamivudine to efavirenz-tenofovir DF-emtricitabine as therapy for treatment-naïve individuals. Investigators randomized 364 individuals to each arm and at 48 weeks results demonstrated non-inferiority of the doravirine regimen by FDA snapshot (proportion of participants with HIV RNA below 50 copies/mL was 84.3% in the doravirine arm

versus 80.8% in the efavirenz arm by intention-to-treat analysis). Results also showed that less rash, central nervous side effects, and lipid changes occurred in the doravirine arm and there were overall fewer treatment discontinuations due to adverse effects as compared to the efavirenz arm. In the open-label, active-controlled, non-inferiority [DRIVE SHIFT] trial, investigators enrolled 670 adults who had suppressed HIV RNA levels for at least 6 months and randomized them (2:1) to switch to once-daily single-tablet regimen of doravirine plus tenofovir DF plus lamivudine or to continue on their current antiretroviral regimen. Participants enrolled were taking two nucleoside reverse transcriptase inhibitors (NRTIs) plus either (1) a boosted protease inhibitor, (2) boosted elvitegravir, or (3) a non-nucleoside reverse transcriptase inhibitor.

Adverse Effects

The adverse effects that occurred in trials in more than 5% of participants consisted of dizziness, nausea, and abnormal dreams. Tenofovir DF may cause nephrotoxicity and decreases in bone mineral density. Doravirine-tenofovir DF-lamivudine should not be used in persons with a creatinine clearance less than 50 mL/min.

Use In Pregnancy

There are insufficient data on the use of doravirine-tenofovir DF-lamivudine in pregnancy.

Key Drug Interactions

For complete information on doravirine-tenofovir df-lamivudine-related drug interactions, see the Drug Interactions section in the Doravirine-Tenofovir DF-Lamivudine (*Delstrigo*) Prescribing Information.