Background

- The once-daily protease inhibitor atazanavir (ATV) boosted with low-dose ritonavir (RTV) and combined with other antiretrovirals is approved for the treatment of HIV-1 infection.

- Development of ATV/COBI 300/150 mg Fixed-Dose Combination (FDC) with a light meal and a high-fat meal was assessed.

- The bioavailability of ATV administered as an FDC was similar to ATV + COBI administered as individual components when given with a light meal.

- The bioavailability of ATV administered as an FDC was similar to ATV + COBI administered as individual components when given with a high-fat meal.

- All ATV PK parameter adjusted Geometric Mean Ratios fell within the predefined limits indicating bioequivalence of the FDC to ATV 300 mg and COBI 150 mg coadministered individually.

Methods

- Study design: This was an open-label, single-dose, 1-period (1-day) trial with four periods (2 periods with each of 2 treatments) followed by an open-label treatment period (Period 2) to assess the bioavailability of ATV administered as an FDC.

- PK parameters: PK parameters were used to assess the bioequivalence of the FDC to ATV 300 mg and COBI 150 mg coadministered individually.

- Pharmacokinetic and safety analyses: Pharmacokinetic and safety analyses of ATV and COBI were performed to assess the bioequivalence of the FDC to ATV 300 mg and COBI 150 mg coadministered individually.

- For the primary objective, complete data from all subjects were included.

- Linear mixed-effects models with natural logarithms of ATV or COBI as response variable and treatment, period, sequence and random effects as covariates were used to assess the bioequivalence of the FDC to ATV 300 mg and COBI 150 mg coadministered individually.

- For the secondary objective, a simpler linear mixed-effects model was used with natural logarithms of ATV or COBI as response variable and treatment, period, sequence, and baseline values as covariates.

Results

- The bioavailability of ATV administered as an FDC was similar to ATV + COBI administered as individual components when given with a light meal.

- The bioavailability of ATV administered as an FDC was similar to ATV + COBI administered as individual components when given with a high-fat meal.

- All ATV PK parameter adjusted Geometric Mean Ratios fell within the predefined limits indicating bioequivalence of the FDC to ATV 300 mg and COBI 150 mg coadministered individually.

- All ATV PK profile - FDC vs Single Agents with a Light Meal

- All ATV PK profile - FDC vs Single Agents with a High Fat Meal

- All ATV PK profile - Cardiovascular events

- All ATV PK profile - Safety and Tolerability

References


2. Xiaolu Tao, Bruijn-Myers Squibb, Pennington, NJ, USA; Bruijn-Myers Squibb, Princeton, NJ, USA.

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