

ASPIRE activation: Where we are and where we are headed

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ASPIRE Protocol Team Meeting
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MTN-020 / ASPIRE





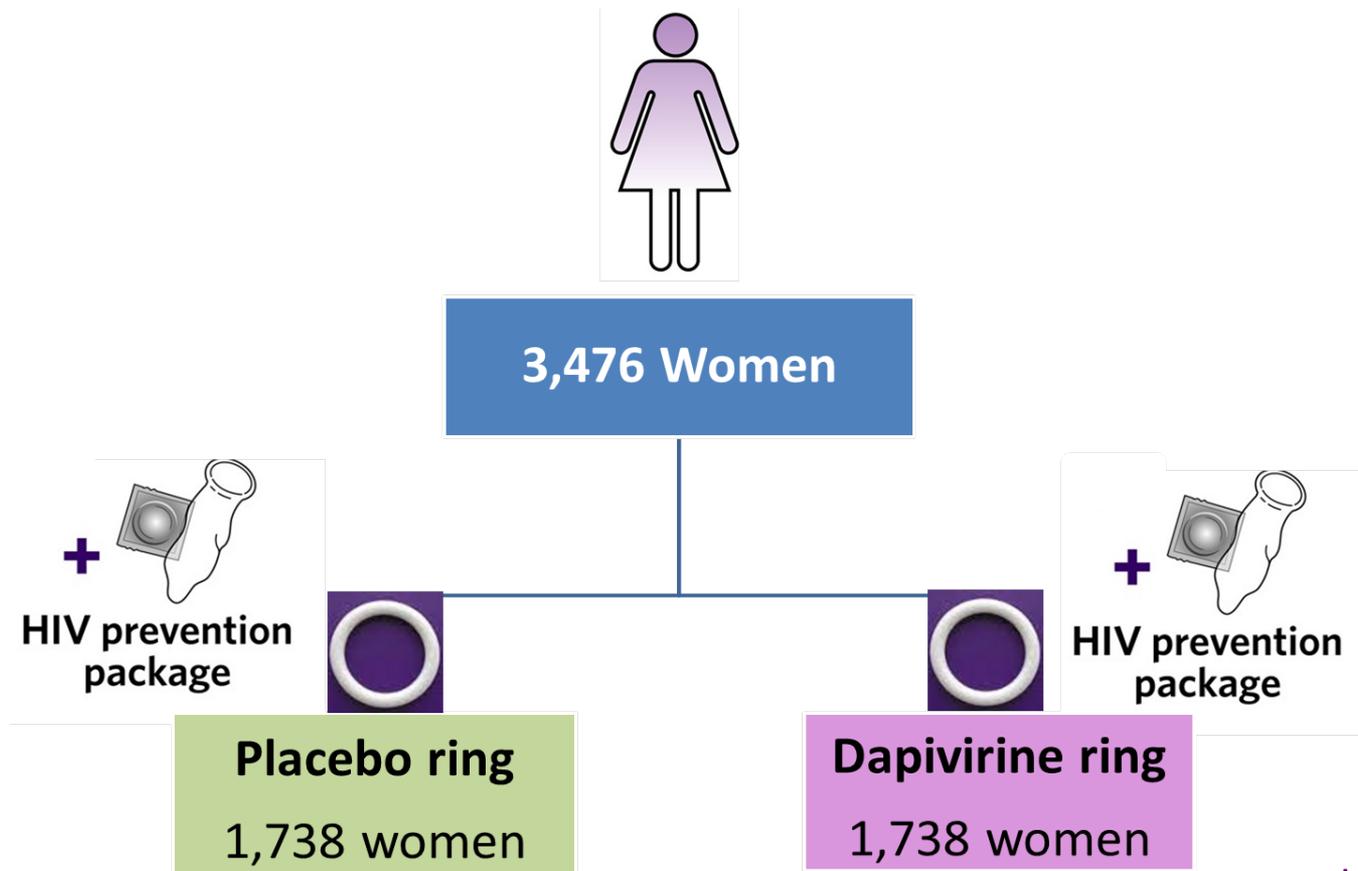
Where we are

MTN-020 / ASPIRE

- **A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase III Safety and Effectiveness Trial of a Vaginal Matrix Ring Containing Dapivirine for the Prevention of HIV-1 Infection in Women**



ASPIRE Overview



ASPIRE to date

- January - March 2011
 - Concept approved by MTN Executive Committee
 - Protocol Consultation Meeting with Site Investigators
- May – July 2011
 - NIAID SWG, PSRC
- September 2011
 - v1.0 to sites for IRB submission
- October 2011
 - Community Consultation, Operational Walk-Through
- January 2012
 - DSMB protocol review
- June, July 2012
 - First site training (Cape Town), first activation (Kampala)
- August 21, 2012
 - First enrollment (Kampala)

Site activations

Site	Date of activation	Site	Date of activation
MA – Blantyre	APPROVALS PENDING	SA – MRC/Verulam	28 AUG 2012
MA - Lilongwe	APPROVALS PENDING	SA – MRC/Umkomaas	28 AUG 2012
SA – Cape Town	4 SEP 2012	SA – WRHI	POISED
SA – CAPRISA eThekwini	13 SEP 2012	UG – Kampala	19 JUL 2012
SA – MRC/Botha’s Hill	28 AUG 2012	ZA – Lusaka	APPROVALS PENDING
SA – MRC/Chatsworth	28 AUG 2012	ZI – Seke South	POISED
SA – MRC/Isipingo	28 AUG 2012	ZI – Spilhaus	POISED
SA – MRC/Tongaat	28 AUG 2012	ZI – Zengeza	POISED

Communications

- Weekly Protocol Management calls (W, 6 AM Pacific)
- Biweekly CRM calls with sites
- Weekly priority emails from FHI360 to sites – collating protocol team priorities
- Monthly team calls = site-driven exercises – sharing experiences
- Listservs : cross-site communications/sharing

Numbers that matter

- 3476 = total number of women enrolled
- >95% = retention, product distribution
- 100% = attention to data quality, safety

Everything else flows from these



Where we are going

Timeline

2011

- Initiate site IRB and regulatory approval process

2012

- IRB/regulatory approvals, trainings, first enrollment, next DSMB 9 November 2012

2013

- Enrollments and follow-up continue

2014

- End of participant follow-up

2015

- Results

The Big Five

Accrual

Retention



**Clinical and
Laboratory
Participant
Safety**

Adherence

**Data Quality
and Timeliness**

ASPIRE
A Study to Prevent Infection
with a Ring for Extended Use



Accrual

Enrollments (27 SEP 2012)

Site	First enr	# scr	# enr	scr:enr ratio
SA – Cape Town	19 SEP 2012	5	3	1.7
SA – CAPRISA eThekwini		1	0	-
SA – MRC/Botha's Hill	10 SEP 2012	39	14	2.8
SA – MRC/Chatsworth	11 SEP 2012	27	11	2.5
SA – MRC/Isipingo	19 SEP 2012	13	4	3.3
SA – MRC/Tongaat	17 SEP 2012	25	5	5.0
SA – MRC/Verulam	13 SEP 2012	33	8	4.1
SA – MRC/Umkomaas	14 SEP 2012	26	13	2.0
UG – Kampala	21 AUG 2012	52	35	1.5
TOTAL		221	93	2.4

Enrollment timelines

- N=3476
- Estimated that accrual will require **approximately** 12 months, with total study duration approximately 24 months
 - Regulatory preference that all participants will achieve 12 months on study product
 - Balance efficient / rapid recruitment with quality
 - Continuous involvement of community (and not just for enrollments)

Site targets

Site	Date of activation	Site	Date of activation
MA – Blantyre	150	SA – MRC/Verulam	216
MA - Lilongwe	150	SA – MRC/Umkomaas	216
SA – Cape Town	150	SA – WRHI	200
SA – CAPRISA eThekwini	150	UG – Kampala	200
SA – MRC/Botha's Hill	216	ZA – Lusaka	150
SA – MRC/Chatsworth	216	ZI – Seke South	150
SA – MRC/Isipingo	216	ZI – Spilhaus	150
SA – MRC/Tongaat	216	ZI – Zengeza	150
ASSIGNED TOTAL		2896	
UNASSIGNED		580	

Getting to 3476

- To date, defined site targets for start-up
 - Additional assignments pending site capacity, performance, etc.
 - Discussions between now and early 2013 for remaining numbers
 - *We are all in this as a team*



Adherence

Learning from PrEP trials

	HIV protection <u>efficacy</u> for FTC/TDF versus placebo in randomized comparison	% of blood samples with tenofovir detected
Partners PrEP	75%	81%
TDF2	62%	79%
iPrEx	44%	51%
FEM-PrEP	6%	26%

Clear dose-response between evidence of use & HIV protection

Adherence is key...

- Products don't work if they aren't used
- How can we set up a culture in ASPIRE so that women can openly report non-use?



Retention



Retention is adherence

- Every missed visit is a month of **zero** adherence

Retention starts before day 1

- Every enrolment should be considered
 - ASPIRE is a monthly, multi-hour commitment until sometime in 2014....
 - Trust your instincts, trust team instincts

- How can we continue to create cultures that make sites places where participants want to spend several hours each week?
 - How do we remind ourselves and participants about their important volunteerism?



Safety

Safety

- Safety is the co-primary endpoint of the study
 - Evaluating whether the product is safe is just as important as whether the product is effective for HIV prevention
 - Regulatory authorities will scrutinize safety data and careful attention to safety documentation is critical

Laboratory

- Laboratory results and archived samples are central to this study
 - Careful attention to performance of every lab test, every sample for storage is critical



Quality

We are all in this together

- We all work together – all parts of the study are all our business

Recruitment

Retention

Adherence

Sample collection

Staff morale

Community/outreach

Communications

Lab quality

QC/QA

Regulatory

Safety Monitoring

Space/facilities

Study drug/pharmacy

Contraception

Lab-clinic interface

Monitoring follow-up

Mistakes happen

- We all make errors
 - But recognizing and acknowledging errors and then developing corrective and preventative action plans is key
- No one knows how to do this perfectly
 - Cross-site, cross-team sharing is important
- Do not let protocol deviation policies become paralyzing

Pay attention to the data

- Follow the metrics –
 - Enrollments
 - Retention
 - Contraceptive use
 - QCs
 - Etc.



Pay attention to the participants

- Participants give much to be in this study
 - Time
 - Blood
 - Privacy
 - Effort

We have much to learn from them.

MTN-020 / ASPIRE



IT TAKES A TEAM



Malawi College of
Medicine – JHU
Research Project



UNC Project -
Malawi



INTERNATIONAL
PARTNERSHIP FOR
MICROBICIDES



University of Zimbabwe,
School of Medicine

