**Pharmacokinetics and Safety of Twice Daily Atazanavir 300 mg and Raltegravir 400 mg in Healthy Subjects**

L. Zhu1, L. Mahnke1, J. Burtterton2, A. Persson1, M. Stonier1, W. Comisar2, D. Panebianco2, S. Breiding2, J. Zhang1 and R. Bertz1

1Bristol-Myers Squibb R&D, Hopewell, NJ and Merck Research Laboratories, PA and MA.

**BACKGROUND**

- **Objectives**: To assess the safety and tolerability of the co-administration of ATV 300 mg BID with RAL 400 mg BID in healthy subjects.
- **Methods**: An open-label, sequential, multiple-dose study in 22 healthy HIV-negative subjects, aged 18 to 45, inclusive, with no clinically relevant abnormalities.
- **Study Design**: Subjects were screened and enrolled within 21 days of Day 1. After a 7-day single-dose sequence, subjects received ATV 300 mg BID alone, followed by ATV 300 mg BID + RAL 400 mg BID for 26 days. Safety and tolerability were assessed through clinical evaluations, vital signs, laboratory tests, and adverse events.

**RESULTS**

- **Safety**:
  - No drug-related serious adverse events were reported.
  - Two (2) subjects discontinued prior to labs.
  - Grade 2 abnormalities were observed in 1%, 0%, and 2% of subjects in ATV, ATV/RTV, and RAL, respectively.
  - Three (3) subjects discontinued due to an AE following administration of ATV 300 mg BID.

- **Pharmacokinetics**:
  - ATV AUC(0-24h) [calculated as 2 x AUC(0-12h)] appeared to be similar to historical values previously observed in healthy subjects following the same treatment (ATV 300 mg BID) in a previous healthy volunteer study.
  - RAL Cmax following RAL 400 mg BID alone was similar to historical values previously observed in healthy subjects following the same treatment (RAL 400 mg BID) in a previous healthy volunteer study.
  - There was a 11%, 17%, and 29% lower Cmax and AUC(0-24h) for ATV when co-administered with RAL, respectively.
  - Both ATV and RAL are individually well-tolerated, with low rates of GI intolerance and minimal impact on lipids.

- **Pharmacodynamics**:
  - PR and QTcF intervals were measured.
  - No ECG PR, QRS, or QT interval changes were observed with ATV 300 mg once daily (QD) has been demonstrated to be highly effective and well-tolerated in both ARV naïve and experienced patients.
  - RAL alone

**TABLES**

1. Summary and Statistical Analyses for ATV Pharmacokinetic Parameters
2. Summary and Statistical Analyses for ATV Pharmacodynamic Parameters
3. Summary and Statistical Analyses for Raltegravir Pharmacokinetic Parameters
4. Summary and Statistical Analyses for Raltegravir Pharmacodynamic Parameters

**REFERENCES**