VOICE Study Update

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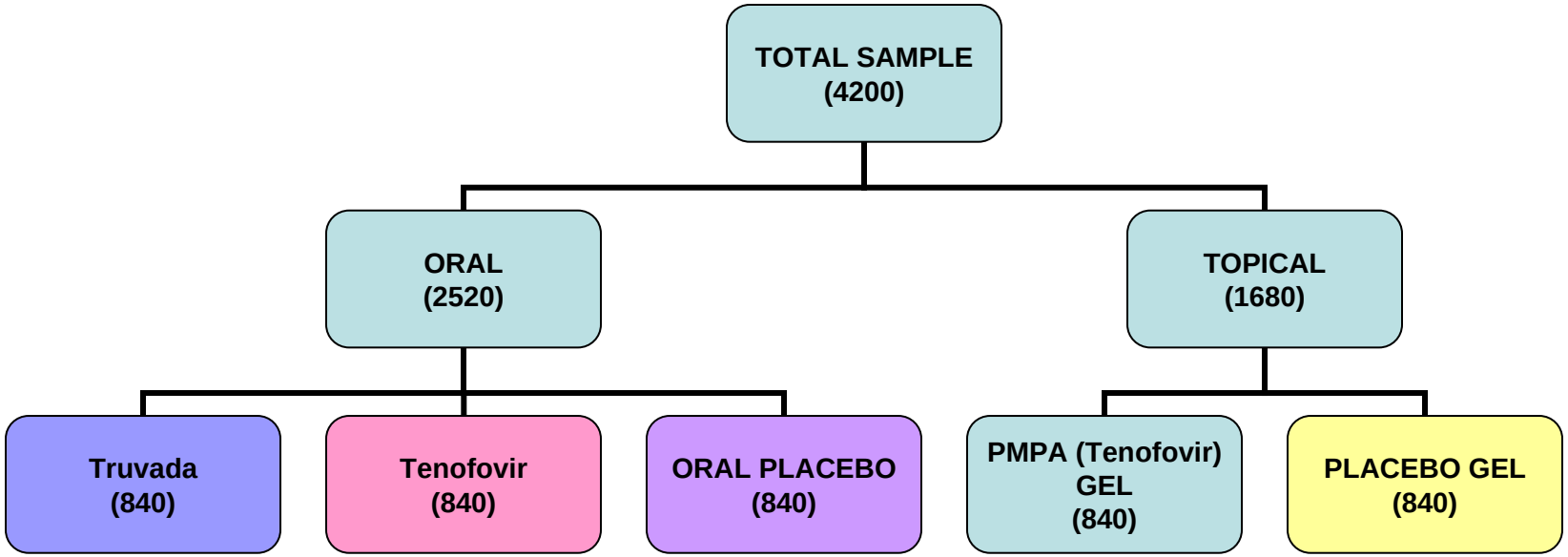
MTN
microbicide trials network

Overview

- Rationale, design & objectives
  - Why is VOICE unique in PrEP landscape?
- Sites
- Milestones achieved to date

The VOICE Study: Design

- Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, TDF (Tenofovir) Tablet and FTC/TDF (Truvada) Tablet for Prevention of HIV Infection in Women
- Five-arm, multi-site, randomized trial
- Expected duration of accrual 21 months
- Women will use product for average of 22 months



Current PrEP Trials

Candidate	Sponsor	Formulation / Design	Population	Sites
Tenofovir	CDC	Once daily oral dose Phase III	2,000 injecting drug users	Thailand
Truvada ***Switched from tenofovir***	CDC	Once daily oral dose Phase III	1,200 heterosexual men & women	Botswana
Tenofovir	CDC	Clinical safety and behavior in once daily oral dose Phase II	400 men who have sex with men	United States
Truvada	NIH	Once daily oral dose Phase III (iPrex)	3,000 men who have sex with men	Peru / Ecuador/ Thailand/ S. Africa

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Tenofovir / Truvada	Gates	Once daily oral dose Phase III	3,900 HIV discordant couples (Partners in Prevention)	Kenya, Uganda
Truvada	USAID	Once daily oral dose Phase II	3,800 high risk women (FemPrEP)	Kenya, S. Africa
Tenofovir topical gel	NIH	Coitally dependent vaginal application Phase III	980 high risk women (CAPRISA)	Durban, S. Africa

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Why is VOICE unique?

Tenofovir Tablets

Tenofovir Gel

Truvada Tablets

Which is effective?

Which will women use?

Is each safe?

Study Objectives

Primary:

- Estimate the effectiveness of daily tenofovir 1% gel compared to a vaginal placebo gel, and the effectiveness of oral TDF and oral FTC/TDF compared to an oral placebo in preventing HIV infection among women at risk for sexually transmitted infection (STI)
- Evaluate the extended safety of daily tenofovir 1% gel, oral TDF, and oral FTC/TDF in women at risk for sexually transmitted HIV infection

Study Objectives

Secondary:

- Adherence/Behavioral:
  - Evaluate adherence to daily regimens of vaginal gel vs. oral tablets used to prevent HIV infection
  - Evaluate whether key behaviors (sexual activity, condom use, intravaginal practices) change over time in women who use either daily vaginal gel or daily oral tablets
- HIV-1 Drug Resistance:
  - Assess the frequency of HIV-1 drug resistance in women who acquire HIV-1 while using study product by standard genotype analysis and more sensitive methods to detect low frequency drug-resistant variants

Study Objectives

Secondary:

- Pharmacokinetic:
  - Evaluate the pharmacodynamic (PD) relationship between plasma drug concentrations and study outcomes (HIV seroconversion, toxicity, viral resistance) using PD-PK models
- Delayed seroconversion:
  - Assess incidence of HIV seroconversion in each study product group during the approximate 8 weeks of follow-up off study product between the Product Use End Visit and the Termination Visit

Advantages of 5-Arm Design

- Straightforward and simultaneous comparison for each active product relative to its corresponding control
  - All participants don't need to receive both interventions
- Allows assessment of placebo gel effect
  - vs. oral placebo
- **Permits simultaneous assessments of different prevention strategies (active vs. placebo; oral vs. topical) compared with appropriate controls**

Accrual Plan

- No. of participants: 4200
- Expected baseline HIV incidence: 4.76%
- Accrual period: 21 months
- Expected average follow-up: 22.5 months
- Total follow-up: 7088 person-years
- Endpoints: 228

VOICE Sites

Malawi

College of Medicine JHU CRS (Queen Elizabeth Central Hospital), Blantyre
UNC Lilongwe CRS (Kamuzu Central Hospital), Lilongwe

Uganda

Makerere University - JHU Research Collaboration CRS , Kampala

South Africa

South African Medical Research Council (MRC), Durban, Kwa-Zulu Natal
Botha's Hill CRS; R.K. Kahn CRS; Umkomaas CRS; Overport CRS

RHRU, University of the Witwatersrand (Soweto)

Zambia

Kamwala Health Centre CRS, Lusaka

Zimbabwe

University of Zimbabwe-UCSF Prevention Trials Unit
Spilhaus CRS, Harare ; Seke South CRS & Zengeza CRS, Chitungwiza;

Site Milestones

- Based on MTN Executive Committee review
- With input from DAIDS, Protocol Chairs, MTN CORE
- Additional site-specific study activation requirements may be specified by DAIDS

Site Milestones

- Purpose:
  - Proactive planning for high quality study implementation
  - Proactive planning for timely study initiation at all sites
- Process:
  - Initial milestone letters sent to sites in April
  - Follow-up letters early July

Site Milestones

- Submission of protocol and informed consent forms to drug regulatory authorities (DRAs) and IRBs/ECs within one month after protocol finalization
- Develop community involvement plan
  - First draft due May 26th
  - Complete by end of August
- Review, translation, and pre-testing, behavioral data collection instruments

Site Milestones

- Additional site specific milestones
  - Pre-study visits for new sites
  - Assurance of realistic screen to enroll ratio
  - Assurance of adequate staffing
  - Assurance of adequate planning to conduct VOICE and other similar studies

VOICE Study Timeline

SWG*	Develop protocol	NIAID PSRC**	DAIDS*** approval	IRB/EC approval	Start accrual	Complete accrual	Complete follow-up
June 2007	Q3 2007	Q4 2007	Q2 2008	Q3 2008	Q1 2009	Q3 2010	Q3 2011
Present study concept to SWG	Select protocol co-chairs and write protocol	Submit protocol to Prevention Science Review Committee	Revise protocol as needed for Medical Officer and Regulatory approval	Obtain IRB/EC approval at study sites	Recruit, screen and enroll study participants	Follow-up period	

*Strategic Working Group, Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID)
** Prevention Sciences Review Committee, NIAID
***Division of AIDS, NIAID

VOICE Timeline

- Need to incorporate ancillary study protocols and DRA and IRB/EC review of these
- IRB/EC review of other materials
  - Recruitment materials
  - Informed consent support materials
  - Case report forms
- Anticipate enrollment to begin Q1 2009

Thank you

For all the incredibly hard work done by the sites to get us to this point!