Rilpivirine pharmacokinetics in HIV-1-infected adolescents: a substudy of PHASE II trial

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Introduction

- The NNRTI rilpivirine (RPV, TMC278) combined with other antiretrovirals (ARVs) is approved for use in treatment-naive, HIV-1-infected adults with a viral load >100,000 to ≤500,000 copies/mL at entry into Phase III trials. RPV is recommended for use in treatment-naive HIV-infected adults and adolescents. A recently published meta-analysis identified 301 adolescents with HIV-1 infection who participated in three Phase III clinical trials of RPV. The meta-analysis compared RPV with efavirenz (EFV) and found that RPV had similar or improved efficacy compared with EFV in adolescents. However, the study did not explore the potential impact of sex and race on the pharmacokinetics of RPV.

Methods

- **Study design and treatment**
  - **PAINT** is an ongoing Phase 3, open-label single arm trial (Figure 1).
  - The eligible treatment population is ARV-naive and includes adolescents aged 12 to 17 years and weighing ≥35 kg.
  - Patients were randomized in a 1:1 ratio to receive RPV 25 mg once daily or placebo.
  - Following enrolment, 2, 4, or 6 weeks of ARV-naive RPV dosing was followed by a 12-week phase in which all patients received the background regimen.
  - The 35 mg/dosed three-drug regimen was used in Part 1a and the 25 mg/dosed three-drug regimen was used in Part 1b.
  - Data were presented for Part 1 overall (Part 1a + 1b).

- **Study population**
  - Every patient who received the study drugs was included in the analysis.
  - Median age: 15.6 years (range: 12.2–18.1 years).
  - Median duration of HIV infection: 2.97 years (range: 0.19–10.23 years).
  - Median body weight: 50.7 kg (range: 12.3–83.4 kg).
  - Rockyou score: 56.1 (range: 0–100).
  - The most common adverse events (AEs) were grade 1 or 2 in severity.

- **RPV pharmacokinetics**
  - RPV plasma concentration-time curves were generated for children and adolescents using a non-compartmental model (NCA) approach.
  - The ratios of the geometric mean PK parameters for adolescents (PAINT Part 1)/adults (ECHO/THRIVE PK substudy) were all >0.80 and <1.25 (Table 1).

Results

- **Study design and treatment**
  - A total of 50 adolescents were treated on the study drugs at 12-week visit.

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Conclusions

- The majority of patients were treatment-experienced in Part 1a and Part 1b.
- The safety and efficacy of RPV in HIV-1-infected adolescents was shown to be similar to that observed in adults.
- RPV was well tolerated and safe in adolescents and did not show any notable differences in safety profiles compared to adults.
- The results of this study support the potential use of RPV in adolescents and provide a basis for further clinical trials.

Acknowledgments and disclosures

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References