1574. Safety Profile of HIV-1 Attachment Inhibitor Prodrug BMS-663068 in Antiretroviral-Experienced Subjects: Week 24 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 an ongoing, Phase IIb, randomized, active-controlled trial investigating the safety, efficacy and dose–response of BMS-663068 vs atazanavir/ritonavir (ATV/r) in treatment-experienced (TE), HIV-1-positive subjects (sbj). At Week 24, response rates across the BMS-663068 arms were consistent with ATV/r.

Methods. Antiretroviral TE sbj (exposure to ≥1 antiretroviral for ≥1 week) with susceptibility to all study drugs (including 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 arm (ATV/r 300/100 mg QD), with tenofovir disoproxil fumarate (TDF) -+ raltegravir (RAL). The complete safety profile through Week 24 is reported.

Results. In total, 251 sbj were treated (BMS-663068, 200; ATV/r, 51). No BMS-663068-related adverse events (AEs) led to discontinuation. Grade 2–4 drug-related AEs occurred in 17/200 (8.5%) sbj across the BMS-633068 arms; however, these events were mostly single instances and no dose-relationship was seen. Similarly, no noticeable trend for Grade 3–4 laboratory abnormalities was seen and Grade 3–4 hematologic changes and liver chemistry elevations were uncommon (neutropenia, 2.5%; AST/ALT elevations, 1% [n = 196]). In the ATV/r arm, Grade 2–4 drug-related AEs occurred in 14/51 (27.5%) sbj and were mostly secondary to gastrointestinal and/or hepatobiliary disorders. Serious adverse events (SAEs) occurred in 13/200 (6.5%) and 5/51 (9.8%) sbj receiving BMS-663068 and ATV/r, respectively; most were secondary to infections and none were related to study drugs. The most common AE reported for BMS-663068 was headache (28/200, 14%), occurring in 5/51 (10%) sbj in the ATV/r arm; in the BMS-663068 arms this was not dose-related. There were no deaths.

Conclusion. BMS-663068 was generally well tolerated across all arms, with no related SAEs or AEs leading to discontinuation and no dose-related safety signals. There were no trends for Grade 2–4 AEs or clinical laboratory abnormalities. These results support continued development of BMS-663068.

Disclosures. **C. Brinson**, Bristol-Myers Squibb: Investigator, employer received monies for conducting the trial, Contract Principal Investigator for clinical trials; Gilead: Board Member and Speaker, advisory board member, education board member, personal fees Investigator, Contract Principal Investigator for clinical trials; Boehringer Ingelheim: Investigator, Contract Principal Investigator for clinical trials; ViiV: Investigator, Contract Principal Investigator for clinical trials; GlaxoSmithKline: Investigator, Contract Principal Investigator for clinical trials; Shionogi: Investigator, Contract Principal Investigator for clinical trials; AstraZeneca: Investigator, Contract Principal Investigator for clinical trials; Pfizer: Investigator, Contract Principal Investigator for clinical trials; Janssen: Investigator, Contract Principal Investigator for clinical trials; Sangamo: Investigator, Contract Principal Investigator for clinical trials; Taimed: Investigator, Contract Principal Investigator for clinical trials; Theratechnologies: Investigator, Contract Principal Investigator for clinical trials; Serono: Investigator, Contract Principal Investigator for clinical trials; Achillion: Investigator, Contract Principal Investigator for clinical trials **J. Echevarría**, Bristol-Myers Squibb: Grant Investigator, Grant recipient **S. Treviño-Pérez**, Bristol-Myers Squibb: Grant Investigator, Grant recipient **J. R. Bogner**, All companies involved in antiretroviral therapy: Speaker's Bureau, Speaker honorarium **D. Stock**, Bristol-Myers Squibb: Employee and Shareholder, Salary **S. R. Joshi**, Bristol-Myers Squibb: Employee and Shareholder, Salary **G. J. Hanna**, Bristol-Myers Squibb: Employee and Shareholder, Salary **M. Lataillade**, Bristol-Myers Squibb: Employee and Shareholder, Salary