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ORAL COMMUNICATION

Tailored approaches to antiretroviral therapy

OC 36 CD4 T-cell, CD4/CD8 ratio improvement and a general reduction in inflammatory biomarkers with low level viremia (LLV) up to Week 192 with Fostemsavir (FTR) based regimens in individuals with multidrug-resistant (MDR) HIV-1

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ABSTRACT

Background: Persistent LLV (40-1000 copies/mL) remains a challenge in the era of high effective ART, which is associated with the emergence of virological failure, drug resistance and an increased risk of immune system activation and inflammation, that may impact morbidity and mortality. FTR, the prodrug of the first-in-class attachment inhibitor Temsavir, is indicated in combination with other antiretrovirals (ARVs) for heavily treatment-experienced (HTE) individuals with MDR HIV-1 who are unable to construct suppressive regimens. BRIGHTE participants were not obligated to stop treatment due to LLV, here we describe outcomes and inflammatory biomarkers measured through Week 192 in participants with low level viremia (<40, 40-400, 400-1000 and >1000 copies/mL) on FTR based regimens from the Randomized Cohort (RC) in the BRIGHTE study.

Methods: BRIGHTE was a Phase III international registrational study 2016- ongoing [n= 371; randomized cohort (RC), n=272; non-randomized cohort n=99], in adults who were failing their current ARV regimen (HIV-1 RNA >400 c/mL) with ≤2 fully active and approved ARVs. Participants with 1 or 2 active ARVs entered the RC and received open-label FTR + optimized background treatment (OBT) after an 8-day blinded placebo-controlled period. Virologic and immunologic responses were analysed by baseline (BL) demographics and disease characteristics.

Results: At baseline in the RC, 89% of participants had a CD4 T-cell count <350 cells/mm3, with 5% between 350-<500 cells/mm3 and 6% ≥500 cells/mm3. The mean CD4 T-cell increase observed in the <40 copies/mL (n=142) group was 331 cells/mm3, 40-400 copies/mL (n=25) was 263 CD4 T-cells/mm3, 400-1000 copies/mL (n=2) was 218 CD4 T-cells/mm3, and in participants with >1000 copies/mL (n=10) it was 107 CD4 T cells/mm3. A similar mean increase in CD4/CD8 T cell ratio was observed across those individuals with LLV; the ratio in the <40 copies/mL (n= 142) group was 0.38, in

those with a VL 40-400copies/mL (n=25) it was 0.31, 400-1000 copies/mL (n=2) it was 0.32, and in the >1000 copies/mL (n=10) group it was 0.09. Biomarkers measured as part of the BRIGHTE showed a mean general reduction in the study; <40 copies/mL [sCD14: -371ug/L (n=133); sCD163: -134 ug/L (n=40); D-Dimer: 0.16mg/L (n=1/39)], 40-400copies/mL [sCD14: -428ug/L (n=21); sCD163: -80ug/L (n=5); D-Dimer: -0.14mg/L (n=22)], 400-1000 copies/mL [sCD14: 1174ug/L (n=2); sCD163: no data; D-Dimer: 0.04mg/L (n=2)], >1000 copies/mL [sCD14: 271ug/L (n=10); sCD163: 107ug/L (n=3); D-Dimer: 0.08mg/L (n=10)].

Conclusions: In those individuals with LLV there is a persistent increase in CD4 T cell number and an improvement in CD4/CD8 ratio, with a general reduction of inflammatory markers (sCD14, sCD163, D-Dimer) up to week 192. These results highlight the value of FTR-based regimens for a sustained improvement where there is incomplete virologic suppression.