2001: A Phase I/II Trial of the Pharmacokinetics, Tolerability, and Safety of Once-Weekly RIF and INH in HIV-1-infected and HIV-1-uninfected Pregnant and Postpartum Women with Latent Tuberculosis Infection

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2001 Screening

• After mother signs Informed Consent, obtain Screening Number (PS########) by completing the PS2001 IMPAAACT Screening Checklist in the Subject Enrollment System on the DMC Portal
2001 Screening

- If mother does not enroll *for any reason*, complete the screening failure CRF (SCR0053) and submit to DMC database.
2001 Enrollment

• Enter the Screening Number PS####### into the Eligibility Checklist (required)
  
  Q0002
  Enter the participant's screening number.

• Mother-infant pairs are enrolled using the Subject Enrollment System (one checklist/pair)

• Questions are asked for the MOTHERS, for example:
  
  Q0009
  What is the participant's sex at birth?
  
  □ Male [Ineligible]
  □ Female [next question]
  □ Ambiguous Genitalia [Ineligible]
  □ Unknown [Ineligible]
Schedules: Maternal

• Cohort 1 and Cohort 2 mothers use same schedules
• Entry and 11 weekly visits = 12 doses
• Postpartum visit (if eligible)
• Monthly visits until 24 weeks after delivery (Study Exit)
Schedules: Infant

- Infant schedule begins when the **EVW0292 – Pregnancy Outcome (Infant Enrolled)** form is submitted **under the Mother’s patid**

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**DATA COLLECTION FORMS SCHEDULE**

<table>
<thead>
<tr>
<th>STUDY 2001</th>
<th>03-17-16</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFANT BOOK 1</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE:** The columns are marked with either an “X” or “V” to indicate data and evaluations required at each visit.

- **X** = Required form.
- **V** = Evaluation required; data may be required.

<table>
<thead>
<tr>
<th>WEEKS</th>
<th>BIRTH (Within 3 Days of Life)</th>
<th>ON STUDY</th>
<th>OFF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
</tbody>
</table>

***Key this form **promptly** after infant’s birth to update the MASTER tables***

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a. Infant PID Number: ..........................................................................................................................

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4. What is the delivery date?........

    dd  mmm  yyyy
Schedules: Maternal & Infant

• Mother’s visits and Infant’s visits will ideally be scheduled to occur on the same day
Premature Discontinuation

• Women who withdraw from study participation will be requested to complete the Study Exit visit, if possible

• Women (and their infants) who permanently discontinue the study drug regimen prematurely will remain on study and follow the visit schedule until 24 weeks postpartum (Study Exit visit)
CRFs: Maternal

• Some forms are **ONLY** required for HIV-1 Infected Mothers:
  1. LBW0054 - Lymphocyte Subsets – III
  2. PE0043 - WHO Staging System For HIV Infection and Disease for Adolescents and Adults (≥ 15 Years) – Revised
  3. PE0045 - WHO Nadir CD4+ Lymphocyte Subset and Immunological Classification
  4. PE0421 - Antiretroviral Concomitant Medications - II
SVW0284 – IMPAAACT 2001
Maternal Study Event Tracking

1. Is this a postpartum visit? ............................................................... (1-Yes, 2-No)
   If No, STOP.
   If Yes, complete the IMPAAACT 2001 Infant Feeding Practices (QLW0272) form and continue.

2. Has the participant given birth at this visit or since the last visit? .......... (1-Yes, 2-No)
   If No, continue.
   If Yes, complete the Pregnancy Outcome (Infant Enrolled) (EVW0292) form and continue.

4. Has the participant completed the study-defined drug regimen (RPT/INH/vitamin B6) with adequate adherence per Protocol Section 5.1.2 (i.e. at least 11 doses within a 16-week window) since the last visit? ............................................................... (1-Yes, 2-No)
   If No, STOP.
   If Yes, continue.

5. Has the participant given birth within 3 days of this visit? ..................... (1-Yes, 2-No)
   If No, STOP.
   If Yes, complete the evaluations listed under the Postpartum Visit column on the Maternal Book 2 DCFS and STOP.

6. Is the participant currently breastfeeding her child who is enrolled in IMPAAACT 2001? ............................................................... (1-Yes, 2-No)
   If No, STOP.
   If Yes, continue.

7. Indicate which postpartum visit this represents: ................................... 1-First weekly visit after delivery
   If 4, STOP.
   If 1-3, complete the IMPAAACT 2001 Breast Milk and Plasma Pharmacokinetics (PKW0394) form and STOP.
   2-Second weekly visit after delivery
   3-Last dose visit
   4-None of these
PKW0394 - IMPAACT 2001 Breast Milk and Plasma Pharmacokinetics

• Women eligible ONLY if:
  1. Still taking study drug regimen postpartum
  2. Breastfeeding

• Eligibility for breast milk and plasma PK sample collection is established by completing the SVW0284 from (previous slide)

• Collect specimens at:
  1. First weekly visit after delivery (3 hours post dose)
  2. Second weekly visit after delivery (6 hours post dose)
  3. Last dose visit (24 hours post dose) (breast milk only)
PKW0392 - IMPAACT 2001
Maternal Pharmacokinetics

• Required twice:
  1. First dose visit (Entry, Week 0) = INTENSIVE PK
  2. Last dose visit (Week 11) = SPARSE PK

• NOTE: Header Date is the date when PK sampling begins
PKW0392 - IMPAAACT 2001
Maternal Pharmacokinetics

• Required twice:
  1. First dose visit (Entry, Week 0) = INTENSIVE PK

<table>
<thead>
<tr>
<th>Expected Draw Time</th>
<th>Specimen Obtained?</th>
<th>Date Specimen Obtained (dd/mmm/yyyy)</th>
<th>Actual Time Specimen Obtained (hh:mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dose</td>
<td>1-Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2-No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3-Not Required</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. 0 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Collect within 30 minutes prior to dosing)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. 0.5 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. 1 hour*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. 2 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. 4 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. 5 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. 8 hours*</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>h. 12 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. 24 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>j. 48 hours*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>k. 72 hours*</td>
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<td></td>
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</tr>
</tbody>
</table>

*15-minute collection window
**PKW0392 - IMPAACT 2001**

**Maternal Pharmacokinetics**

- Required twice:
  2. Last dose visit (Week 11) = SPARSE PK

<table>
<thead>
<tr>
<th>Expected Draw Time</th>
<th>Specimen Obtained?</th>
<th>Date Specimen Obtained (dd/mmm/yyyy)</th>
<th>Actual Time Specimen Obtained (hh:mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. 1 hour*</td>
<td>1-Yes 2-No 3-Not Required</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. 4 hour*</td>
<td>1-Yes 2-No 3-Not Required</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. 24 hours*</td>
<td>1-Yes 2-No 3-Not Required</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. 48 hours*</td>
<td>1-Yes 2-No 3-Not Required</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*15-minute collection window</td>
<td></td>
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</tr>
</tbody>
</table>
TXW0304 – IMPAACT 2001 Study Treatment Record

- Be sure to report **ALL three** study medications

1. Were there any modifications to study medication at this visit or since the study participant's last visit? (This includes all initial doses, modifications, interruptions, and permanent discontinuation.) (1-Yes, 2-No) □

   **NOTE:** Study medication is defined as rifapentine (RPT), isoniazid (INH), pyridoxine (vitamin B₆).

   If No, go to question 2.
   If Yes, continue. *Use the Tab Key after the last entry.*

   Specify Drug [70]:
   Dose Status [ ]:
   Total Daily Dose (mg):

   a. Manufactured Type:
   If Generic Code ‘2’ or ‘3’, Specify Manufacturer [70]:
   Date Modification Started (dd/mmm/yyyy):
   Formulation [ ]:

   If 98 or 99, Specify [70]:
   Reason for Modification [ ]:
   Specify Reason [70]:
   Toxicity Grade [ ]:
PKW0393 – IMPAAACT 2001 Infant PK and Cord Blood Collection

1. Were specimens obtained for infant pharmacokinetics at this visit? ........................................................................ (1-Yes, 2-No) □
   If Yes, go to question 2.
   If No, complete 'a-e' and go to question 3. Indicate the reason(s) infant PK specimens were not obtained:

   a. Infant’s birth weight < 1000 grams: ................................................................. □
   b. Infant receiving disallowed medications as indicated in Protocol Section 5.5: ......................... □
   c. Infant has any severe congenital malformation or other medical condition not compatible with life, or that would interfere with study participation or interpretation, as judged by the site investigator: ................................................................................................. □
   d. Mother’s most recent dose taken more than 72 hours before drawing the infant’s blood: .................................................................................................................. □
   e. Other, specify .......................................................................................................................... Specify [70]: ..............................

3. Was a cord blood specimen obtained for pharmacokinetics during labor/delivery? ... (1-Yes, 2-No) □
   If Yes, go to question 4.
   If No, complete 'a-c' and go to question 6. Indicate the reason(s) cord blood specimens were not obtained:

   a. Mother’s most recent dose taken more than 72 hours prior to delivery: ........................ □
   b. No site capacity for collecting cord blood specimens: .................................................. □
   c. Other, specify .......................................................................................................................... Specify [70]: ..............................
Event Directed TBW forms

• Triggered from TRK0159 - IMPAACT 2001 TB Exposure or Active TB Diagnosis Tracking:

Mothers AND Infants

TBW0045

TBW0029

TBW0039

TBW0034

TBW0048
Questions??

• Schedules, CRFs, LCs, etc:
  • Stephanie Popson: popson@fstrf.org

• eData, Smart Update, technical issues:
  • User Support: user.support@fstrf.org

• Patient management, protocol:
  • 2001 Protocol Team: impaact.team2001@fstrf.org

• Used by protocol team to convey information to registered sites:
  • impaact.prot2001@fstrf.org