CROI 2018 PRESS CONFERENCE ABSTRACTS
Monday, March 5, 2018
Contents embargoed until: Monday, March 5, 2018 at 12:00 pm ET

Abstract Number 30LB - (Oral)

RESULTS OF ACTG A5288: A STRATEGY STUDY IN RLS FOR 3RD-LINE ART CANDIDATES

Clinical: (G) Antiretroviral Therapy: Pre-Clinical and Randomized Trials

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Background: Individuals presenting for 3rd line ART are a challenge in resource limited settings (RLS) because of uncertain ARV susceptibility and limited data on virologic responses to remaining available ARV regimens.

Methods: A5288 is an open-label strategy study in RLS in HIV-1 infected individuals presenting with confirmed plasma HIV RNA (VL) ≥ 1000 copies after > 24 weeks of protease-based (PI) 2nd line ART. Primary objective was to use novel antiretrovirals and contemporary management tools, including standard genotyping to select an appropriate 3rd-line regimen, interventions to improve adherence, and VL monitoring, to achieve virologic suppression in ≥65% at 48 weeks of follow-up. Review of prior ART, combined with real-time standard genotype, determined Cohort A-D assignment (Table). An exploratory randomized comparison in Cohort B of NRTIs+DRV/r+RAL (B1) versus ETR+DRV/r+RAL (B2) among HBV Ab- participants was performed; HBV Ab+ participants in B received DRV/r + RAL + TDF/FTC or TDF+3TC (B3). Suppression of VL ≤200 copies/mL at 48 weeks and virologic failure (VF, two consecutive ≥1000 copies/mL ≥ 24 weeks) were 1o and 2o endpoints.

Results: From 2013-2015, 545 participants in 10 countries in Africa, Asia, South America and the Caribbean enrolled: 47% females; median age 41 years, median CD4 count 175 cells/mm3. At enrollment, drug resistance (moderate or high-level) to 0, 1, 2, and 3 ARV classes was identified in 22%, 20%, 30% and 27% of participants, respectively. Overall, 64% (95% CI 60, 68%) had VL ≤ 200 copies/mL at week 48. Viral suppression and VF differed across cohorts (Table). By week 48, Cohort A had the most Grade ≥ 3 adverse events (39%) and regimen discontinuations (13%). No differences in VL ≤ 200 copies/mL at week 48 or VF ≥ 24 weeks were observed in the randomized comparison of B1 & B2 cohorts.

Conclusion: Regimens containing DRV/r and RAL with or without ETR were highly effective for participants with LPV/r resistance who presented for 3rd line ART. More than half of participants without LPV/r resistance and who remained on 2nd line ART did not achieve viral suppression at week 48. This subgroup requires additional interventions to achieve viral suppression. Targeted real-time genotyping to select regimens for 3rd line ART can appropriately allocate more costly ARVs to those with greater resistance.