To compare rilpivirine AUCs, clearance, and troughs during pregnancy.

To investigate the pharmacokinetics of rilpivirine during pregnancy.

To determine if the pharmacokinetics of rilpivirine differ during pregnancy compared to postpartum.

Method:

IMPACT Protocol P0128s is a Phase IV study of the pharmacokinetics and safety of ARVs, including a rilpivirine arm, in pregnant women. Protocol 1026s (IMPAACT Protocol P1026s) is an ongoing, multicenter, non-blinded, non-randomized study evaluating the pharmacokinetics and safety of ARVs in pregnant women that included a cohort of US pregnant women receiving as part of clinical care.

Results:

RPV PK data were available for 26 women. PK parameters are presented in the table below. Between trimester comparisons were performed using a two-sided Wilcoxon signed rank test. Pairwise comparisons within each subject between time points were performed using a two-sided Wilcoxon signed rank test. Results: PK data were available for 26 women. Parameters were compared between trimester and postpartum. Maternal and umbilical cord blood samples were collected at term and 6-12 weeks postpartum. The impact of pregnancy on RPV pharmacokinetics (PK) is unknown.

Methods:

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Results (cont.)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC&lt;sub&gt;0-24&lt;/sub&gt; (mg·hr/mL)</td>
<td>1.36 (0.97 - 1.82)</td>
<td>1.01 (0.67 - 1.28)</td>
<td>0.67 (&lt;10 - 1.96)</td>
</tr>
<tr>
<td>C&lt;sub&gt;0&lt;/sub&gt; (mg/mL)</td>
<td>53 (12 - 140)</td>
<td>19 (5 - 57)</td>
<td>12 (&lt;10 - 68)</td>
</tr>
<tr>
<td>T&lt;sub&gt;1/2&lt;/sub&gt; (hr)</td>
<td>9 (6 - 15)</td>
<td>5 (4 - 8)</td>
<td>4 (3 - 7)</td>
</tr>
<tr>
<td>C&lt;sub&gt;min&lt;/sub&gt; (mg/mL)</td>
<td>19 (6 - 61)</td>
<td>10 (&lt;10 - 22)</td>
<td>5 (&lt;10 - 20)</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (mg/mL)</td>
<td>61 (37 - 105)</td>
<td>56 (18 - 101)</td>
<td>51 (&lt;10 - 200)</td>
</tr>
</tbody>
</table>

Conclusions:

Rilpivirine pharmacokinetic parameters showed high variability.

The following factors: 27.90% (0.05 - 0.83). RPV was well tolerated. There were 4 maternal grade 3 or 4 AEs (1 preterm birth; 1 neonatal death; 1 ventilator support; 1 preterm birth). There were 4 infant grade 3 or 4 AEs (1 preterm birth; 1 neonatal death; 1 ventilator support; 1 preterm birth).

Rilpivirine was generally tolerated well. There were 4 maternal grade 3 or 4 AEs (1 preterm birth; 1 neonatal death; 1 ventilator support; 1 preterm birth). There were 4 infant grade 3 or 4 AEs (1 preterm birth; 1 neonatal death; 1 ventilator support; 1 preterm birth).

Rilpivirine pharmacokinetic parameters differed during pregnancy compared to postpartum.

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