Ongoing and Planned IMPAACT Studies in Pregnant Women

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IMPAACT Network Mission

- To decrease incident HIV and HIV-associated infections including mother-to-child transmission among infants, children, youth and pregnant/postpartum women
- To decrease HIV-associated mortality and morbidity among these populations

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

IMPAACT Network

- Scientific Committees
  - Treatment
  - Prevention
  - Cure
  - Tuberculosis
  - Complications & Comorbidities
- Investigators, clinicians and site staff, community representatives
- 52 sites in 16 cities in the US and 13 countries

Track Record of Success
Enrolling Pregnant Women into Studies

- PROMISE Studies:
  - Designed to address in an integrated and comprehensive fashion three critical questions:

    -What is the optimal intervention for the prevention of transmission of HIV?

    -What is the optimal intervention for the prevention of transmission in breastfeeding infants?

    -What is the optimal intervention for the preservation of maternal health
  - 3747 pregnant HIV+ women and their infants enrolled
- H1N1 Study:
  - Multi-center, Phase II, open label study of an inactivated Influenza A (H1N1) 2009 monovalent vaccine. Designed to determine safety and antibody response after each of two doses of Influenza A (H1N1) 2009 Monovalent Vaccine in HIV-1 infected pregnant women
  - Enrollment completed in 6 weeks; N=130 HIV+ pregnant women

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Group

Prevention

- **IMPAACT 2009**: Pharmacokinetics, Feasibility, Acceptability, and Safety of Oral **Pre-Exposure Prophylaxis (PrEP)** for Primary HIV Prevention during Pregnancy and Postpartum in Adolescents and Young Women and their Infants (Protocol chairs: Ben Chi, Lynda Stranix-Chibana and Sybil Hosek)
- Purpose
  - PK component: To establish, among young HIV-uninfected women, plasma drug concentrations associated with daily directly observed oral PrEP during pregnancy and postpartum.
  - PrEP Comparison Component: To determine feasibility, acceptability, and safety of oral PrEP during pregnancy and postpartum among young HIV-uninfected women and their infants

IMPAACT 2009

- Study population:
  - Pregnant HIV-uninfected women, 16-24 years of age, with confirmed singleton pregnancy of ≤ 32 weeks gestation, and their infants
    - Cohort 1: Mother **accepts PrEP** initiation during pregnancy at study entry
    - Cohort 2: Mother **declines PrEP** initiation during pregnancy at study entry
- N=350 mother-infant pairs
- Intervention: Daily oral PrEP 200 mg FTC/300 mg TDF
- Status: Planned; *initiation anticipated mid-2018*

Treatment

- **P1026s**: PK properties of ARV therapies during pregnancy/postpartum (Study Chairs: Mark Mirochnick, Alice Stek)
  - *Enrolling*: As of February 2018: 977 mothers enrolled
  - Completed pregnancy arms for 17 ARVs, including darunavir, rilpivirine, maraviroc, dolutegravir and elvitegravir
  - Presented 32 abstracts and published 20 manuscripts
  - P1026s PK data cited for 63% (17) of the 27 ARV drugs in the current published HHS perinatal guidelines
  - P1026s responsible for 32% (24) of the 76 PK in pregnancy studies cited in perinatal guidelines
- 25 women per study arm

IMPAACT P1026s V10 Current enrollment status

Arm	Number Enrolled	Target Accrual	% Completed
Antepartum/HIV-infected Arms			
DRV/r (800/100)	24	25	96%
DRV/r (900/100)	2	25	8%
TAF 25 mg w/o COBI or ritonavir	13	25	52%
TAF 25 mg with COBI or ritonavir	1	25	4%
TAF 10 mg with COBI	30	25	100%
DRV/COBI	11	25	44%
ATZ/COBI	2	25	8%
TB Arms			
First line TB drugs with EFV	15	25	60%
First line TB drugs with LPV/r	1	25	4%
TB Only	8	25	32%
Second Line TB drugs (HIV-infected and uninfected)	1	25	4%
Postpartum Contraception Arms			
EFV + oral contraceptive	27	25	100%
DRV/COBI or ATZ/COBI + oral contraceptives	0	25	0%
DRV/COBI or ATZ/COBI + etonogestrel	0	25	0%

Upcoming Changes for P1026s

New Arms to Evaluate:

- Bictegravir/FTC/TDF
- Doravirine
- Intracellular TAF with and without boosting
- ARV and TB therapies in the pipeline for treatment of adults to be studied
  - LA Cabotegravir
  - LA Rilpiverine
  - Bedaquiline
  - Delaminid

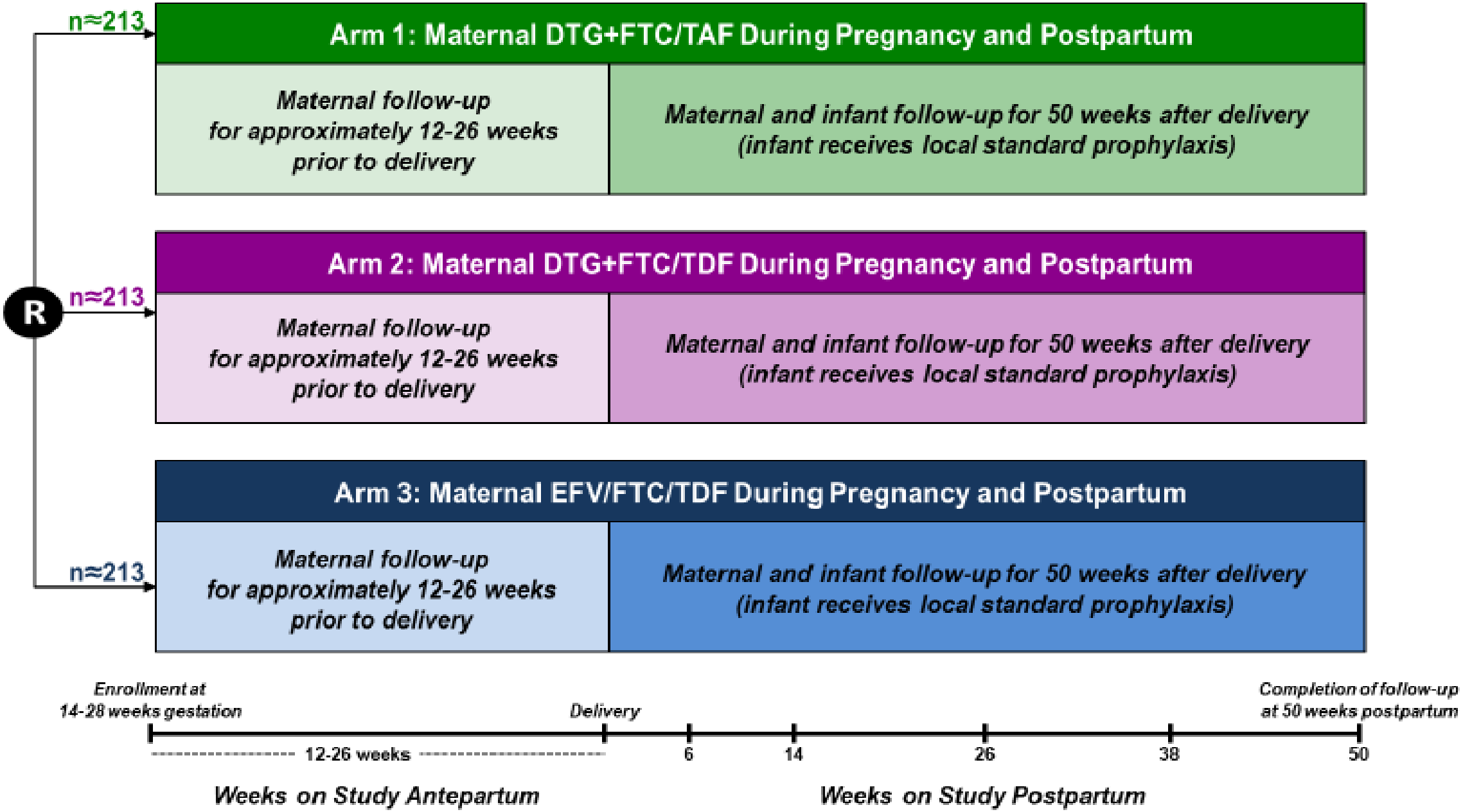
IMPAACT 2010 aka "VESTED Study"

Virologic Efficacy and Safety of ART Combinations

(Study Chairs: Shahin Lockman and Lameck Chinula)

- Purpose: To compare the virologic efficacy and safety of three ARV regimens – combinations of TAF/TDF, EFV, and DTG – for HIV-1-infected pregnant women and to compare the safety of these regimens for their infants
- Sample size: 639 mother-infant pairs (approximately 213 per arm)
- Status: ***Enrolling***; anticipated study completion mid-2020

VESTED Study Design



Tuberculosis

- **IMPAACT P1078**: Phase IV Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Safety of Immediate (Antepartum-Initiated) Versus Deferred (Postpartum-Initiated) Isoniazid Preventive Therapy Among HIV-Infected Women in High TB Incidence Settings
  - *Closed*
- **IMPAACT 2001**: Phase I/II Trial of the Pharmacokinetics, Tolerability, and Safety of Once-Weekly Rifapentine and Isoniazid in HIV-infected and HIV-1-uninfected Pregnant and Postpartum Women with Latent Tuberculosis Infection
  - *Enrolling*

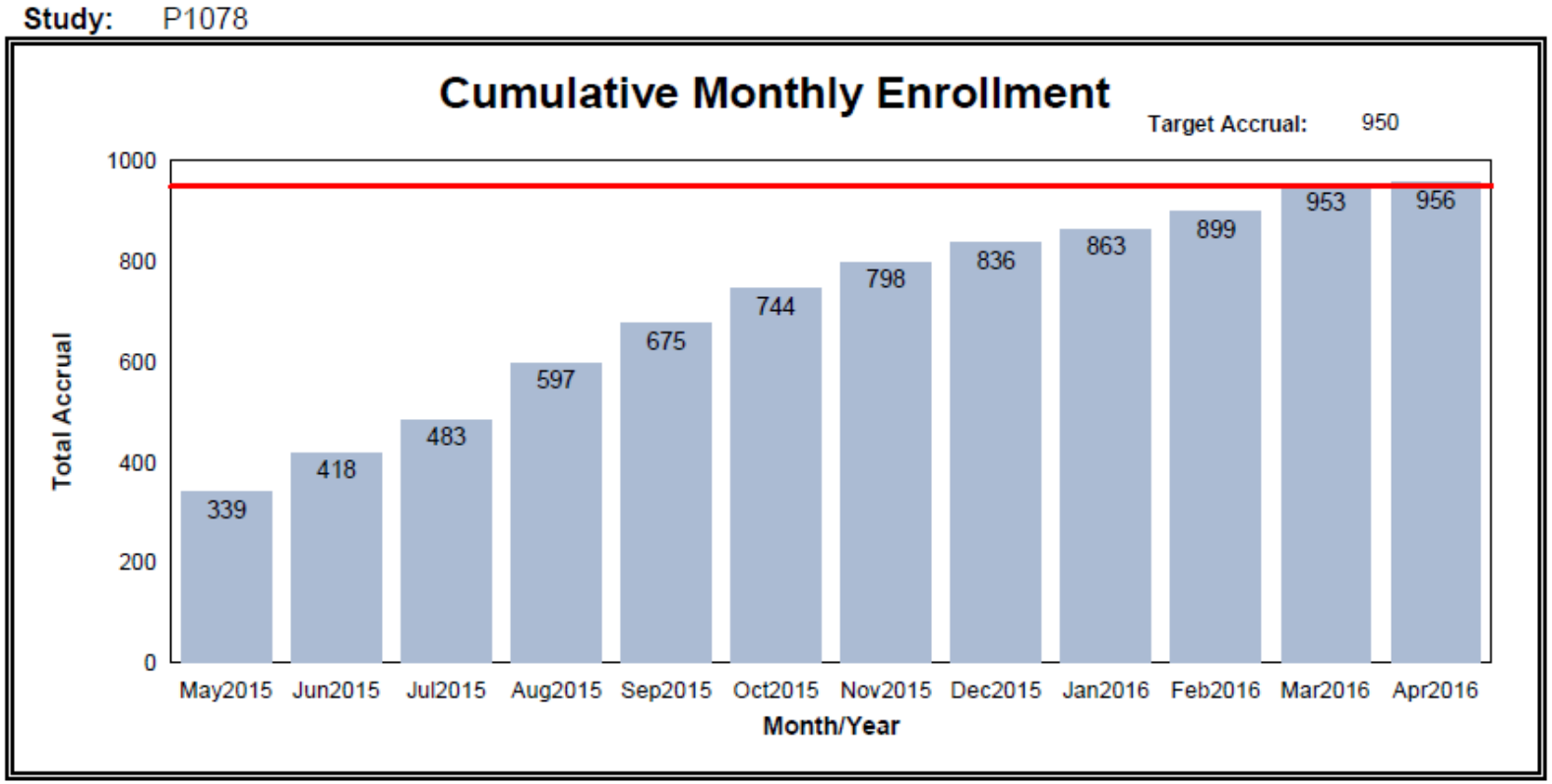
IMPAACT P1078 aka "TB APPRISE Study"

(Study Chair: Amita Gupta)

- Purpose: Phase IV, randomized, double-blind, placebo-controlled non-inferiority study to determine overall safety as well as the other risks and benefits of **immediate versus deferred INH in HIV-infected pregnant women and their infants**, enrolled at ≥ 14 through ≤ 34 weeks (34 weeks, 6 days) gestation, **at high risk for TB** (i.e., reside in high TB prevalence area, defined as having 60 TB cases per 100,000 population in the WHO TB annual report or documented local burden)
- Sample size: 950 women and their infants (475 women per study arm)
- Study treatment: At study entry, randomized in a 1:1 ratio to Arm A (immediate INH treatment) OR Arm B (deferred INH treatment)

TB APPRISE Study Completed

- **Enrollment completed ahead of schedule**
- Closed to follow-up in Sept 2017
- Results presented in late breaker at CROI 2018
- www.impaactnetwork.org



IMPAACT 2001

(Study Chair: Jyoti Mathad)

- Purpose: To describe the pharmacokinetics and safety of once-weekly doses of **rifapentine (RPT) and isoniazid (INH) in pregnant and postpartum women with latent TB** and inform the practice on usage of this regimen in the second and third trimesters of pregnancy
- Sample size: up to 82 pregnant women and their infants
- Study treatment: 12 directly observed once-weekly doses of RPT (900mg) and INH (900mg) taken with pyridoxine (25 to 100mg)
- Status: ***Enrolling***; study completion anticipated mid-2019

In Summary

- Focused maternal child network with critical mass of investigators
- Ability to react quickly to pathogens of high importance
- Close collaboration with sites and community

Ask the questions

Design the studies

Enroll rapidly

Get the answers…

Future plans…

To continue to excel in clinical research of topics that affect our populations

Thank you to our funders,

our families and our sites