Initial plasma HIV-1 RNA and CD4+ T-cell count are determinants of virological outcomes with initial integrase inhibitor-based regimens: a prospective multinational RESPOND consortium.

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Background and Aim

There are conflicting data regarding baseline determinants of virological non-suppression outcomes in people living with HIV who initiate antiretroviral treatment (ART). We evaluated the impact of different baseline variables in the RESPOND cohort consortium.

Methods

We included treatment-naive participants aged ≥18 who initiated 3-drug ART (two nucleos(t)ides and either dolutegravir, ritonavir-boosted atazanavir, darunavir, or raltegravir), 2014-2020. We assessed the odds of virological suppression (VS) (HIV-1 RNA <50 copies/mL) at week 48 and 96, using logistic regression. The incidence of viral blips isolated (VHI) (HIV-1 RNA >50 copies/mL following VS), residual viremia (RV) (HIV-1 RNA 20-49 copies/mL for assay with limit of detection of 20 copies/mL following VS), and virological failure (VF) (two consecutive HIV-1 RNA ≥50 copies/mL, or them ≥200 copies/mL following VS) were assessed using Cox regression. The outcomes assessment was based on an intention-to-treat (ITT) analysis including all participants starting their ART regimen in the defined period and having HIV-1 RNA in the relevant time point, imputing missing values as excluded.

Results

Out of 4,310 eligible participants, 72.3% initiated integrase inhibitor (INSTI)-based regimens, of whom 1,970 (63%) initiated dolutegravir (Table 1). VHI at week 48 and 96 with a 12-week window on either side, and Kaplan-Meier estimates of the proportion with viral blips, LTV, RV, and VF at 12 months were assessed (Table 2). In the multivariate analysis (Table 3 and figure 1), baseline HIV-1 RNA >100,000 copies/mL, and CD4+ count <200 cells/µL were negatively associated with VS at weeks 48 and 96, and with significantly higher rates of blips, LTV, RV, and CD4+ count <200 cells/µL was associated with higher risk of VF. Results were consistent in those starting INSTIs compared to other regimens or those initiating dolutegravir compared to other INSTIs (p<0.05, tests for interaction).

Table 1. Baseline characteristics of participants in the intention-to-treat exposed population.

Table 2. Virological outcomes in the intention-to-treat exposed population.

Table 3. Logistic regression analysis (multivariate) of factors associated with virological suppression at week 48 and 96, for all participants included.

Conclusions

- Initial high HIV-RNA and low CD4+ count are associated with lower rates of VS at 48 and 96 weeks and higher rates of viral blips, LTV, RV. Low baseline CD4+ count is associated with higher VF rates.
- These associations remain with INSTI- and specifically dolutegravir-based regimens.
- While we cannot exclude confounding by indication, these findings suggest the impact of these baseline determinants is independent of the ART regimen initiated.

References


Appendix

Table 4. Additional factors associated with viral blip (A), low viremia (B), residual viremia (C) and virological failure (D), for all participants included in a multivariate analysis.

Figure 1. Forest plots showing adjusted hazard ratio of factors associated with viral blip (A), low viremia (B), residual viremia (C) and virological failure (D), for all participants included in a multivariate analysis.