

# HPTN 084

**A Phase 3 Double Blind Safety and Efficacy Study of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women**

**Version 3.0/ OLE laboratory training**

# Overview of new Steps in OLE

- 1) Step 4a- Procedures for Participants Initially Randomized to TDF/FTC Who Elect to Move to OL CAB LA with Optional Oral Lead-in first (may be up to 56 weeks instead of 48)
- 2) Step 4b- Procedures for Participants Initiating or Re-starting CAB LA without the Optional Oral Lead-in; the Initial Dose Visit
- 3) Step 4c- Procedures for Participants on Maintenance Doses of CAB LA or TDF/FTC
- 4) Step 4d- Procedures for Pregnant/Breastfeeding Participants
- 5) Step 5- Procedures for Participants Taking OL TDF/FTC for 48 Weeks after Premature CAB LA discontinuation

# Length of study

For the majority of participants, the HPTN 084 OL component will last a minimum of approximately **48 weeks and a maximum of 52 weeks**, per participant. In specific circumstances, participants may be in the study for longer timeframes:

- Participants starting/re-starting CAB LA who elect to do the oral run-in will be followed for **56 weeks**. These participants will complete 4 weeks of an oral run-in plus a 4-week injection loading period.
- Only a minority of participants will be followed for up to 100 weeks (those who discontinue CAB LA prematurely during the OL component and are offered 48 weeks of TDF/FTC to cover the pharmacokinetic (PK) “tail”).
- Pregnant participants may be enrolled in the study for up to 148 weeks (four-week OLI optional, plus 48 weeks OL CAB LA (and only if pregnancy occurs within 8 weeks of last injection) plus 96 weeks of follow-up through pregnancy and post-partum period with final assessment of infant outcome at 48 weeks post-partum).

\*\*\*NEW\*\*\*

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- HIV RNA testing in addition to HIV rapid and instrumented testing
- ✓ Check lab reports and report any detectable VL results regardless of rapid and instrumented results to the HIV alias
- ❖ Ensure that data entry on the eCRF is correct - watch the reporting of Detectable versus Target Not Detected

# Lab

- Check the footnotes carefully regarding the chemistry analytes.
- **Albumin** has been added and only
- CPK, Phosphorous, Glucose, Amylase, Lipase and Calcium have been removed

# 4a: SoE for those on TDF/FTC who want CAB with oral lead-in

	DAY 0/ of Step 4a
<b>ADMINISTRATIVE, BEHAVIORAL, REGULATORY</b>	
Informed consent	X
Locator information	X
Offer CAB LA and counseling on direct to inject vs. oral lead in	X
Acceptability assessment	X
Behavioral assessment	X
HIV prevention counseling	X
Offer condoms	X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>	
Medical history, con meds, targeted physical exam (with pulse, BP, weight and BMI calculated at each visit)	X
Blood collection	X
Urine collection <sup>1</sup>	X
For those who select oral lead in: Dispense study product (enough for 4 weeks)	X
Adherence counseling <sup>2</sup>	X
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>	
HIV testing <sup>3</sup>	X
HIV viral load testing <sup>4</sup>	X
Pregnancy testing <sup>1</sup>	X
CBC with differential, if not done in Step 4a	X
Chemistry testing <sup>5</sup>	X
Liver function tests <sup>6</sup>	X
Fasting lipid profile, if not done in Step 4a <sup>7</sup>	X
Plasma storage <sup>8,9</sup>	X
DBS storage <sup>9</sup>	X

# 4b: Initiating or re-starting CAB LA without oral lead-in (initial dose visit)

	DAY 0 of Step 4b
<b>ADMINISTRATIVE, BEHAVIORAL, REGULATORY</b>	
Informed consent, if not obtained in Step 4a	X
Locator information	X
Offer CAB LA and counseling on direct to inject vs. oral lead in, if not done in Step 4a	X
Acceptability assessment, if not done in Step 4a	X
Behavioral assessment, if not done in Step 4a	X
HIV prevention counseling	X
Offer condoms	X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>	
Medical history, con meds, targeted physical exam (with pulse, BP, weight and BMI calculated at each visit)	X
Blood collection	X
Urine collection <sup>1</sup>	X
Adherence counseling <sup>2</sup>	X
Dispense and administer CAB LA $\pm$	X
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>	
HIV testing <sup>3</sup>	X
HIV viral load testing <sup>4</sup>	X
Pregnancy testing <sup>1</sup>	X
CBC with differential, if not done in Step 4a	X
Chemistry testing <sup>5</sup>	X
Liver function tests <sup>6</sup>	X
Fasting lipid profile, if not done in Step 4a <sup>7</sup>	X
Plasma storage <sup>8,9</sup>	X
DBS storage <sup>9</sup>	X

# 4c: Maintenance doses of CAB LA or TDF/FTC 48 weeks

Time on OL Study Product	Week 0 of Step 4c	Week 8	Week 16	Week 24	Week 32	Week 40	Week 48
Informed Consent**	X						
Locator information	X	X	X	X	X	X	X
Acceptability assessment	X			X			X
Behavioral assessment	X	X	X	X	X	X	X
HIV prevention counseling	X	X	X	X	X	X	X
Offer condoms per local SOC	X	X	X	X	X	X	X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>							
Medical history, concomitant medications, targeted physical exam (with pulse, BP, weight and BMI calculated at each visit)	X	X	X	X	X	X	X
Blood collection	X	X	X	X	X	X	X
Urine collection <sup>1</sup>	X	X	X	X	X	X	X
Vaginal swab collection <sup>2</sup>	X			X			X
Adherence counseling <sup>3</sup>	X	X	X	X	X	X	X
Dispense/administer product as is appropriate	X	X	X	X	X	X	X
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>							
HIV testing <sup>4</sup>	X	X	X	X	X	X	X
HIV viral load testing <sup>2</sup>	X	X	X	X	X	X	X
Pregnancy testing <sup>1</sup>	X	X	X	X	X	X	X
CBC with differential, if not done in Step 4a or 4b	X			X			X
Chemistry testing, if not done in Step 4a or 4b <sup>6</sup>	X			X			X
Liver function testing <sup>7</sup>	X			X			X
Fasting lipid profile <sup>8</sup>							X
Syphilis testing	X			X			X
Vaginal GC/CT and TV testing <sup>2</sup>	X			X			X
Urinalysis (protein, glucose)	X			X			X
Plasma storage <sup>9,10</sup>	X	X	X	X	X	X	X
DBS storage <sup>10</sup>	X	X	X	X	X	X	X



# 4d: Pregnancy

Time on Pregnancy and Infant Sub-study	Week 0	Week 1-4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Delivery	Week 2, PP	Week 4, PP	Week 8, PP	Week 16, PP	Week 24, PP	Week 32, PP	Week 40, PP	Week 48, PP	
<b>Maternal assessments</b>																					
Informed Consent	X																				
Locator information	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	X	X	
Acceptability assessment	X			X					X								X			X	
Behavioral assessment	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	X	X	
HIV prevention counseling	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	X	X	
Offer condoms per local SOC	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	X	X	
Medical history, concomitant medications (including folate intake)	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	X	X	
Targeted physical exam including antenatal assessment per SOC	X	X	X	X	X	X	X	X	X	X	X				X					X	
Ultrasound or refer to ultrasound				X																	
Blood collection	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Urine collection <sup>1</sup>	X						X													X	
Vaginal swab collection <sup>1</sup>	X						X								X					X	
Breastmilk Collection, 5mLs <sup>1</sup>													X	X	X	X	X				
Adherence counseling <sup>2</sup>	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	X	X	
Contraceptive counseling															X	X	X	X	X	X	
Dispense/administer study product, as is appropriate	X		X		X		X		X		X				X	X	X	X		X	
ISR Assessment, only for PPTs receiving CAB LA injections		X		X		X		X		X					X					X	
HIV testing <sup>3</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
HIV viral load testing <sup>4</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy testing <sup>5</sup>															X	X	X	X	X	X	
CBC with differential	X						X			X					X					X	
Chemistry testing <sup>6</sup>	X						X			X					X					X	
Liver function testing <sup>7</sup>	X						X			X					X					X	
Syphilis testing	X						X								X					X	
Vaginal GC/CT and TV testing <sup>1</sup>	X						X								X					X	
Urinalysis (protein, glucose)	X						X			X					X					X	
Plasma storage <sup>8,9</sup>	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Breastmilk storage <sup>8,10</sup>													X	X	X	X	X				
DBS storage for women on TDF/FTC only <sup>11</sup>	X	X	X	X	X	X	X	X	X	X	X	X			X	X	X				
<b>Infant assessments</b>																					
Pregnancy outcome assessment including abbreviated infant examination <sup>12</sup>															X					X	
Infant feeding history															X	X	X				
Infant HIV testing, if the mother is confirmed to have HIV infection <sup>13</sup>																					
Cord blood storage <sup>14</sup>												X									
Infant plasma storage <sup>14</sup>										X	X	X	X	X	X	X	X			X	

# Breast Milk

- Breast Milk samples
  - Collect 3 to 5 mL into a 50 mL conical tube
  - Store at 4°C within 10 minutes of collection
  - Send to the lab on wet ice,
  - processed within 6 hrs
  - Log into LDMS and make 3 to 5 @ 1mL aliquots

# LDMS entry

- Whole blood Breast Milk
  - Primary BMK
  - Additive NON
  - Derivative BMK
  - Sub add/der N/A

Ultra low freezer

# Cord Blood

- Cord Blood samples
  - Collect 5 mL into a K2 EDTA
  - Process within 6 hours
  - Single spun!
  - processed within 6 hrs
  - 2 @ 1 mL

# LDMS entry

- Cord Blood
  - Primary CRD
  - Additive DPE (EDT)
  - Derivative PL1
  - Sub add/der N/A

Ultra low freezer

# Infant Plasma

- Infant Plasma samples
  - Collect 500uL to 2 mL into a spray dried EDTA
  - Process within 6 hours
  - Single spun!
  - processed within 6 hrs
  - Minimum 250uL
  - Store what you can

# LDMS entry

- Infant Plasma
  - Primary BLD
  - Additive DPE
  - Derivative PL1
  - Sub add/der N/A

Ultra low freezer

# Infant Testing

- Per local guidelines.



## Step 5- TDF/FTC tail coverage ONLY for those who had to prematurely d/c CAB during the Step 4

Time in Step 5	Step 5, Day 0*	Step 5, Week 12	Step 5, Week 24	Step 5, Week 36	Step 5, Week 48
<b>ADMINISTRATIVE, BEHAVIORAL, REGULATORY</b>					
Locator information	X	X	X	X	X
Acceptability assessment	X				X
Behavioral assessment (if done in last 4 weeks, skip D0 and start at W12)	X		X		X
HIV prevention counseling	X	X	X	X	X
Offer condoms	X	X	X	X	X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>					
Medical history, concomitant medications, targeted physical exam (with pulse, BP, weight and BMI calculated at each visit)	X	X	X	X	X
Blood collection	X	X	X	X	X
Urine collection	X <sup>7</sup>	X	X	X	X
Vaginal swab collection <sup>1</sup>	X <sup>7</sup>		X		X
Adherence counseling <sup>2</sup>	X	X	X	X	
Dispense pills to all participants	X	X	X	X	
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>					
HIV testing <sup>3</sup>	X	X	X	X	X
HIV viral load testing <sup>4</sup>	X	X	X	X	X
Pregnancy testing <sup>5</sup>	X	X	X	X	X
Chemistry testing <sup>6</sup>	X		X		X
Liver function testing <sup>7</sup>	X				X
Syphilis testing	X <sup>7</sup>		X		X
GC/CT and TV testing <sup>1</sup>	X <sup>7</sup>		X		X
Plasma storage <sup>8,9</sup>	X	X	X	X	X
DBS storage <sup>9</sup>	X	X	X	X	X

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