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Paper Poster Session III

HIV/AIDS

Efavirenz-based versus two ritonavir-boosted protease inhibitor regimens in HIV-1-infected patients with advanced disease: 96-week results of a randomized trial (Advanz-3 Trial)

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Background: We studied immune reconstitution in very immunosuppressed antiretroviral-naïve HIV-1-infected patients by comparing an efavirenz-based regimen with 2 ritonavir-boosted protease inhibitor–based antiretroviral regimens.

Methods: Randomized, controlled, open-label clinical trial (ClinicalTrials.gov NCT00532168) in 5 Spanish hospitals in which 90 HIV-1-infected antiretroviral-naïve patients with <100 CD4 cells/mm^3 were randomly assigned in a 1:1:1 ratio to efavirenz (group A, 28 patients), atazanavir-ritonavir (group B, 30 patients), or lopinavir-ritonavir (group C, 29 patients) plus tenofovir + emtricitabine (Truvada®) at standard doses. The primary endpoint was the change in CD4 cell count at weeks 48 and 96.

Results: Median (IQR) age was 38 (33-43) years and 82% were men. HIV-1 infection was sexually transmitted in 86%. AIDS-defining opportunistic infections were diagnosed in 56% of cases. Baseline median (IQR) CD4 cells/mm^3 was 32 (20-59) and plasma viral load (pVL) was 5.2 (4.8-5.7) log_{10}/mL (no differences between the arms). Antiretroviral therapy (ART) was changed in 17 cases (20%) because of toxicity (7), virological failure (6), and medical decision (4). Ten patients (11.5%) developed a new AIDS-defining event and 11 (12.6%) developed IRIS (no differences between the arms). No patients died. Ten patients (11.5%) were lost to follow-up (group A, 3; group B, 4; group C, 3). The proportion (95% confidence interval) of patients achieving pVL <50 copies/mL in the intention-to-treat analysis in groups A, B, and C was 75% (56.6-87.3%), 73.3% (55.6-85.8%), and 69% (50.8-82.7%) at week 48 (p=0.90) and 60.7% (42.4-76.4%), 56.7% (39.2-72.6%), and 55.2% (37.5-71.6%) at week 96 (p=0.73). The median (IQR) CD4 cell increase in the on-treatment analysis in groups A, B, and C was 196 (119-349), 196 (153-238), and 205 (178-327) cells/mm^3 at week 48 (p=0.60) and 288 (175-430), 275 (220-391), and 334 (215-443) cells/mm^3 at week 96 (p=0.61). The reduction in immune activation (CD8+CD38+ T cells) was higher in the efavirenz arm at 48 weeks (-35%, -22%, and -29% for groups A, B, and C; p=0.04) but not at week 96 (-48%, -49%, and -45% for groups A, B, and C; p=0.2).

Conclusions: The ART-induced immune reconstitution and reduction in the immune activation at 2 years in very immunosuppressed patients on an efavirenz-based regimen was of similar magnitude to that induced by 2 ritonavir-boosted protease inhibitor-based regimens.