HIV-1 Attachment Inhibitor Prodrug BMS-663068: Interactions with DRV/r and/or ETR

**BACKGROUND**

HIV-1 Attachment Inhibitor Prodrug BMS-663068: Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability

**OBJECTIVES**

- Assess the safety and tolerability of BMS-663068 administered alone and in combination with DRV/r or ETR in healthy subjects.
- Evaluate the pharmacokinetic (PK) characteristics of BMS-663068 and its active moiety BMS-626529.
- Assess the effects on the PK of BMS-626529 of coadministering BMS-663068 with DRV/r or ETR.
- Evaluate the effect of BMS-663068 on the PK of RTV.

**RESULTS**

- **Study Design**
  - **Eligible subjects** were randomly assigned to Cohort 1, 2 or 3 before dosing on Day 1 (Figure 1).
  - **Treatment and comparison** included BMS-663068 600 mg BID and ETR 200 mg BID.
  - **A previous Phase I study** (n=44) of BMS-663068 1200 mg BID/single dose (SD), RTV 100 mg BID/SD was terminated due to one instance of anaphylaxis.

- **PK Characteristics**
  - **Coadministration of DRV/r with BMS-663068 increased peak plasma concentration and AUC** compared to BMS-663068 alone.
  - **Coadministration of BMS-663068 with DRV/r resulted in no change for C**.
  - **GMRs comparing BMS-663068 + ETR versus ETR were contained within the predefined 90% CI limits (0.75–1.70)**.

- **Adverse Events**
  - **Overall, no treatment-related serious adverse events were reported**.
  - **The most common adverse events were local skin rash (23.1%) and nausea (13.0%).**

**CONCLUSIONS**

- **BMS-663068 and the active moiety BMS-626529 had no clinically relevant effect on the PK of DRV/r or ETR**.
- **BMS-663068 alone contained the predefined 90% CI limits of 0.75–1.70**.
- **BMS-663068 was well tolerated in healthy subjects when administered alone or in combination with DRV/r or ETR**.

**REFERENCES**

- Data on File. AI438009 CSR. BMS, Princeton, NJ.

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**METHODS**

- **Study population**
  - Healthy male and female volunteers, 18 to 50 years of age and eligible to contribute to the study: 36 subjects (12 per cohort).

**Figure 1: ACOBRO study design**

**Figure 2: Mean (+/-SD) plasma concentration–time profiles for the effect of BMS-663068 on PK of RTV**

**Figure 3: PK results and statistical analysis: DRV**

**Figure 4: PK results and statistical analysis: ETR**

**Table 3: PK results and statistical analysis: DRV**

**Table 4: PK results and statistical analysis: RTV**

**Table 5: Summary of AEs experienced by all subjects**