Dolutegravir plus Abacavir-Lamivudine for the Treatment of HIV-1 Infection

Walmsley SL, Antela A, Clumeck N, et al. for the SINGLE Investigators

N Engl J Med 2013; 369: 1807-1818

Background: Dolutegravir (S/GSK1349572), a once-daily, unboosted integrase inhibitor, was recently approved in the United States for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in combination with other antiretroviral agents. Dolutegravir, in combination with abacavir-lamivudine, may provide a simplified regimen.

Methods: We conducted a randomized, double-blind, phase 3 study involving adult participants who had not received previous therapy for HIV-1 infection and who had an HIV-1 RNA level of 1000 copies per milliliter or more. Participants were randomly assigned to dolutegravir at a dose of 50 mg plus abacavir-lamivudine once daily (DTG-ABC-3TC group) or combination therapy with efavirenz-tenofovir disoproxil fumarate (DF)-emtricitabine once daily (EFV-TDF-FTC group). The primary end point was the proportion of participants with an HIV-1 RNA level of less than 50 copies per milliliter at week 48. Secondary end points included the time to viral suppression, the change from baseline in CD4+ T-cell count, safety, and viral resistance.

Results: A total of 833 participants received at least one dose of study drug. At week 48, the proportion of participants with an HIV-1 RNA level of less than 50 copies per milliliter was significantly higher in the DTG-ABC-3TC group than in the EFV-TDF-FTC group (88% vs. 81%, P = 0.003), thus meeting the criterion for superiority. The DTG-ABC-3TC group had a shorter median time to viral suppression than did the EFV-TDF-FTC group (28 vs. 84 days, P<0.001), as well as greater increases in CD4+ T-cell count (267 vs. 208 per cubic millimeter, P<0.001). The proportion of participants who discontinued therapy owing to adverse events was lower in the DTG-ABC-3TC group than in the EFV-TDF-FTC group (2% vs. 10%); rash and neuropsychiatric events (including abnormal dreams, anxiety, dizziness, and somnolence) were significantly more common in the EFV-TDF-FTC group, whereas insomnia was reported more frequently in the DTG-ABC-3TC group. No participants in the DTG-ABC-3TC group had detectable antiviral resistance; one tenofovir DF-associated mutation and four efavirenz-associated mutations were detected in participants with virologic failure in the EFV-TDF-FTC group.

Conclusions: Dolutegravir plus abacavir-lamivudine had a better safety profile and was more effective through 48 weeks than the regimen with efavirenz-tenofovir DF-emtricitabine. (Funded by ViiV Healthcare; SINGLE ClinicalTrials.gov number, NCT01263015.)

IL/DLG/0049/14 ; Sep 2014