Project Brief: IMPAACT 2009

Full Title of Study/Programme	Pharmacokinetics, Feasibility, Acceptability, and Safety of Oral Pre-Exposure Prophylaxis for Primary HIV Prevention during Pregnancy and Postpartum in Adolescents and Young Women and their Infants
Technical Focus Area	Research (Paediatrics and Maternal)
Rationale	Feasibility, Acceptability and Safety of pre-exposure prophylaxis during Pregnancy and Breast Feeding to establish drug thresholds for optimal adherence when FTC/TDF is administered daily under direct observation during pregnancy and in the postpartum period.
Primary Objectives	• To characterize PrEP adherence among HIV-uninfected adolescent and young adult women (aged 16-24 years) who initiate once-daily emtricitabine-tenofovir disoproxil fumarate (FTC/TDF) in pregnancy and are followed through 6 months postpartum, when offered adherence support through mobile technology and drug level-directed counseling. • To compare maternal and infant adverse events (including pregnancy outcomes) between women who initiate PrEP and women who decline PrEP over the observation period.
Secondary Objectives	• To identify individual, social, and structural barriers and facilitators to PrEP uptake during pregnancy, and to adherence and continued use during pregnancy and postpartum. • To compare reported sexual risk behavior and incidence of sexually transmitted infections among women who initiate PrEP during pregnancy and those who decline PrEP over the observation period. • To compare HIV incidence in women who initiate PrEP during pregnancy and those 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
Primary Endpoint/Outcome	N/A
Secondary Endpoint/Outcome	N/A
Study Design	IMPAACT 2009 comprises two distinct components: The PK Component is a pharmacokinetic study to establish drug thresholds for optimal adherence when FTC/TDF is administered daily during pregnancy and in the postpartum period. The PrEP Comparison Component is a cohort study that will assess the feasibility, acceptability, and safety of PrEP when provided to adolescents and young women during pregnancy and postpartum.
Study Population	This study will be conducted among approximately 390 women and their infants (40 in the PK Component, and 350 in the PrEP Comparison Component) who will be selected for the study according to the criteria in Sections 4.1-4.3. The study-specific

	approach to recruitment, screening, and enrollment is described in Section 4.4. Considerations related to participant retention and withdrawal from the study are provided in Sections 4.5 and 4.6, respectively. A slightly different population for the two components will be recruited from. In the PrEP Comparison Component, adolescent girls and young women aged 16-24 years are of interest, because this is window of elevated HIV risk for pregnant women. In the PK Component, the lower age limit will be 16 years of age. However, the team has elected not to include an upper age limit. Instead, HIV-uninfected pregnant women 16 years or older can be considered for enrollment, so long as they meet site-specified criteria that account for the social and cultural aspects of daily PrEP adherence. Each site will be asked to develop locally relevant criteria, though this may include factors such as the disclosure of HIV status to family members or the identification of a support partner for daily adherence. Maternal participants will not be stratified in the PK group by age because: a) the overall sample size remains relatively small, limiting its utility for sub-analysis, b) the team looks to enroll rapidly into this initial PK component, and c) the physiological differences between the age groups (i.e., 16-24 years vs. 25 years and older) are unlikely to influence PK parameters over the observation period.
Study Sample Size	FTC/TDF will be provided to relevant maternal participants as one fixed dose oral combination tablet (FTC 200 mg/TDF 300 mg) taken by mouth once daily, with or without food.
Follow-up/Duration	ponent All PK Component participants will initiate FTC/TDF at entry. Maternal participants will be directed to take one FTC/TDF tablet by mouth once daily with or without food for 12 weeks. Dosing will be directly observed and participants will be encouraged by the study team to continue dosing throughout follow-up. mparison Component Participants who initiate PrEP during pregnancy and participants who decline PrEP will be followed through the first 26 weeks postpartum. Drug Formulation FTC/TDF is a fixed dose combination tablet containing 200 mg of emtricitabine (FTC) and 300 mg of tenofovir disoproxil fumarate (TDF) in each tablet. FTC/TDF, Truvada®: study tablets must be stored at 25°C (77°F); excursions permitted to 15-30°C (59°86°F) (see USP Controlled Room Temperature). FTC/TDF tablets must be stored in the original container. Each container is packaged with a child-resistant screw cap and contains a silica gel to protect the product from humidity.

	FTC/TDF 200 mg/300 mg is available as Truvada®, a medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of HIV-1 infection and for PrEP to reduce the risk of sexually acquired HIV in adults at substantial risk. Further information on Truvada is available in the current package insert available at http://rsc.tech-res.com/safetyandpharmacovigilance
Study/Programme Sites	• Wits RHI Shandukani Research Centre (SRC) • Other sites not specified
Study/Programme Duration	January 2017 -2018
Investigators	Dr Lee Fairlie, Principal Investigator Dr Masebole Masenya, Sub Investigator
Other Partners & Collaborators	
Sponsors/Donors	IMPAACT
Publications/Key Presentations to Date	None as yet
Progress Update as at 11/2016	N/A
Frequency of Donor Narrative Report	Monthly
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