Rilpivirine Pharmacokinetics Without and With Darunavir in Adolescents and Young Adults

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BACKGROUND & OBJECTIVE

- Rilpivirine (RPV) is a second generation non-nucleoside reverse transcriptase inhibitor (NNRTI).
- Once daily (QD) dosing of RPV is approved at 25 mg for HIV-infected adolescents and young adults.
- Once daily dosing of RPV makes it an attractive option for HIV-infected adolescents and young adults.
- Primary Objective: To assess the steady state pharmacokinetics of rilpivirine 25 mg QD with and without darunavir/ritonavir (DRV/r 800/100 mg) once daily administered to adolescents and young adults.
- Secondary Objective: To assess steady state pharmacokinetics of DRV/r 800/100 mg QD with RPV 25 mg QD administered to adolescents and young adults.

METHODS

- IMPACT P1058A is a multi-centered observational study designed to evaluate the PK of antiretroviral drug combinations commonly used by HIV-infected children, adolescents, and young adults [clinicaltrials.gov: NCT0077756].
- Two of the RPV regimens under study in protocol Version 2.0 included: RPV exposure after 25 mg dosing in conjunction with DRV/r 800/100 mg once daily was two to three fold higher for all tested parameters when compared to the RPV 25 mg QD alone regimen.
- The study was approved by the Institutional Review Board at each site.
- Sample size was selected to have power to identify situations in which DRV/r led to pharmacokinetic parameter values outside the target range.
- The study was supported by the Review Board at each site.

RESULTS

- The study was an observational, non-randomized study.
- The study did not prescribe therapy or provide medications, and did not dictate subject management.
- Eligible subjects included HIV-infected patients aged 12 to 24 years of age on one of the regimens of interest for at least 30 days at an IMPACT site in the United States.
- Subjects were excluded if they had any clinical or laboratory toxicity of grade 2 or higher, a hemoglobin level of <8.5 gm/dl, or were receiving a drug that might interact with the drugs of interest.
- A negative pregnancy test was required at enrollment for females of child-bearing capacity.
- PK Results were communicated to the local investigator in real-time but there were no protocol-mandated dosage adjustments.

Table 1. Baseline Patient Demographics

<table>
<thead>
<tr>
<th>Gender</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Male</td>
<td>13 (87)</td>
</tr>
<tr>
<td>Female</td>
<td>2 (13)</td>
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</tbody>
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Table 2. Rilpivirine Pharmacokinetics without and with administration of Darunavir

<table>
<thead>
<tr>
<th>PK Parameters (90% CI)</th>
<th>RPV 25 mg QD</th>
<th>RPV 25 mg QD + DRV/r 800/100 mg QD</th>
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<tbody>
<tr>
<td>AUC (µg/mL)</td>
<td>2.38 (1.32-2.4)</td>
<td>6.74 (4.56-9.26)</td>
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<tr>
<td>Cmax (µg/mL)</td>
<td>1.3 (0.9-1.4)</td>
<td>3.24 (1.13-7.96)</td>
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<tr>
<td>Cmin (µg/mL)</td>
<td>0.81 (0.61-1.08)</td>
<td>0.52 (0.38-0.72)</td>
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CONCLUSIONS

- RPV exposure after 25 mg dosing without DRV/r in our cohort, median age 20, was similar to adults, although slightly above the standard AUC range of 1.4-2.2 µg/mL (Table 2).
- Greater variability in concentration-time curves was seen in those patients receiving RPV plus DRV/r (Figure 1).
- RPV exposure after 25 mg dosing in conjunction with DRV/r 800/100 mg once daily was two to three fold higher for all tested parameters (AUC, Cmax, Cmin, Clast) when compared to RPV alone (Table 2 and Figure 2).
- DRV exposure after 800/100 mg dosing did not appear to be affected by concomitant RPV use (Table 2 and Figure 3).
- All patients had RPV Cmax, above the RPV half maximal effective concentration (EC50) of 0.03-0.37 ng/mL for wild-type HIV.
- Further studies are required to determine if changes in RPV dose are needed when used in combination with DRV/r in this age group.

REFERENCES