

Where Do We Go from Here?

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MTN Annual Meeting
Bethesda, MD
February 12th, 2013



Overview

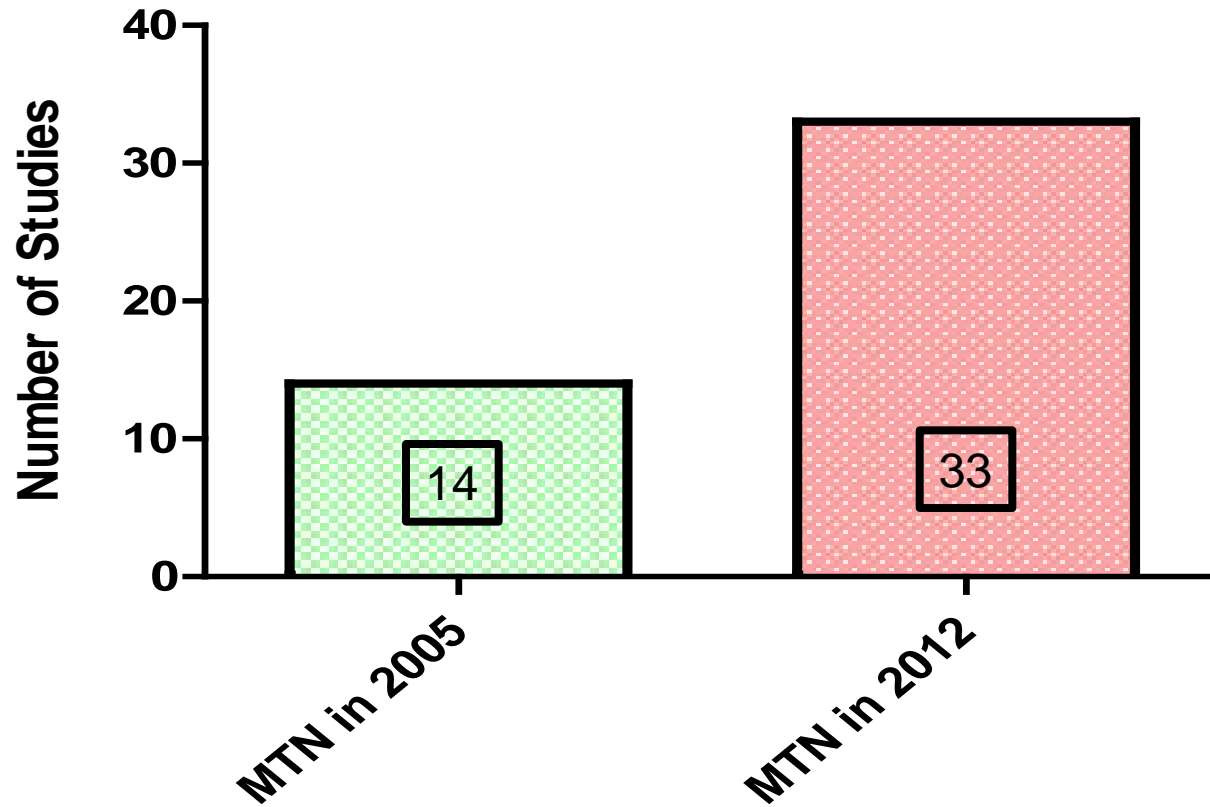
- Where are we in 2013
 - What has the MTN accomplished?
 - What else has happened in PrEP?
- The MTN recompetition submission:
 - New products
 - New strategies
 - New populations
- Important timelines



The MTN Research Portfolio

- Clinical evaluation of candidate microbicides
 - Vaginal microbicides
 - Rectal microbicides
 - PrEP
 - Vaccines
- Special populations
 - Pregnancy
 - Adolescence
 - MSM & Transgender women
- Integrated behavioral and biomedical research agenda

The MTN Scorecard in 2013





HIV Prevention in 2013

- The successes
 - CAPRISA 004 (Tenofovir gel)
 - Partners PrEP (Oral tenofovir & Truvada)
 - CDC TDF-2 study (Truvada)
 - iPrEx study in MSM (Truvada)
 - FDA licenses Truvada for PrEP
- Studies without evidence of efficacy
 - FEM-PrEP (Truvada)
 - VOICE (Oral tenofovir and tenofovir gel)



Divergent PrEP Results: Why?

- Different PrEP regimens
- Different populations
- Differential adherence
- Pharmacokinetics
- Virology
- Hormonal contraception
- Product induced mucosal “injury”

Adherence in PreP Studies

	Age	Married or stable partner	Efficacy	Adherence as per drug levels
CAP 004	24	88%	39% [CI = 6-60]	40%*
iPrEx	27		42% [CI = 18-60]	51%
Partners PrEP	36	98%	67% [CI = 44-81] TDF 75% [CI = 55-87] FTC/TDF	81%
TDF-2	25	6%	62% [CI = 22-83]	79%
FEM-PrEP	24	31%	6% [CI = -52-41]	26%
VOICE-SA	25	8%	<i>March 2013</i>	
VOICE-Ug	28	50%	<i>March 2013</i>	
VOICE-Zim	28	94%	<i>March 2013</i>	
FACTS	<i>2015</i>			



Ongoing PrEP Studies in 2013

- Effectiveness studies
 - The ASPIRE study (MTN-020; DPV IVR)
 - The RING study (IPM-027; DPV IVR)
 - FACTS-001 (BAT TFV gel)
- Roll-over studies
 - iPrEx OLE (Truvada)
 - CAPRISA-008 (TFV gel)
 - CDC TDF-2 study (Truvada)



MTN Studies Planned for 2013

- MTN-014
 - Rectal & vaginal tenofovir PK
- MTN-017
 - Phase 2 tenofovir rectal safety study
- MTN-022
 - HIV vaccine + oral / vaginal PrEP
- MTN-023
 - Dapivirine ring safety in adolescents
- MTN-024
 - Dapivirine ring safety in post menopausal women

Creating Desire in MTN Trials



The advertisement features a superhero character in a blue suit with a white 'G' on his chest, pointing forward. A circular logo with a 'G' and bubbles is in the top right. The text 'SOY GELLUX' is written in a stylized font. Below it, the text reads: 'Y traigo una nueva opción que nos podría ayudar a prevenir el VIH... Los Microbicidas Rectales'. At the bottom, it says 'herqes' with a male symbol over the 'q' and a female symbol over the 'e', followed by 'Ser Voluntario' and the 'Impacta' logo. Contact information and a Facebook link are at the bottom left.

Para disfrutar primero te lo debes aplicar

SOY GELLUX

Y traigo una nueva opción que nos podría ayudar a prevenir el VIH...
Los Microbicidas Rectales

herqes

Ser Voluntario

Impacta

INFÓRMATE MÁS LLAMANDO AL 0-800-1-7432

f Gellux.Impacta

To enjoy (the gel) first you need to use it

Looking Towards the Future



The MTN Recompetition

- Safe and effective vaginal microbicides
- Safe and effective rectal microbicides
- Combination hormonal contraceptive and antiretroviral vaginal ring
- Special populations
 - Pregnancy
 - Adolescence
 - Post menopausal women
 - MSM and transgender women



Behavioral Research Agenda

- Maximizing adherence to study products
- Understanding differential adherence
- Determining product preferences
- Investigating changes in risk behavior during trials
- Identifying the most reliable and informative measures of acceptability and adherence
- Understanding motivations and characteristics of trial participants
- Examining participant comprehension of partial efficacy

Biomedical Research Agenda

- To test and evaluate novel biomarkers within MTN protocols:
 - Efficacy
 - Safety
 - Adherence
 - HIV risk
- Determine impact of microbicides on:
 - Host microbiome
 - Host mucosal immune response
- Impact of mucosa on antiretrovirals:
 - Transporters, metabolism, and dNTP pools



New Products & Formulations

□ Candidates

- Griffithsin
- 5P12-RANTES
- MIV-150
- IQP-0528

□ Formulations

- Intravaginal rings
 - Combination antiretroviral and contraceptive
- Vaginal films
- Suppositories
- Rectal-specific formulations

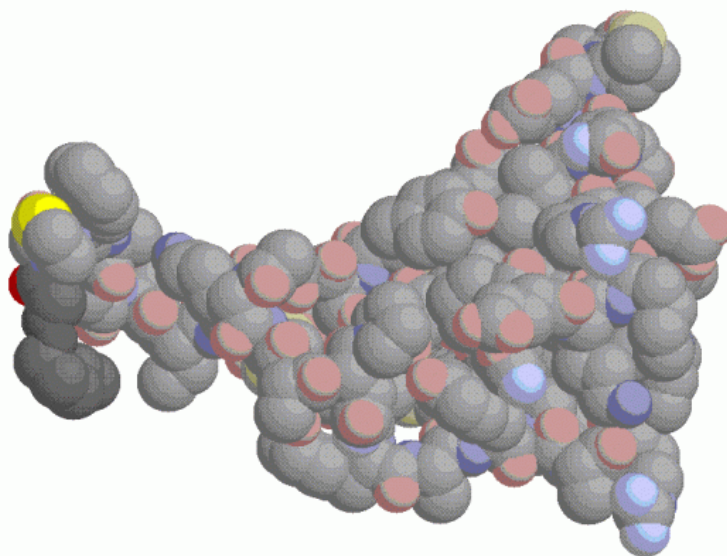
Griffithsin

- Product class
 - Protein isolated from the red algae
- Sponsor
 - NCI/Kenneth Palmer
- Formulation
 - Gel
- Development stage
 - Preclinical toxicology (rectal and vaginal)
- Unique features
 - Could be used in HIV-positive women

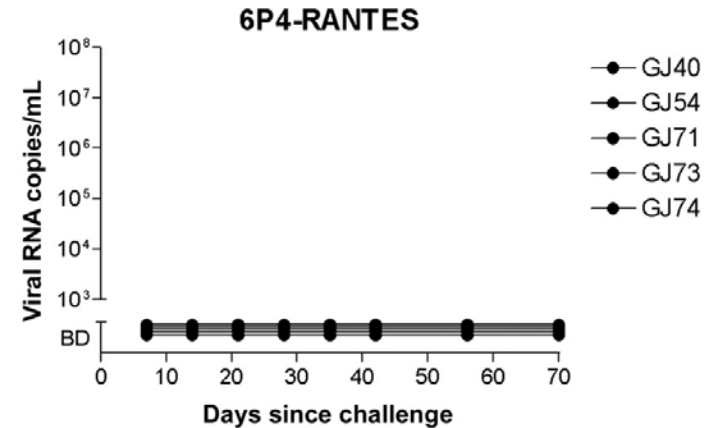
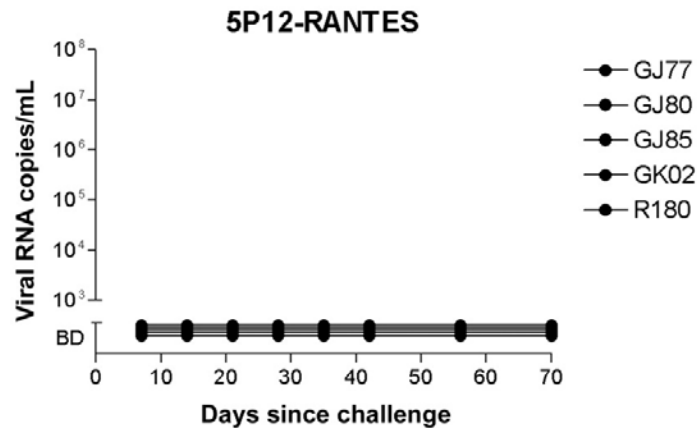
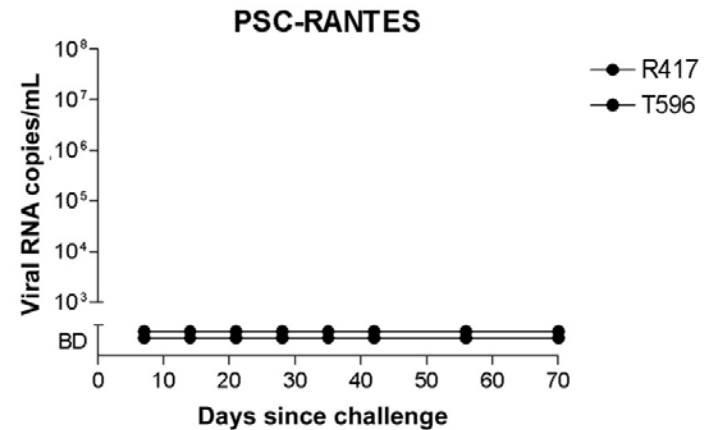
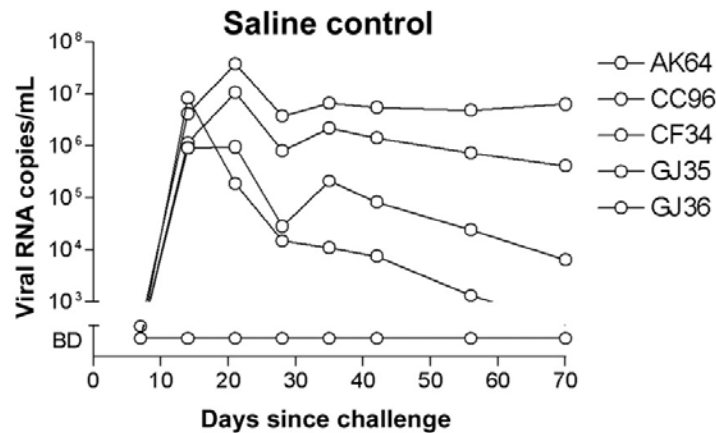


5P12-RANTES

- Product class
 - CCR5 antagonist
- Sponsor
 - Mintaka Foundation, Geneva
- Formulation
 - PBS
- Development stage
 - Protection in macaque challenge model

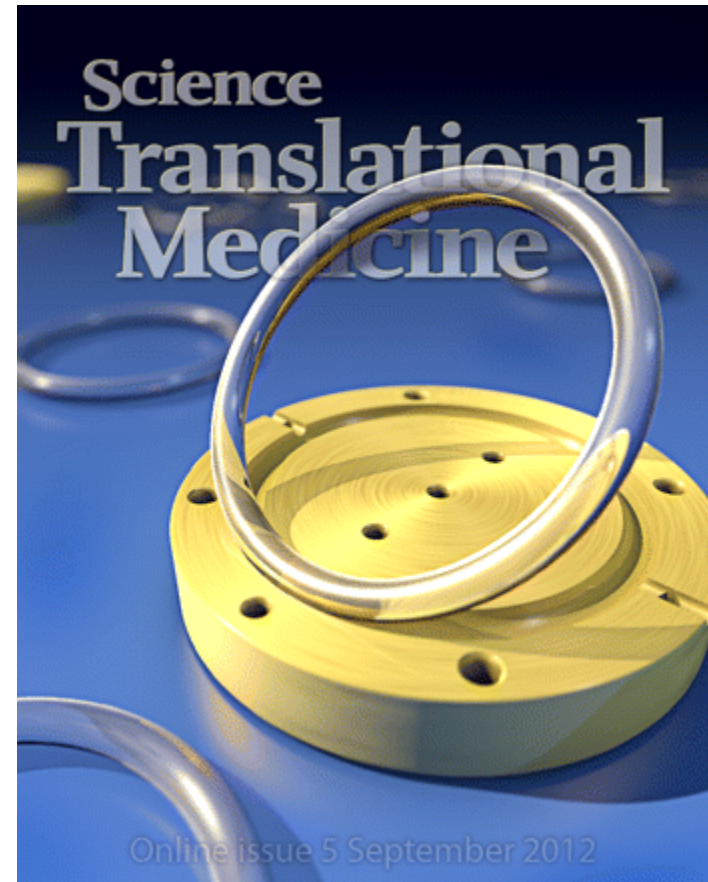


5P12-RANTES Macaque Study



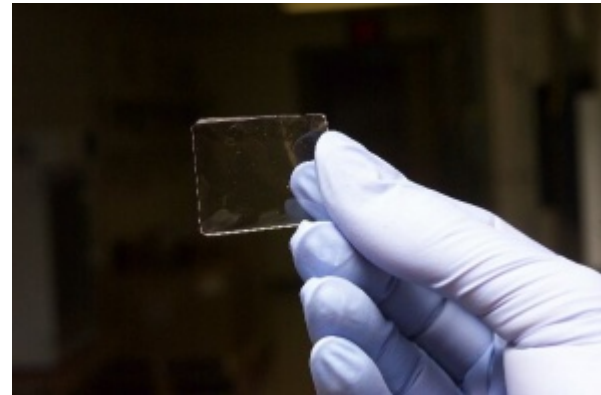
MIV-150

- Product class
 - NNRTI
- Sponsor
 - Population Council
- Formulation
 - Gel and ring
- Development stage
 - Protection in vaginal and rectal macaque studies



IQP-0528

- Product class
 - Pyrimidinedione
- Sponsor
 - ImQuest Biosciences
- Formulation
 - Films
 - Gels
- Development stage
 - Preclinical



The MTN Portfolio

Study	Product	Formulation	Population	Phase	N	2013	2014	2015	2016	2017	2018	2019	2020
MTN-015	N/A	N/A	Seroconverters	N/A	N/A								
MTN-016	N/A	N/A	Pregnancy and infants	N/A	N/A								
MTN-020 (ASPIRE)	Dapivirine	Ring	Women	3	3476								
MTN-018 (CHOICE)	Truvada	Oral	Women	3B	TBD								
MTN-017	Truvada and TFV	Oral / Rectal Gel	MSM TG	2	186								
MTN-026	Maraviroc	Rectal Gel	Men/Women	1	45								
MTN-027	TFV	Rectal Gel	Men/Women	1	45								
MTN-028	MIV-150	Vaginal Gel / Ring	Women	1	45								
MTN-029	MIV-150	Rectal Gel	Men/Women	1	45								
MTN-030	TFV	Rectal Gel	MSM/TG	3	5000								
MTN-031	HC/ART	Ring	Women	1	45								
MTN-032	IQP-0528	Vaginal Gel	Women	1	45								
MTN-033	5P12-RANTES	Rectal Gel	Men/Women	1	45								
MTN-034	Dapivirine	Film	Women	1	45								
MTN-035/HVTN 117	HIV Vaccine/TFV	Oral/Rectal Gel	Men/Women	1	120								
MTN-036	TBD	Rectal Gel	Men/Women	1	45								
MTN-037	HC/ART	Ring	Women	2	200								
MTN-038	Griffithsin	Vaginal Gel	HIV+ Women	1	45								
MTN-039	Dapivirine	Film	Women	2	200								
MTN-040	Dapivirine	Film	Pregnancy	1	45								
MTN-041	HC/ART	Ring	Women	3	5000								
MTN-042	TDF	Ring	Women	2	200								
MTN-043	IQP-0528	Ring	Women	1	45								
MTN-044	Griffithsin	Rectal Gel	Men/Women	1	45								
MTN-045	Dapivirine	Film	Adolescent girls	1	45								
MTN-046	HC/ART	Ring	Lactating women	1	45								

Vaginal Microbicides

Study	Phase	Population	Product(s)	N
MTN-028	1	Women	MIV-150 gel/ring	45
MTN-032	1	Women	IQP-0528 gel	45
MTN-034	1	Women	DPV film	45
MTN-038	1	HIV + Women	Griffithsin gel	45
MTN-039	2	Women	DPV film	200
MTN-040	1	Pregnancy	DPV film	45
MTN-042	2	Women	TDF ring	200
MTN-043	1	Women	IQP-0528 ring	45
MTN-045	1	Adolescents	DPV film	45
MTN-046	1	Lactation	HC/ARV	45

Rectal Microbicides

Study	Phase	Population	Product(s)	N
CHARM-03 / MTN-026	1	Men/Women	MVC gel	45
MTN-027	1	Men/Women	TFV gel	45
MTN-029	1	Men/Women	MIV-150	45
MTN-030	2B/3	MSM and Transgender women	TFV gel	5,000
MTN-033	1	Men/Women	5P12-RANTES	45
MTN-035 HVTN 117	1	MSM and Transgender women	Oral TDF/FTC TFV gel HIV vaccine	120
MTN-036	1	Men/Women	TBD	45
MTN-044	1	Men/Women	Griffithsin	45

Combination Rings

Dual Protection VR	Indications	Status	Developer
TFV + LNG	HIV + pregnancy (+ HSV)	Preclinical	CONRAD
MIV-150+ZN acetate + LNG	HI + pregnancy + HSV (+HPV)		Population Council
DPV + HC (TBD)	HIV + pregnancy		IPM
TDF + progestin type HC	HIV + pregnancy		AECOM, U Utah
AZT + ferrous gluconate	HIV + pregnancy		Weill COM, Cornell
AZT + l-ascorbic acid	HIV + pregnancy		Weill COM, Cornell
Nuvaring + ARV (TBD)	HIV + pregnancy		Merck

Proposed Ring Studies

Study	Phase	Population	Product(s)	N
MTN-031	1	Women	HC/ARV ring	45
MTN-037	2	Women	HC/ARV ring	200
MTN-041	3	Women	HC/ARV ring	5,000

MTN Affiliated Sites



Country	Sites
USA	9
Malawi	2
Zambia	1
Uganda	1
Zimbabwe	3
South Africa	12
India	1
Thailand	2
Peru	1
Total	32



Important Dates

- 29th September, 2012
 - MTN recompetition submitted
- 4th March, 2013
 - Presentation of the VOICE data at CROI
- 9th May, 2013
 - MTN Virtual Reverse Site Visit
- 31st December, 2013
 - End of current MTN funding cycle



Summary

- Development of safe and effective PrEP agents including microbicides remains a critical focus for HIV prevention research
- Increased interest in sustained delivery products
- Rectal microbicide development important for both domestic and international MSM and others at risk of infection through RAI
- Innovative trial design will be needed to sustain the HIV prevention research agenda

The Need Remains



The size of your dreams must always exceed your current capacity to achieve them. If your dreams do not scare you, they are not big enough.

Ellen Johnson Sirleaf

MTN Partners



BILL & MELINDA
GATES *foundation*

The National Institutes of Health



NIAID



National Institutes of Health
Eunice Kennedy Shriver
National Institute of Child Health & Human Development



Thank You
