PREDICTORS OF VIROLOGIC OUTCOME WHILE CONTINUING A PI-BASED ART REGIMEN IN ACTG A5288

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Introduction

A5288 was an open-label phase IV, prospective intervention study conducted at 19 urban sites in 10 countries evaluating a strategy for individuals experiencing virologic failure on their second-line regimen. As part of this strategy, participants with no lopinavir/ritonavir (LPV/r) resistance and susceptibility to at least one NRTI were enrolled in Cohort A of the study and continued their second-line PI-based regimen with possible change in NRTIs. Key inclusion/exclusion criteria included: virologically infected adults aged ≥18 years, two prior ARV regimens, including at least one NRTI-based regimen replaced by a PI-based regimen, with the change due to toxicity or failure. Our objective was to evaluate demographic and clinical predictors of virologic outcomes in this subpopulation (Cohort A) of the A5288 study population.

Methods

Real-time HIV drug resistance results, treatment history, and, if available, any historical resistance results were used to assign participants to one of four treatment cohorts (Figure 1). Participants at most sites were also randomized to receive a cell phone adherence support intervention in addition to standard of care (CPI-SOC) or SOC adherence support. These analyses focus on participants enrolled in Cohort A. Logistic regression models were used to evaluate sex, age, baseline HIV-1 RNA, CD4 count, presence of resistance to at least one NRTI, and randomized adherence support intervention (CPI-SOC vs SOC) as predictors of failure to meet the study’s primary endpoint: suppression of HIV-1 RNA <200 c/mL at week 48 (ITT, irrespective of ART changes). Similarly, proportional hazards models were used to assess predictors of time to confirmed virologic failure (VF) ≥1000 c/mL. Kaplan-Meier plots show results for time to VF by categories of age, CD4 count and resistance status. Similar analyses were conducted to evaluate sex, age, baseline HIV-1 RNA, CD4 count, resistance status, and history of ART failure at screening, with confirmed virologic failure at screening.

Cohort Allocation

Screening Process up to 120 days

Participants with no lopinavir/ritonavir (LPV/r) resistance and susceptibility to at least one NRTI were enrolled in Cohort A of the study and continued their second-line PI-based regimen with possible change in NRTIs. Categories of age and CD4 count were then combined in the analysis population and findings. All participants received 3TC or FTC with N TAM. Those with confirmed VF had a new NRTI, a second NRTI, and in some cases, a third NRTI.

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Conclusions

- Less than half of the participants who remained on second-line ART (44%) achieved HIV-1 RNA suppression ≤200 c/mL at 48 weeks in this analysis of participants in RLS, failing 2nd-line PI-containing ART with no LPV resistance and susceptibility to at least one NRTI
- Participants of younger age, baseline HIV-1 RNA, lower baseline CD4 count, and resistance to any NRTI (multivariate only) were less likely to meet the study’s primary endpoint of HIV-1 RNA ≤200 c/mL at week 48
- Participants of younger age, baseline HIV-1 RNA, lower baseline CD4 count, and resistance to any NRTI were more likely to experience confirmed virologic failure during study follow up (median 72 weeks). Sex was statistically significant in univariate analyses and not significant in the multivariate models.
- Individuals who are younger and/or have more advanced disease as indicated by baseline HIV-1 RNA and lower CD4 count, and those with NRTI resistance-associated mutations, are at higher risk of negative virologic outcomes when continuing their 2nd-line regimen and therefore may be candidates for alternative interventions.

Figure 1 (above) displays the criteria used by the study team to determine a participant’s cohort at screening.

Figure 2 (below) displays cumulative Kaplan-Meier plots for the time to confirmed VF outcomes by the categories of the variables specified.

Table 1 (center) displays the univariable and multivariable models assessing each of the displayed relapses for the outcome specified.

Table 2 (below) shows the results for the final Cox regression models assessing predictors of confirmed VF outcomes by the categories of the variable specified.