

Oral Presentation – Abstract O423A

The PROTEA trial: darunavir/ritonavir with or without nucleoside analogues, for patients with HIV-1 RNA below 50 copies/mL

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Introduction: In previous studies, protease inhibitor (PI) monotherapy has shown trends for higher low-level elevations in HIV-1 RNA compared to triple therapy, but no increase in the risk of drug resistance.

Methods: A total of 273 patients with HIV-1 RNA < 50 copies/mL for over 24 weeks on current antiretrovirals switched to DRV/r (darunavir/ritonavir) 800/100 mg once-daily, either as monotherapy ($n = 137$) or with 2NRTIs (nucleoside reverse-transcriptase inhibitors) ($n = 136$), after a 4 week run-in phase with DRV/r + 2NRTI. Treatment failure was defined as HIV-1 RNA levels above 50 copies/mL (FDA Snapshot method) by Week 48, or switches off study treatment. Patients with elevations in HIV-1 RNA on DRV/r monotherapy could be re-intensified with NRTIs. The trial had 80% power to show non-inferiority for the monotherapy arm ($\delta = -12\%$).

Results: Patients were 83% male and 87% Caucasian, with mean age 42 years; 10% were HCV antibody positive. In the DRV/r monotherapy arm, there were more patients with nadir CD4 count below 200 cells/ μ L (30% versus 22%). In the primary efficacy analysis, HIV-1 RNA < 50 copies/mL by Week 48 (intent-to-treat (ITT)) was 118/137 (86.1%) in the DRV/r monotherapy arm versus 129/136 (94.9%) in the triple therapy arm; DRV/r monotherapy did not show non-inferiority versus triple therapy in the primary analysis (difference = -8.7% , 95% CI -15.5 to -1.8%). In the multivariate analysis, the main predictor of treatment failure was nadir CD4 count. For patients with nadir CD4 counts < 200 cells/ μ L, HIV-1 RNA suppression rates at Week 48 were 27/41 (66%) in the DRV/r monotherapy arm and 29/30 (97%) in the triple therapy arm; for patients with CD4 nadir at least 200 cells/ μ L, HIV-1 RNA suppression rates were 91/96 (95%) in the DRV/r monotherapy arm and 100/106 (94%) in the triple therapy arm. In the overall population, by a switch included analysis, efficacy was 92.0% versus 96.3%, showing non-inferiority (difference = -4.3% , 95% CI = -9.7 to $+1.2\%$). No treatment-emergent primary PI mutations were detected in three patients with sustained elevations in HIV-1 RNA at least 400 copies/mL (two on PI monotherapy, one on triple therapy). CD4 counts remained stable during the trial in both arms.

Conclusions: In this study for patients with HIV-1 RNA < 50 copies/mL at baseline, switching to DRV/r monotherapy showed lower efficacy versus triple antiretroviral therapy at Week 48 in the primary switch equals failure analysis (86% versus 95%). However, this lower efficacy was seen mainly in patients with CD4 nadir levels below 200 cells/ μ L. There was no development of PI resistance.

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