What We Will Learm About PrEP from IMPAACT 2009?

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IMPAACT 2009 Pharmacokinetics, Feasibility, Acceptability, and Safety of Oral Pre-Exposure Prophylaxis for Primary HIV Prevention during Pregnancy and Breast Feeding in Adolescents and Young Women

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Lab Center Rep: Carolyn Yanavich

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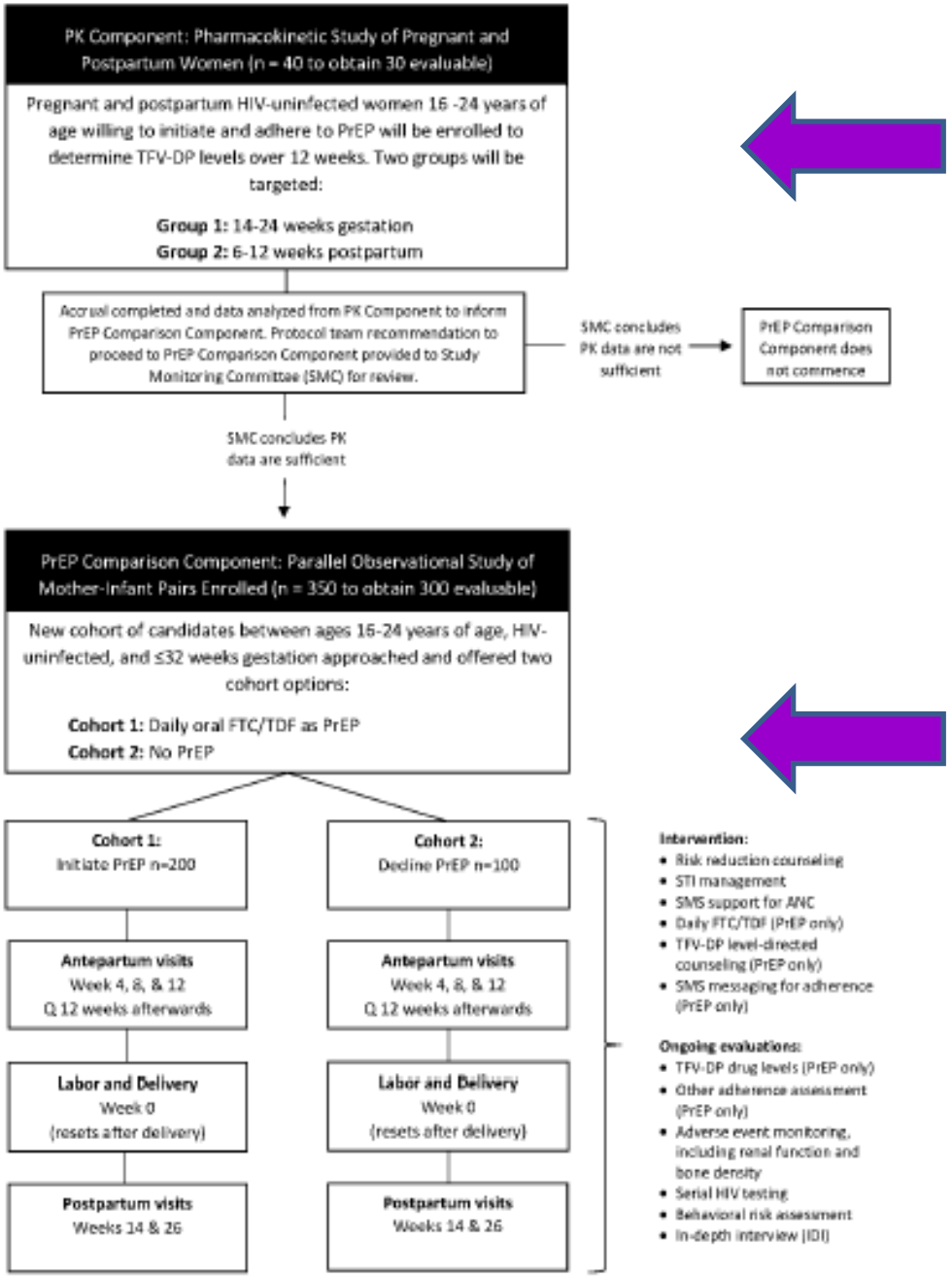
Truvada in Pregnancy: Background

- PrEP could be effective during pregnancy, but data gaps persist:
  - Much of the available safety data on Truvada in pregnancy based on HIV and HBV treatment, a situation where multiple drugs are administered.
  - Possible effects on renal function and bone mineral density, especially given physiologic changes during pregnancy have not been systematically evaluated.
  - Concerns about pregnancy outcomes (e.g., preterm birth)

- Risk: benefit ratio of Truvada may be different in the context of prevention



Component 1: PK study

Component 2: PrEP Users vs Nonusers

Schema – PK Component

Purpose: To establish, among young HIV-uninfected women, the plasma drug concentrations associated with daily oral PrEP during pregnancy and postpartum

Design: PK study with oral PrEP drug concentrations determined under direct observation

Population: HIV-uninfected pregnant women 16-24 years of age and their infants

Group 1: enrolled at 14-24 weeks gestation

Group 2: enrolled at 6-12 weeks following delivery

Sample Size: ~40 women (20 per group) to achieve at least 30 evaluable women (15 per group) and their infants.

Intervention: Fixed dose combination of FTC 200 mg + TDF 300 mg administered once daily for 12 weeks.

IMPAACT 2009 PK Component

- Primary Objective: To determine the concentration of tenofovir diphosphate (TFV-DP) associated with adequate adherence to FTC/TDF among women observed ingesting daily oral PrEP during pregnancy and postpartum
- Secondary Objective: To compare TFV-DP concentrations observed in pregnant and postpartum women

- A total of 40 women will be enrolled in this component
  - If the pharmacokinetic studies suggest that drug levels in pregnant are inadequate to provide robust protection, the phase 2 component of the study will not move forward

Schema – PrEP Comparison Component

Purpose: To determine among young HIV-uninfected women and their infants, the feasibility, acceptability, and safety of oral PrEP during pregnancy and postpartum.

Design: Parallel observational cohort study

Population: Pregnant HIV-uninfected women,16-24 years of age, with a confirmed singleton pregnancy of ≤32 weeks gestation, and their infants.

Cohort 1: Initiates PrEP at study entry

Cohort 2: Declines PrEP at study entry

Sample Size: ~350 women to achieve at least 300 evaluable (200 in Cohort 1 and 100 in Cohort 2) and their infants.

Schema – PrEP Comparison Component

Both cohorts:

Behavioural HIV risk reduction package, including cohort-appropriate SMS messages throughout follow-up.

Cohort 1 only:

- Daily oral PrEP (200 mg FTC)/ 300 mg TDF throughout follow-up.
- Enhanced adherence support, including SMS messaging and feedback of drug levels with tailored counseling.

IMPAACT 2009 PrEP Comparison Component

Primary Objectives:

- To characterize PrEP adherence among HIV-uninfected young women during pregnancy and for six months postpartum, when provided with enhanced adherence support through mobile technology and counseling based on observed drug levels.

- To assess the safety of FTC/TDF PrEP during pregnancy and postpartum by comparing pregnancy outcomes and maternal and infant safety between cohorts.

IMPAACT 2009 PrEP Comparison Component

Secondary Objectives:

- To identify individual, social, and structural barriers and facilitators to PrEP uptake during pregnancy, and to adherence during pregnancy and postpartum.
- To compare reported sexual risk behaviors and incidence of sexually transmitted infections, including HIV infection, among women who initiate PrEP during pregnancy versus women who decline PrEP over the observation period.
- To compare antiretroviral drug resistance among mothers and infants who acquire HIV with and without exposure to FTC/TDF for PrEP, including whether resistance was transmitted or acquired at time of transmission
- To compare bone density in women who initiated PrEP during pregnancy and women who decline PrEP.

IMPAACT 2009 PrEP Comparison Component

- Exploratory objective: To describe the composition of and changes in the maternal vaginal and infant gut microbiomes according to PrEP exposure

Participating Sites

- **Uganda**
  - Baylor CRS
  - Makerere Uni-JHU CRS
- **Malawi:** Blantyre CRS
- **Zimbabwe**
  - Harare Family Care CRS
  - St. Mary's CRS
  - Seke North CRS
- **South Africa:** Shandukani CRS

IMPAACT 2009
n= 300 (200 on TDF/FTC)

MTN 042
n=750 (n=250 on TDF/FTC, 500 on ring

Both studies evaluate safety, adherence, PK , feasibility, acceptability
Both contribute to the body of evidence required around oral PrEP in pregnancy/postpartum

- PK and adherence component (40 women) more intense-observed dosing
- Pregnancy and postpartum cohort
- Young women 16-24 years
- Women self-select using PrEP or not (control group)
- Enrollment 14-24 weeks & 6-12 weeks post partum
- Bone scans of women & infants
- Study completion 26 weeks postpartum
- Evaluation of impact on microbiome

- PK and adherence evaluated-self report, plasma and ring levels
- All women 18-45 years
- Gestational age de-escalating to 12 weeks
- Randomisation 2:1 to dapivirine ring and oral PrEP (truvada)
- Control group=PrEP:
- Expanded birth outcomes of interest given local vaginal product
- DPV levels in pregnant women and infants
- Study completion 6 weeks postpartum

Thank you!

MTN
microbicide trials network