

## **HPTN 084 Open Label Extension FAQ:**

### **1. What is an open-label extension amendment?**

An open-label extension (OLE) amendment is offered after a Phase III trial finds an investigational product safe and effective. Current study participants are then offered the opportunity to enroll and use the investigational product. In addition to offering current participants access to the investigational product, OLEs are typically designed to collect additional information about the investigational product's safety and use.

### **2. Why is the HPTN 084 OLE being done?**

The results from HPTN 084 showed that long-acting injectable cabotegravir (CAB LA) is superior to TDF/FTC for PrEP in women. The OLE amendment is being done to:

- Evaluate the acceptability (uptake, continuation, discontinuation) of open-label CAB LA
- Evaluate the safety of open-label CAB LA with and without the oral lead-in
- Estimate the incidence of pregnancy among participants during the OLE period
- Evaluate safety and infant outcomes among pregnant participants
- Estimate the incidence of HIV among participants who use CAB LA, combining participants from all three steps of the HPTN 084 study

### **3. What will happen to women who decide to join the HPTN 084 OLE?**

Unblinded HPTN 084 study participants will be given the choice to stay on their current study product or switch to the other study product. By offering participants a choice of study products in the OLE, we will learn about preferences for open-label products.

Participants who decide to continue into the HPTN 084 OLE will have visits similar to those in the earlier part of the study. Most study visits will be spaced eight weeks apart (every other month). These next study visits will happen for at least 48 weeks (11 months). Some participants will have visits for as long as 96 weeks (1 year and 10 months). The length of time in HPTN 084 OLE will depend on the study product they choose (either oral TDF/FTC or CAB LA injections) and how soon CAB LA becomes available locally for women who want to stay on it.

### **4. Will pregnant and breastfeeding women be included in the HPTN 084 OLE?**

Yes! There has been an increased number of HPTN 084 participants who want to become pregnant. Contraception is no longer a requirement for participation. Data from the HPTN 084 OLE will help answer the following questions:

- Do pregnant women metabolize CAB LA differently than non-pregnant women?
- Do pregnant women experience side-effects at the same rate as non-pregnant women?
- Is CAB LA transferred to the baby?

### **5. Why was the decision made to include pregnant and breastfeeding women in the HPTN 084 OLE when they were not included in the original study design?**

Pregnant and lactating women have typically been excluded from many clinical trials because of the desire to protect the mother and fetus from potential harms. However, excluding these women from trials has moved the risk of harm from during studies when informed consent and intensive monitoring are practiced to routine care settings in which medications may be used without data for evidence-based management decisions. Excluding pregnant and lactating women from clinical trials to avoid harm has actually had the effect of increasing the risk for larger numbers of women who are exposed to medications with uncertain dosing, safety, and efficacy data.

Early concerns have diminished with accumulating safety data on dolutegravir (DTG) and neural tube defects (NTD). Current evidence suggests the risk is similar to other antiretrovirals (ARVs)

used around the time of conception. We do know that no babies born to women taking CAB LA during HPTN 084 had a spine problem or other birth defect, although the number of deliveries during the trial has been small to date. We also know that in other research studies where pregnant women took CAB LA, no babies had birth defects.

The HPTN 084 study team thinks it is essential to address the use of these products during pregnancy, especially given what we now know about CAB LA safety and effectiveness. Some studies have shown that the late pregnancy and early postpartum periods are times of HIV vulnerability for women because of the biological changes caused by pregnancy hormones which may make them more susceptible to HIV acquisition. If women are sexually active and exposed to HIV, we can presume that they may also be at risk for pregnancy. Women need products that would allow them to safely conceive while being protected from HIV.

Participants who become pregnant on HPTN 084 will now be offered the opportunity to continue CAB LA during pregnancy and breastfeeding under close monitoring.

**6. Since pregnant women will be included in the HPTN 084 OLE, what is happening with the requirement for long-acting reversible contraceptive use?**

In the HPTN 084 OLE, participants get to choose if they want to use contraception. Contraception is no longer a requirement for participation. Participants will be counselled about the risks and benefits of contraception and will be provided with contraceptives if they choose.

**7. What will happen to a woman who falls pregnant during the HPTN 084 OLE?**

If a woman taking CAB LA falls pregnant, she will be permitted to choose whether she wants to stay on CAB LA or switch to TDF/FTC. TDF/FTC is the standard for HIV prevention and is not known to cause any health problems for babies. We will continue to follow pregnant women in the study, and they will have the option of joining a mother-infant sub-study where we will follow both the mother and baby for about a year after birth. We think it is important for women to be able to protect themselves from HIV during pregnancy and breastfeeding. We would like to give women a choice about which product they want to use during this time.