



# IMPAACT 2007

# PHARMACOKINETICS

IMPAACT ANNUAL MEETING JUNE 2017

VERSION 1.0, 13 APRIL 2016

LOA #1, 12 AUGUST 2016



# PK SAMPLING REFERENCES

Consult Section 7 of the Manual of Procedures which is available on the PSWP for guidelines related to PK Sampling

# COHORT 1: ENTRY INTENSIVE PK VISIT

## Cohort 1: Entry - Intensive PK Sampling

Time Points	Pre-dose < 1 hr before dosing	1 – 2 hrs post-dose	4 – 8 hrs post-dose	11 – 13 hrs post-dose	20 – 24 hrs post-dose	48 – 72 hrs post-dose
	Stratum 1B only: Collect single sample for EFV level at any time <u>on the same day</u> as the first dose of maraviroc					

# COHORT I: SEQUENCE OF INTENSIVE PK-RELATED PROCEDURES AT ENTRY (DAY 0-3)

If the mother-Infant pair is not enrolled, confirm final eligibility determination



Enter checklist data into Subject Enrollment System (SES) to enroll mother-infant pair; confirm pair successfully enrolled



Pre-dose PK blood draw



Study drug administered in the clinic within 1 hour of pre-dose PK blood draw



1-2 hour PK blood draw

# SEQUENCE OF INTENSIVE PK-RELATED PROCEDURES

4-8 hour PK blood draw



11-13 hour PK blood draw



20-24 hour PK blood draw



48-72 hour PK blood draw



Provide any available test or laboratory results



Schedule Week 1 visit and provide site contact instructions

# COHORT 1: LIMITED PK VISIT

- A Limited PK collection will be conducted at the Week 1 visit (Day 7-14)
- Collect a pre-dose PK sample **within 48 hours of study-drug dosing**
  - *Note: Second dose of maraviroc should not be administered until Week 1 ALT and AST test results have been reviewed (See Section 8.2.1 in LoA #1 for modified toxicity management guidelines).*
- Limited PK samples should be collected at the following time points:
  - **1-2 hours and 22-26 hours after the observed dose**
- Infants in **Stratum 1B only** should have an additional 0.5 mL sample collected for EFV testing

# COHORT 2: INTENSIVE PK VISITS

## *Weeks 1 and 4*

- Based on data from Cohort 1, the daily dose frequency for Cohort 2 will be communicated via a protocol Clarification Memorandum
- Infants in each stratum will be administered maraviroc either once daily or twice daily.
- The intensive PK sampling timepoints for each stratum in Cohort 2 are dependent on the frequency of daily dosing.

# COHORT 2 INTENSIVE PK – ONCE DAILY DOSING

## Cohort 2: Weeks 1 and 4 - Intensive PK Sampling with Once Daily Dosing

Time Points	Pre-dose < 1 hr before dosing	1 – 2 hrs post-dose	4 – 8 hrs post-dose	11 – 13 hrs post-dose	20 – 24 hrs post-dose
	Stratum 2B only: Collect single sample for EFV level at any time during PK sampling				



# COHORT 2: INTENSIVE PK VISITS

## ONCE-DAILY DOSING

### *Weeks 1 and 4*

- Infants should take study drug for *3 days prior* to the intensive PK visit. If this does not occur, the intensive PK visit should be rescheduled
- PK sampling should be scheduled so that the observed dosing of study drug is ideally **24 hours** (generally 22-26 hours) *after the previous dosing*. *PK sampling must be initiated on the same day as the observed dose of maraviroc*
- A pre-dose PK sample should be collected **within 1 hour before dosing**, and then **1-2h, 4-8h, 11-13h, and 20-24h after dose**
- Infants in **Stratum 2B only** should have an additional 0.5 mL sample collected for EFV testing

# COHORT 2 INTENSIVE PK SAMPLING WITH TWICE DAILY DOSING

## Cohort 2: Weeks 1 and 4 - Intensive PK Sampling with Twice Daily Dosing

Time Points	Pre-dose < 1 hr before dosing	1 – 2 hrs post-dose	3 – 5 hrs post-dose	6 – 8 hrs post-dose	11 – 13 hrs post-dose
	Stratum 2B only: Collect single sample for EFV level at any time during PK sampling				

# COHORT 2: INTENSIVE PK VISITS TWICE-DAILY DOSING

## *Weeks 1 and 4*

- Infants should take study drug for *3 days prior* to the intensive PK visit. If this does not occur, the intensive PK visit should be rescheduled.
- PK sampling should be scheduled so that the observed dosing of study drug is ideally **12 hours** (generally 11-13 hours) *after the previous dosing*.
- A pre-dose PK sample should be collected **within 1 hour before dosing**, and then **1-2h, 3-5h, 6-8h, and 11-13h** after dose.
- Infants in **Stratum 2B only** should have an additional 0.5 mL sample collected for EFV testing.

# COHORT 2: POPULATION PK

## *Week 6*

- A single 0.5 mL sample should be collected for all infants in Cohort 2 (for once or twice daily dosing)
- Infants in **Stratum 2B only** should have an additional 0.5 mL sample collected for EFV testing.



# IMPAACT 2007 PK PROCEDURES

**What are your questions?**