ORAL ABSTRACTS

540. HIV-1 Attachment Inhibitor Prodrug BMS-663068 in Antiretroviral-Experienced Subjects: Week 24 Subgroup Analysis

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Background. BMS-663068 is a prodrug of BMS-626529, an attachment inhibitor that binds directly to HIV-1 gp120, preventing initial viral attachment and entry into the host CD4+ T-cell. AI438011 is a Phase IIb, randomized, active-controlled trial investigating the safety, efficacy and dose–response of BMS-663068 versus atazanavir/ritonavir (ATV/r) in treatment-experienced (TE), HIV-1-positive subjects (sbj).

Methods. Antiretroviral TE sbj (exposure to ≥1 antiretroviral for ≥1 week) with susceptibility to all study drugs (BMS-626529 IC_{50} <100 nM), were randomized equally to four BMS-663068 arms (400 or 800 mg, BID; 600 or 1200 mg, QD) and a control group (ATV/r 300/100 mg QD) with tenofovir disoproxil fumarate (TDF) + raltegravir (RAL). A subgroup analysis of viral efficacy and immunologic reconstitution is presented.

Results. 251 sbj were treated. Median age was 39 years, 60% were male and 38% white. Median baseline (BL) viral load (VL) was 4.85 $\log_{10}$ c/mL (43% >100,000 c/mL) and median CD4+ T-cell count was 230 cells/mm^3 (38% <200 CD4 cells/mm^3). Through Week 24, response rates (HIV-1 RNA <50 c/mL) were comparable across all BMS-663068 arms and the ATV/r arm regardless of gender, age and race. Response rates for sbj with BL VL <100,000 c/mL (BMS-663068, 82–96%; ATV/r, 93%) were higher than those for sbj with BL VL ≥100,000 c/mL (BMS-663068, 70–87%; ATV/r, 73%); however, there were no substantial differences in response across the BMS-663068 and ATV/r arms in either subgroup. Response rates for sbj with BL CD4+ cell counts ≥200 cells/mm^3 (87–96%) were higher than those for sbj with BL CD4+ cell counts <200 cells/mm^3 (62–82%); however no substantial differences in response were seen across the BMS-663068 and ATV/r arms in either subgroup. Mean changes in CD4+ T-cell counts from BL were similar across all arms regardless of gender, age and BL CD4+ T-cell count.

Conclusion. Virologic response rates were similar across the BMS-663068 and ATV/r arms in TE subjects, regardless of BL demographic characteristics (gender, race, age), BL HIV-1 RNA, or BL CD4+ T-cell count. Mean increases in CD4+ T-cell counts across the BMS-663068 arms were consistent with ATV/r, regardless of gender, age and BL CD4+ T-cell count. These results support continued development of BMS-663068.

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