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BHIVA ‘Best of CROI’ Feedback Meetings

London | Edinburgh

Wakefield | Cardiff

Birmingham | Haydock

Newcastle

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- Testing
- Prevention
- MTCT
- Cure

- Testing
- Prevention
- MTCT
- Cure

RCT of rapid HIV screening in US EDs p956

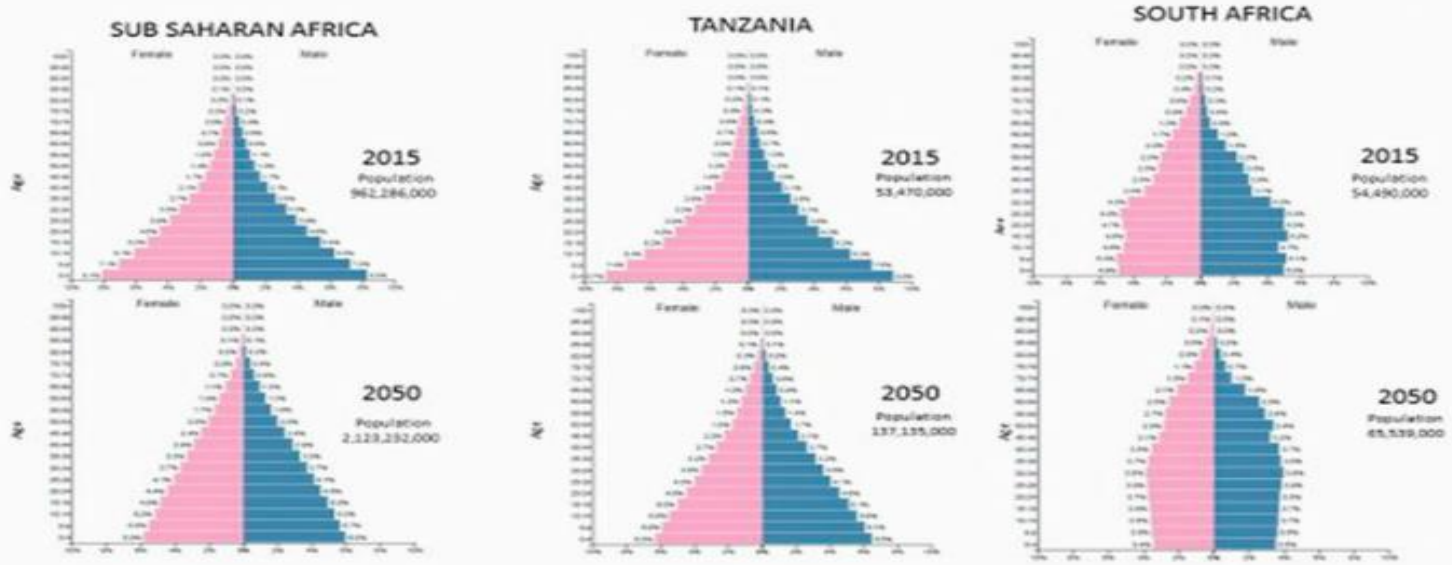
- Enhanced targeted screening (Denver risk score) vs traditional risk screening vs non targeted
- 25,000 each arm however only 4000 per arm tested
- 10+ves in non targeted , 7 in each of others
- All 3 strategies worked and were cost effective
- Risk screening probably not worth doing in ED

Pharmacy based HIV testing p962

- One minute insti test
- No risk assessment or counseling
- 3000+ tests, 25 +ve
- Good coverage of hard to reach groups(men,black africans)
- Most +ves linked to care, only 2 (lost to FU)

Africa's Youth will Age into Young Adulthood

Age Structure Differs—Southern Africa ahead in demographic shift



United Nations, Department of Economic and Social Affairs, Population Division, World Population Prospects: The 2015 Revision. (Medium variant)

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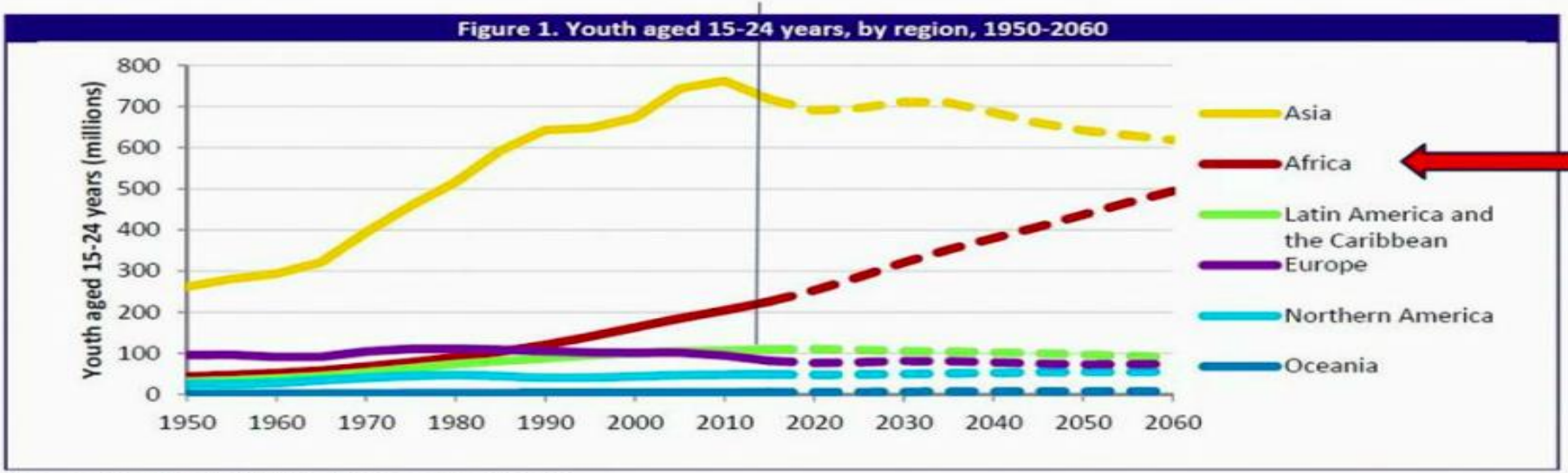
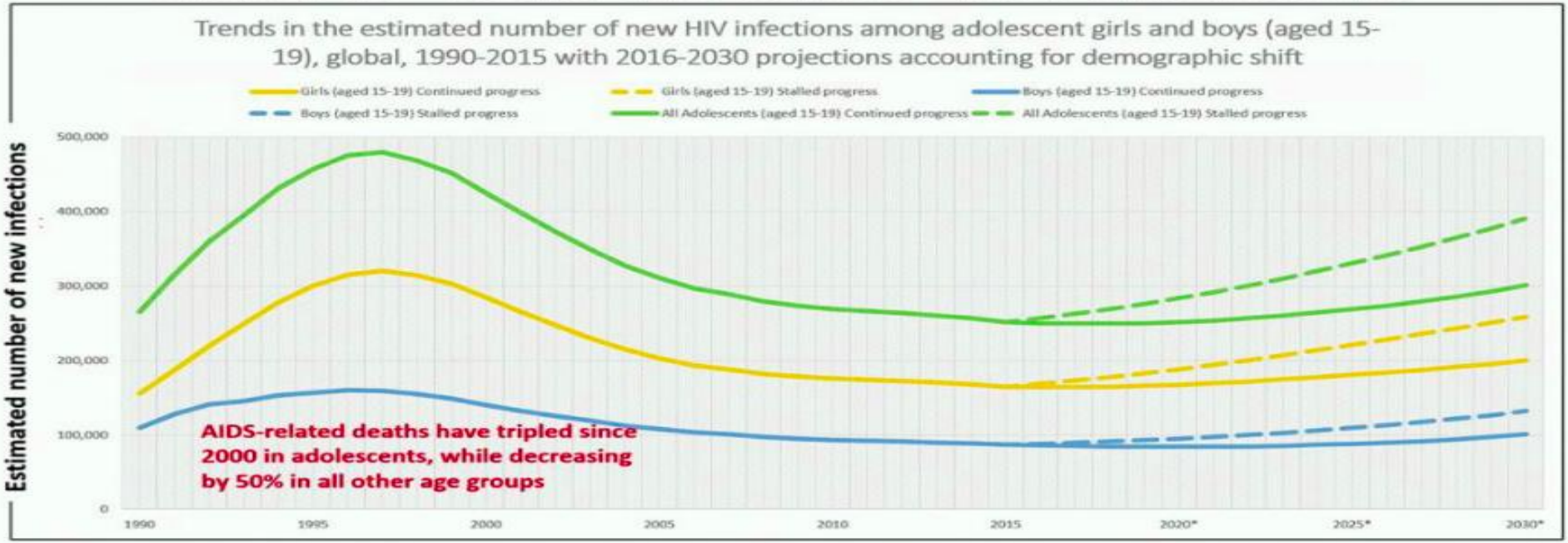
Projected Growth:
Absolute Increase in Africa's Young Adult Population



Data source: United Nations (2013) *World Population Prospects: The 2012 Revision.*

Need to "Bend the Curve" for Adolescents



UNICEF analysis of UNAIDS 1990-2015 HIV and AIDS estimates and United Nations Statistics Division, World Population Prospects 2015 Revision, June 2016

- Testing
- Prevention
- MTCT
- Cure

On Demand Post-Exposure Prophylaxis with Doxycycline for MSM Enrolled in a PrEP Trial

Molina JM, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, Capitant C, Rojas-Castro D, Meyer L, and the ANRS Ipergay Study Group

Hospital Saint-Louis and University of Paris 7, Inserm SC10-US19 Villejuif, Hospital Croix-Rousse, Lyon, Hospital Tenon, Paris, CHU de Nice, AIDES, Pantin, Paris Sud University, France

anrs France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm

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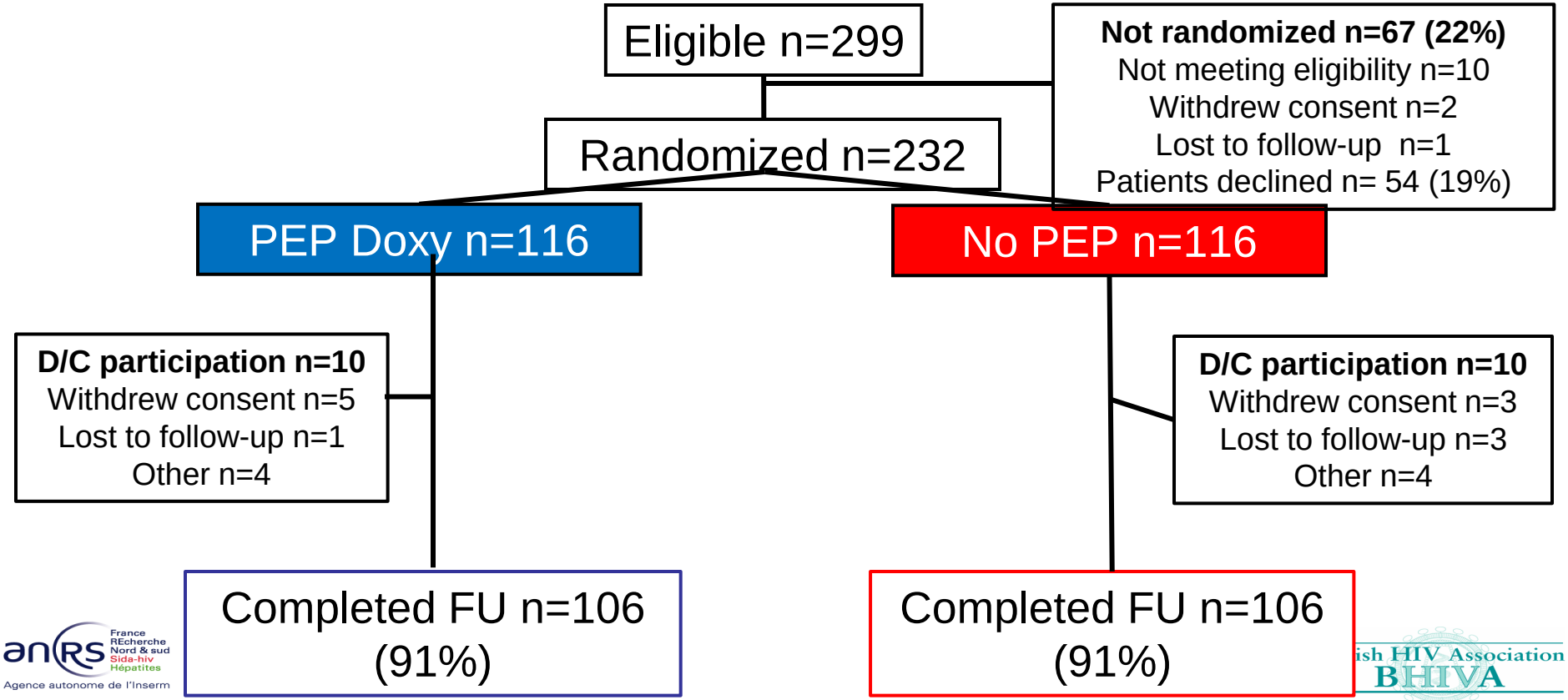
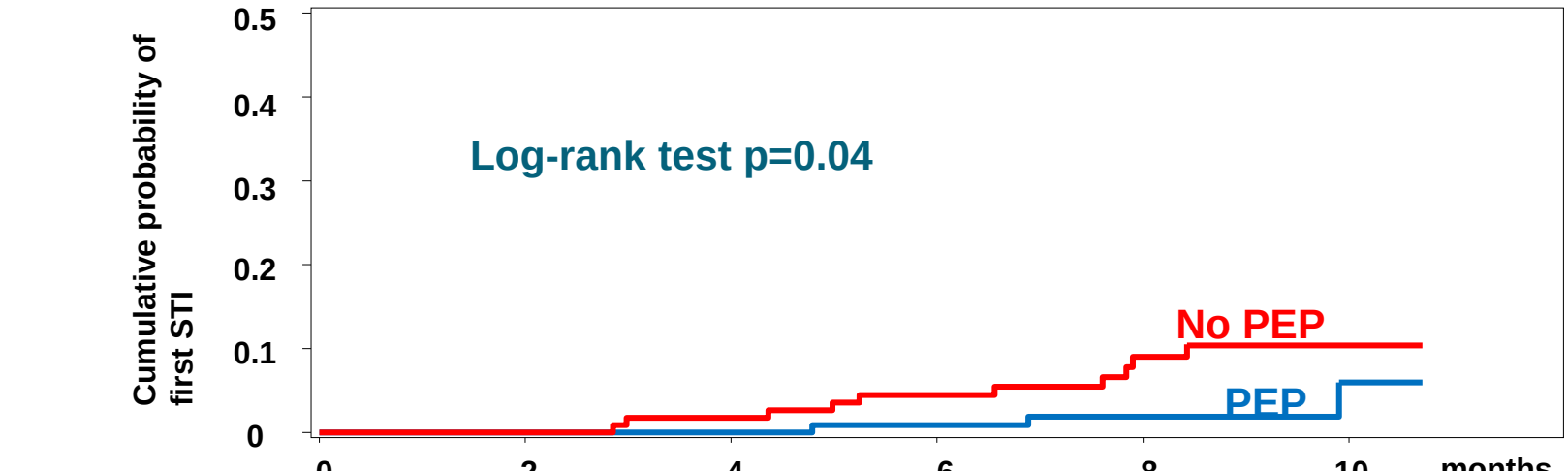
Study Flow-Chart



KM Estimates of Time to a First Syphilis (ITT Population)

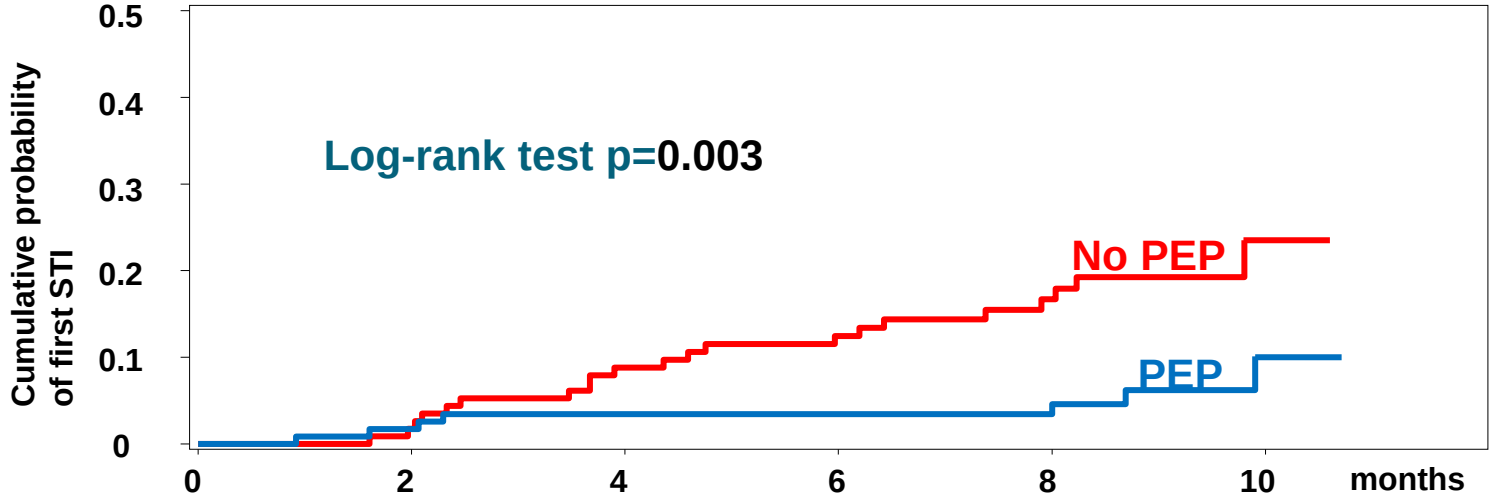


Median follow-up of 8.7 months (IQR: 7.8-9.7): 13 subjects infected

10 in no PEP arm (incidence: 12.9 / 100 PY), **3 in PEP arm** (incidence: 3.7 / 100 PY)

Hazard Ratio: 0.27 (95% CI: 0.07-0.98, p<0.05)

KM Estimates of Time to a First Chlamydia (ITT Population)



Median follow-up of 8.7 months (IQR: 7.8-9.7): 28 subjects infected

21 in no PEP arm (incidence: 28.6/100 PY), **7 in PEP arm** (incidence: 8.7/100 PY)

Hazard Ratio: 0.30 (95% CI: 0.13-0.70, p=0.006)

ipergay
ANRS
Intervention Préventive
de l'Exposition aux Risques
avec et pour les Gays

Conclusions

- PEP with doxycycline reduced the overall incidence of bacterial STIs by 47% in MSM on PrEP (8.7 months of FU)
- No effect on Gonorrhea but strong reduction (70-73%) in Chlamydia and Syphilis incidence
- Acceptable safety profile with mild/moderate GI AEs leading to D/C in only 7% of participants
- No evidence of risk compensation
- Analysis of antibiotic resistance pending
- Long-term benefit of PEP yet unknown
- Antibiotic prophylaxis for STIs still NOT recommended
- More research needed in the field of STIs

anrs France REcherche Nord & sud Sida-hiv Hépatites
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Truvada PrEP failure P953

- MSM 20+ sex partners per month
- Good TDP levels at 0 and month 6
- Flu type illness, HIV Ab +, Ag neg, RNA neg
  - Told to stop PrEP
- 2 weeks later RNA detected, wild type virus
- ? Was this PrEP failure or did he get infected after stopping PrEP
- ?hx ivdu- chem sex likely

Pharmacy PrEP P961

- Single arm n=245 (84% MSM ~34 yrs)
- Only 25% had a care provider
- At 1 yr: 75% retention, 1 new HIV
- HIV testing and PrEP in pharmacy highly acceptable
- BUT dedicated PrEP pharmacist

PrEP and microbiome O85

- IAS 2016 CAPRISA 1% tenofovir gel
  - HIV acquisition associated with absence of lacto bacilli
  - Mechanism proposed: gardnerella degrades TNF
  - Controversial
- Partners PrEP n=1785 oral TDF
  - X sectional study of vaginal swabs
  - BV (nugent score 7-10) was not associated with HIV
  - 73% efficacy v 77% efficacy

Impact of vaginal microbiota on tenofovir O86lb

- 1% TNF gel for 1 week.
- Samples taken day 0 & 7
- BV associated with low TNF levels in vaginal fluid and plasma
- Effect present within 2 hours of dosing

Male Circumcision O87

- VMMC highly effective. mechanism unknown
- VMMC Controls from Rakai cohort
- 16S qPCR of foreskin swabs
- HIV neg (n=136) v HIV seroconverted (n=46)
- HIV acquisition was associated with prevotella, anaerobes and IL-8
  - Modifiable
  - Could they be passing BV to female partners?

- Testing
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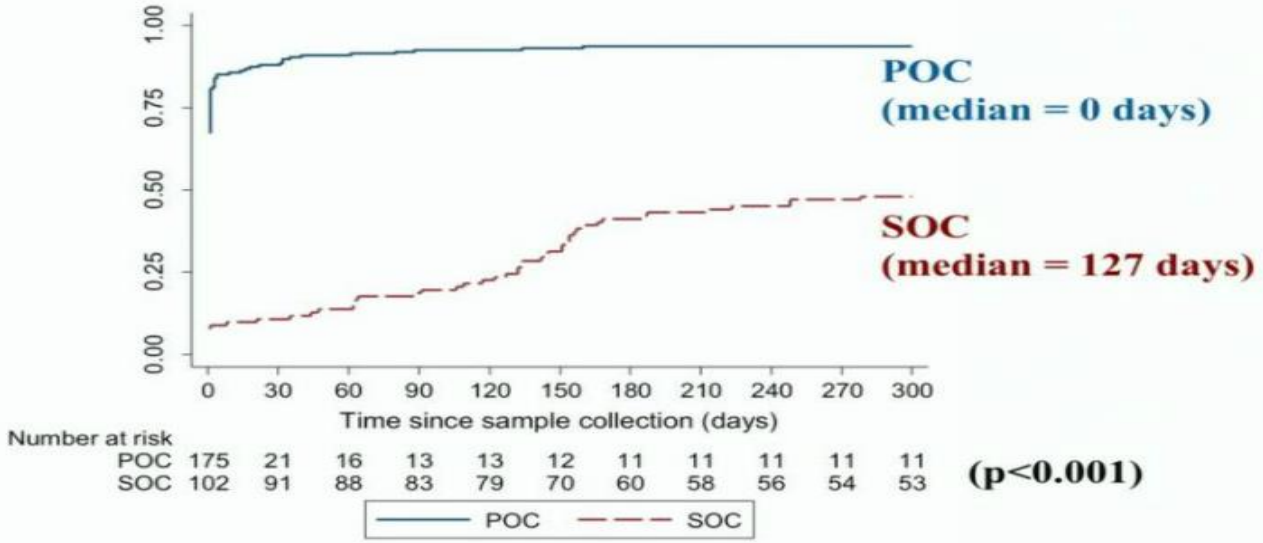
PrEP and pregnancy p934

- Partners PrEP
  - N=30 pregnancies:
    - No pregnancy loss
    - No preterm delivery
    - No poor infant growth

Innovation in infant testing: POC and linkage to care O26

Results (5) - Kaplan-Meier estimate of time from sample collection to initiation of antiretroviral therapy



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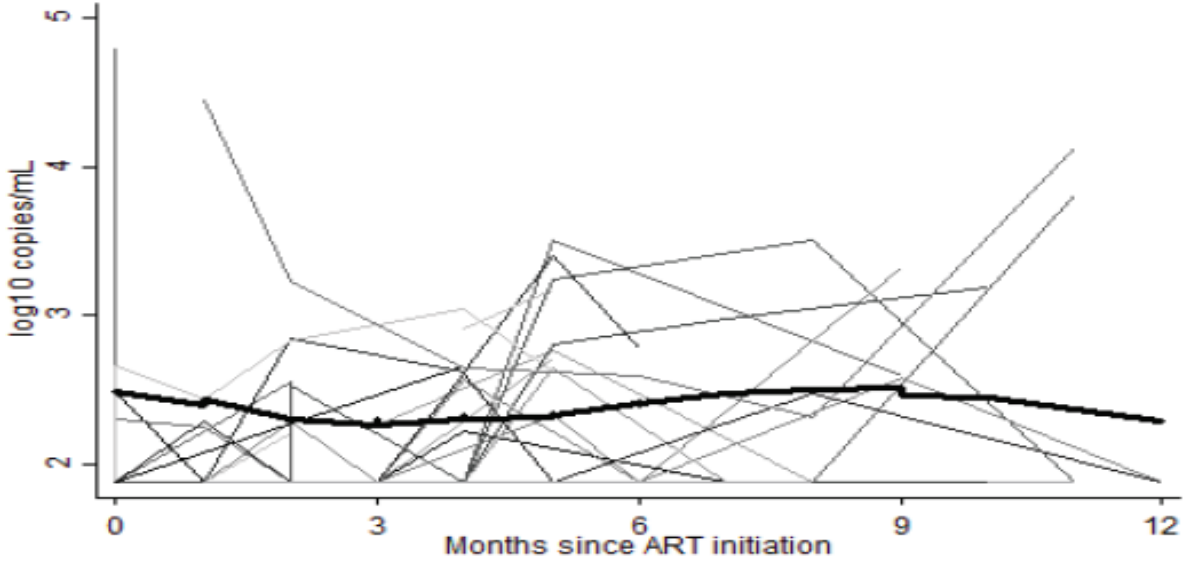
MTCTM: Breast Feeding p765

Figure 1. Breast milk HIV RNA levels



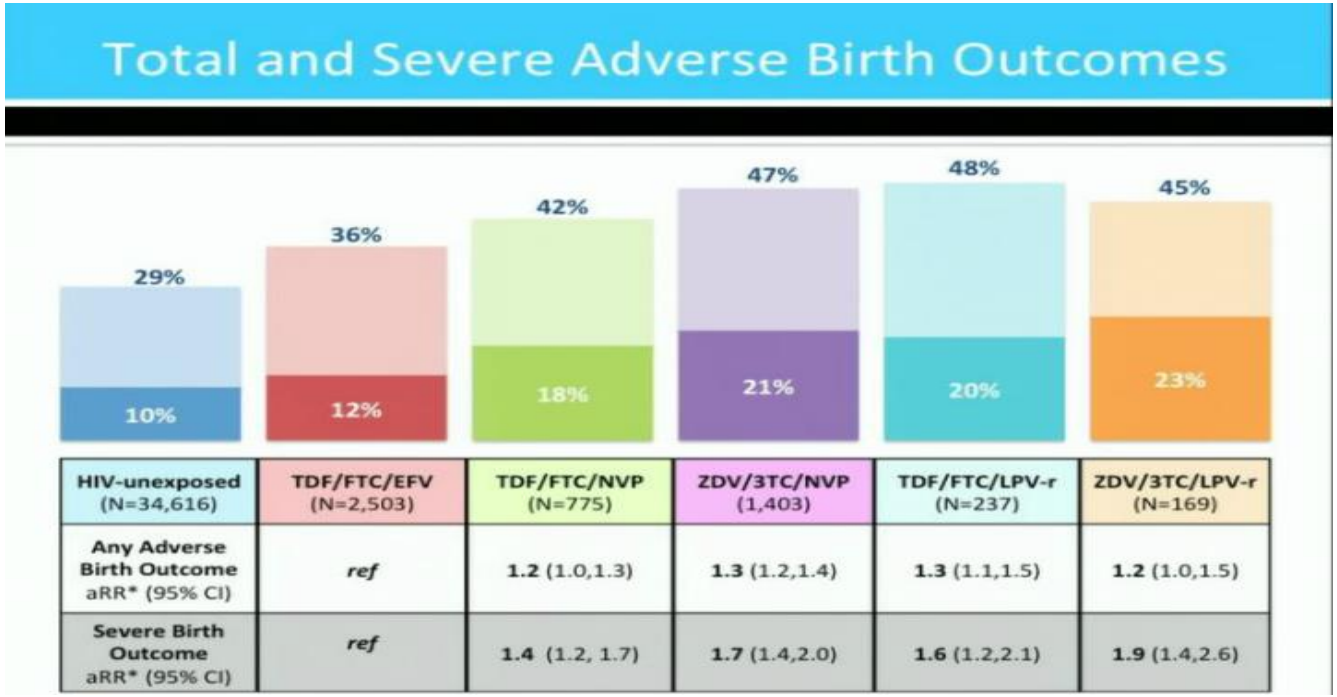
Thick black line is lowess curve, grey thin lines are individual-level breast milk viral loads

DETECTION OF HIV IN BREAST MILK AMONG PREGNANT/POSTPARTUM WOMEN WITH RECENT HIV

Alison L. Drake[1], John Kinuthia[2], Daniel Matemo[2], Barbra A. Richardson[1], Sandy Emery[3], Vrasha Chohan[1], Julie Overbaugh[3], Grace John-Stewart[1]

[1]Univ of Washington, Seattle, WA, USA, [2]Kenyatta Natl Hosp, Nairobi, Kenya, [3]Fred Hutchinson Cancer Rsr Cntr, Seattle, WA, USA

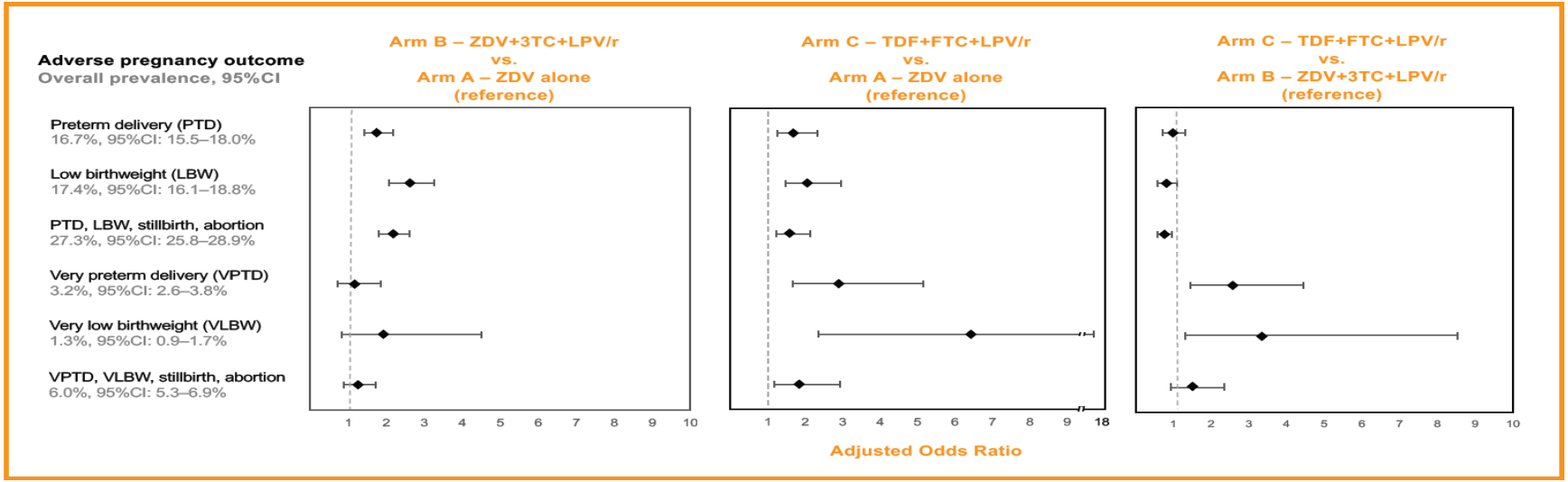
MTCTM: birth outcomes O25



HIV-unexposed (N=34,616)	TDF/FTC/EFV (N=2,503)	TDF/FTC/NVP (N=775)	ZDV/3TC/NVP (1,403)	TDF/FTC/LPV-r (N=237)	ZDV/3TC/LPV-r (N=169)
Any Adverse Birth Outcome aRR* (95% CI)	*ref*	**1.2** (1.0,1.3)	**1.3** (1.2,1.4)	**1.3** (1.1,1.5)	**1.2** (1.0,1.5)
Severe Birth Outcome aRR* (95% CI)	*ref*	**1.4** (1.2, 1.7)	**1.7** (1.4,2.0)	**1.6** (1.2,2.1)	**1.9** (1.4,2.6)

Poster 776

Update from PROMISE on pregnancy outcomes



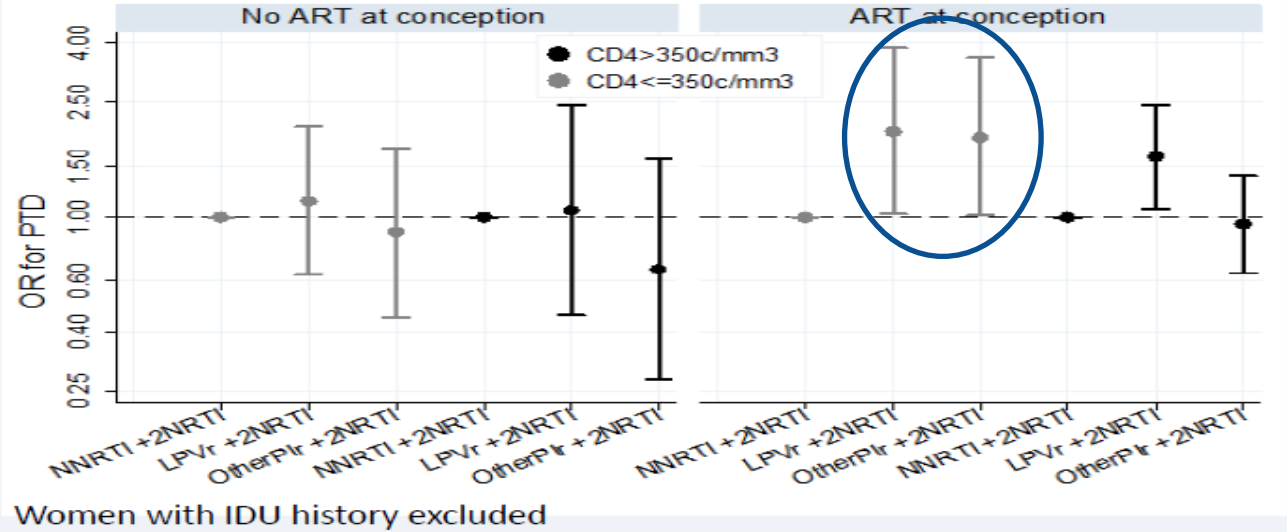
The use of LPV/r-containing antiretroviral regimens (TDF+FTC+LPV/r, ZDV+3TC+LPV/r) was associated with an elevated risk for PTD and LBW, when compared to antenatal ZDV alone.

ZDV+3TC+LPV/r had a somewhat higher risk for severe outcomes, relative to the ZDV alone arm, but this was not statistically significant. However, the TDF+FTC+LPV/r arm had a significantly higher risk than either of the other arms.

P778

Do HIV+ women on PIs deliver pre-term (UK & Ireland cohort)

Fig 1 Adjusted OR for PTD stratified by ART at conception and CD4 count (≤350 and >350 cells/mm³)



Women with IDU history excluded

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It's not the TDF (data from US cohorts)

Table 2. Risk of outcomes by initial regimen

	Initial **antiretroviral** regimen during pregnancy					
	TDF/FTC/LPV/r		TDF/FTC/ATV/r		ZDV/3TC/LPV/r	
	n	Risk (%)	n	Risk (%)	n	Risk (%)
Preterm birth	27	(21.4)	86	(16.1)	184	(19.5)
Very preterm birth	5	(4.0)	26	(4.9)	44	(4.7)
Low birth weight	30	(23.8)	86	(16.2)	175	(18.8)
Very low birth weight	1	(0.8)	10	(1.9)	18	(1.9)
Adverse outcome	36	(28.1)	127	(23.7)	256	(27.2)
Severe adverse outcome	7	(5.5)	28	(5.2)	51	(5.4)

Table 3. Risk ratios and 95% confidence intervals for infant outcomes based on comparisons of initial antiretroviral regimen used during pregnancy

	TDF/FTC/LPV/r vs ZDV/3TC/LPV/r				TDF/FTC/ATV/r vs ZDV/3TC/LPV/r				TDF/FTC/LPV/r vs TDF/FTC/ATV/r			
	Crude		Adjusted		Crude		Adjusted		Crude		Adjusted	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Preterm birth	1.10	(0.77, 1.58)	0.95	(0.66, 1.39)	0.83	(0.65, 1.04)	0.76	(0.59, 0.99)	1.33	(0.91, 1.96)	1.23	(0.84, 1.82)
Very preterm birth	0.85	(0.19, 2.11)			1.04	(0.65, 1.68)			0.82	(0.32, 2.08)		
Low birth weight	1.27	(0.90, 1.78)	1.08	(0.76, 1.54)	0.86	(0.68, 1.09)	0.83	(0.64, 1.09)	1.47	(1.02, 2.13)	1.40	(0.97, 2.03)
Very low birth weight	0.41	(0.06, 3.06)			0.97	(0.45, 2.10)			0.42	(0.05, 3.27)		
Adverse outcome	1.03	(0.77, 1.39)	0.90	(0.66, 1.23)	0.87	(0.72, 1.05)	0.83	(0.67, 1.02)	1.18	(0.86, 1.62)	1.11	(0.81, 1.52)
Severe adverse outcome	1.01	(0.47, 2.17)			0.96	(0.61, 1.51)			1.04	(0.47, 2.34)		

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What happens after pregnancy

FIGURE 1. PROMISE 1077HS study design

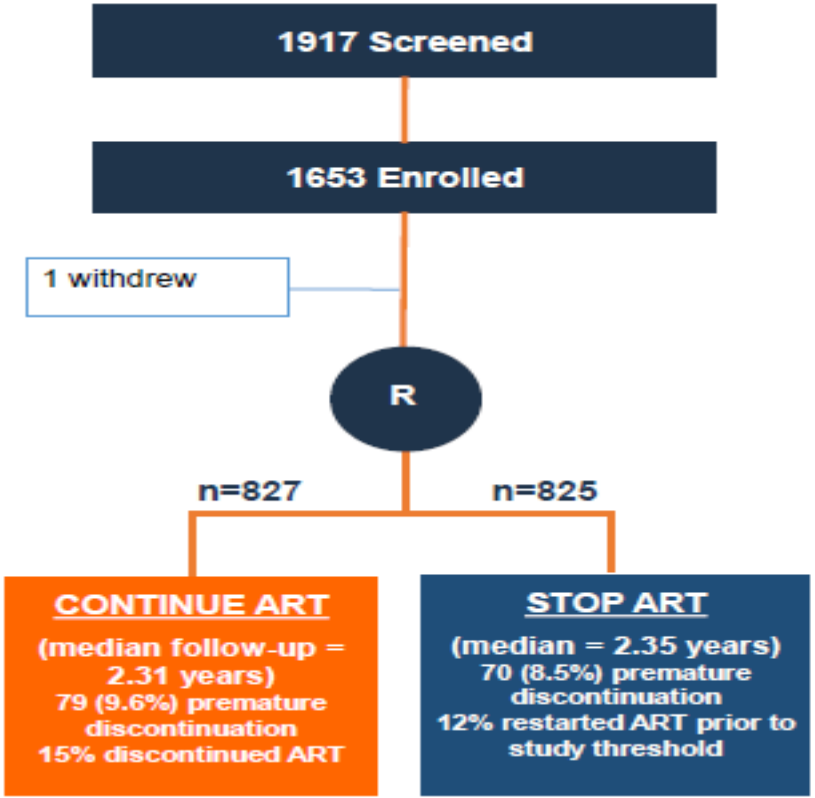

TABLE 2. Pregnancy outcomes recorded for the initial subsequent pregnancy

	HS Randomization Arm		
	Continuation of HAART (N=140)	Discontinuation of HAART (N=126)	P-value
Live Birth	100 (71%)	100 (79%)	
Spontaneous Abortion (<20 weeks)	27 (19%)	13 (10%)	0.06
Stillbirth (IUFD ≥ 20 weeks)	6 (4%)	2 (2%)	0.29
Spontaneous Abortion or Stillbirth	33 (24%)	15 (12%)	0.02

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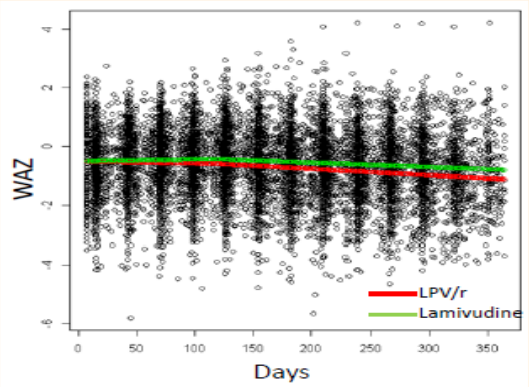
And just to add to the bad news

Weight for Age Z-score (WAZ)

Comparison of WAZ between the two arms		Real Data						Least Squares Means	
		LPV/r		Lamivudine		Difference of Means (95%CI)	P value	Difference of Means (95% CI)	P value
		n	Mean (95%CI)	n	Mean (95%CI)				
Data censored at the end of treatment	6 weeks	541	-0.54 (-0.63 ; -0.46)	547	-0.46 (-0.55 ; -0.37)	-0.08 (-0.20 ; 0.03)	0.16	-0.06 (-0.16; 0.04)	0.25
	26 weeks	474	-0.75 (-0.85 ; -0.65)	487	-0.55 (-0.65 ; -0.44)	-0.20 (-0.35 ;-0.05)	**<0.01**	-0.18 (-0.30; -0.05)	**<0.01**
	50 weeks	115	-1.09 (-1.32 ; -0.86)	128	-0.81 (-1.05 ; -0.57)	-0.28 (-0.61 ; 0.06)	0.10	-0.24 (-0.44; -0.05)	**0.02**



Spline regression model for WAZ

→ Overall, the Mixed Model showed a significant increase of the WAZ difference between arms over time (**p<0.01**)

→ The Spline Model confirmed this result, and showed that the WAZ difference between arms occurred early (**p=0.02**, Knot=118 days).

And finally two PK studies showing significantly reduced concentrations in pregnancy

Figure 1. Median Elvitegravir Concentrations

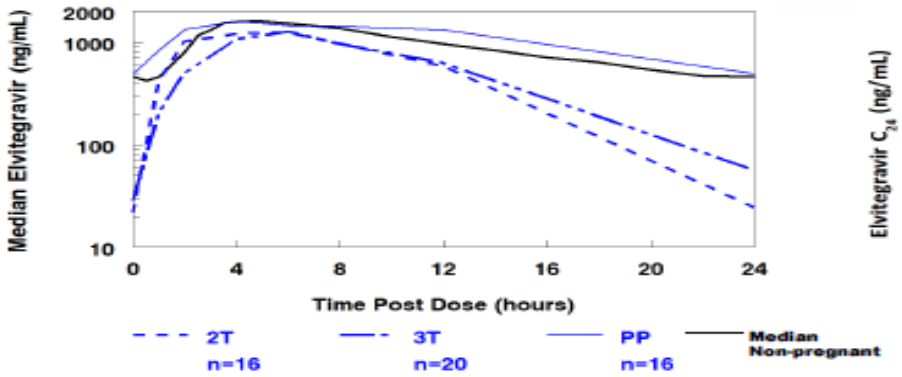


Figure 2. Elvitegravir C_{24} Ante- and Postpartum

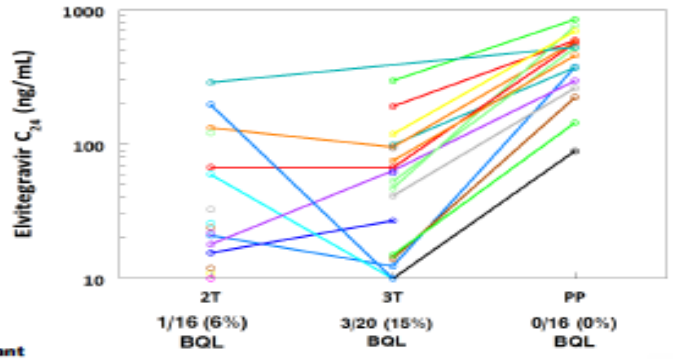


Figure 3. Median Cobicistat Concentrations

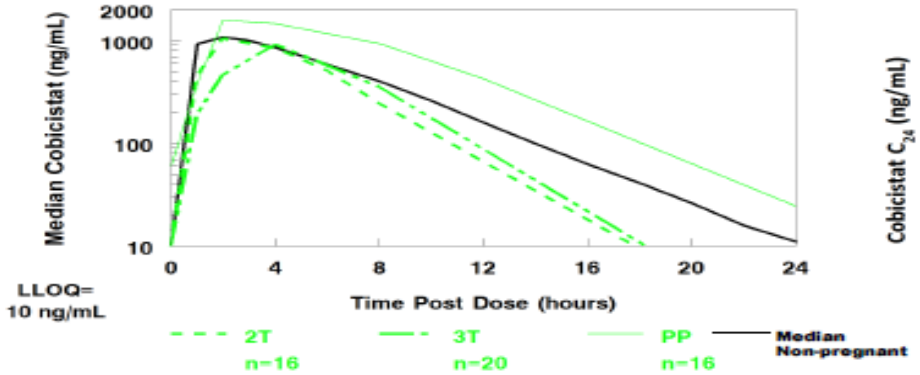
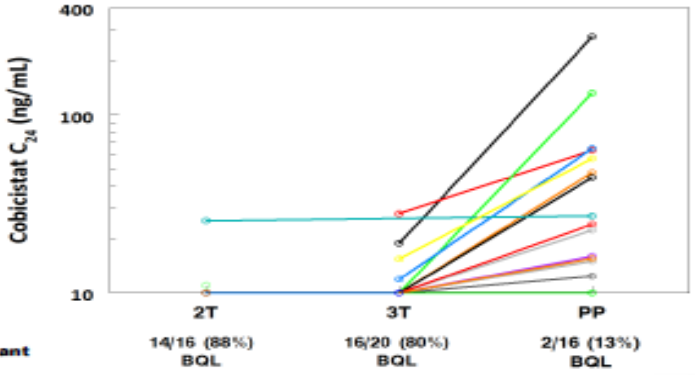


Figure 4. Cobicistat C_{24} Ante- and Postpartum



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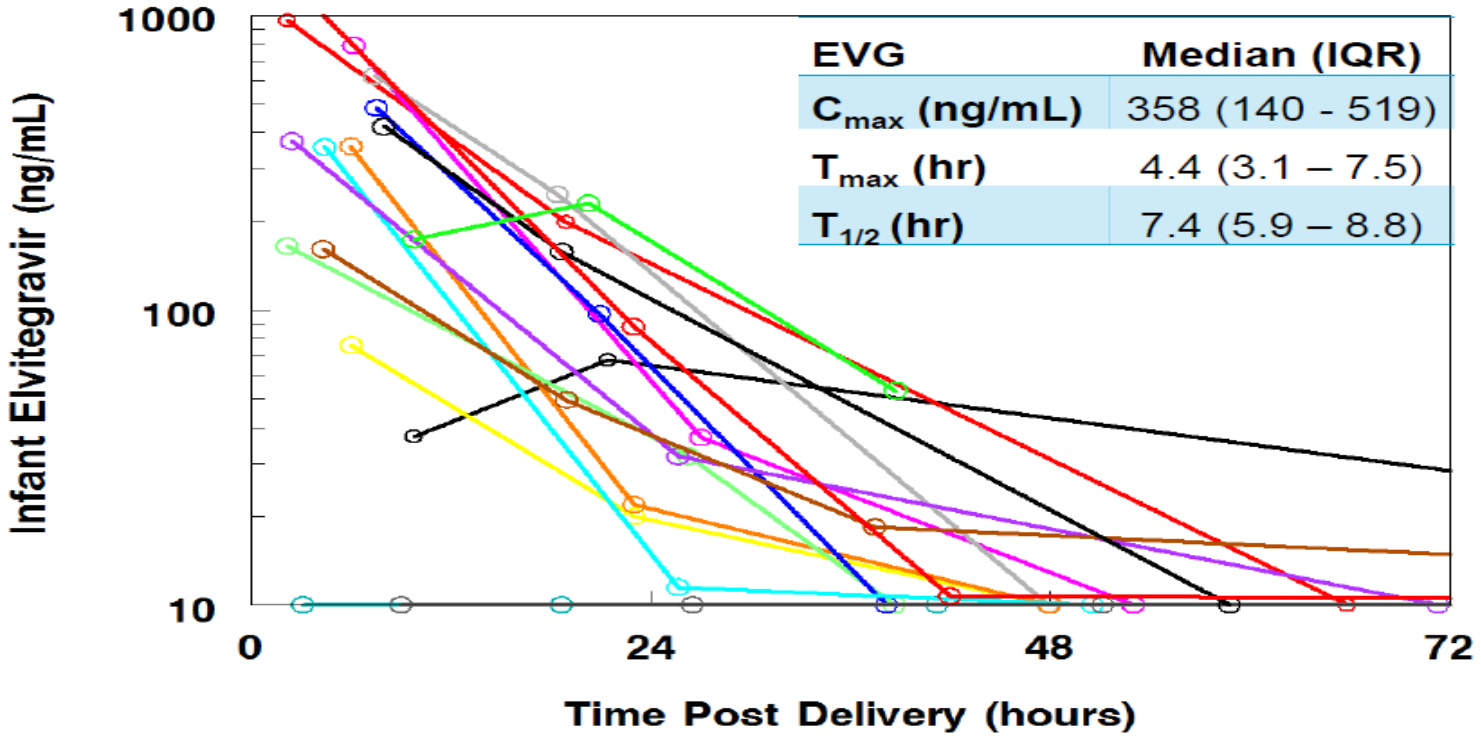
Elvitegravir but not Cobi crosses the placenta

Figure 5. Infant Elvitegravir Concentrations



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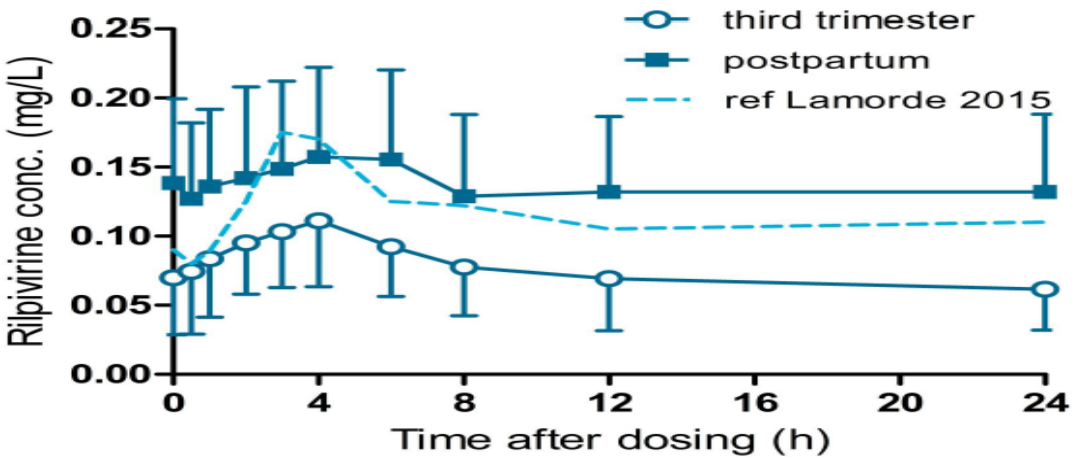
#754

Substantially lower rilpivirine conc in pregnancy

Cord:maternal ratio 0.5

2/16 had sub-therapeutic rilpivirine in T3

Figure 1: Mean (±%CV) concentration-time profile after administration of RPV 25mg QD during third trimester and postpartum



Pharmacokinetic Parameters	Third Trimester (n=16)	Postpartum (n=15)	GM Ratio (%) [90% CI] Third trimester / postpartum
$AUC_{0\text{-}24h}$ (h*mg/L)	1.71 (37)	3.04 (39)	55 (46-66)
C_{max} (mg/L)	0.11 (36)	0.17 (34)	65 (55-76)
C_{min} (mg/L)	0.05 (50)	0.10 (42)	51 (41-63)

Rilpivirine PK in pregnancy is highly variable

Tran et al JAIDS 2016;72:289-296

25mg daily with 500 Cal food 1 hour after medication	T3 (n=30)	PP (n = 28)
AUC ng*hr/mL (range)	1669 (556 – 4312)	2387 (188 – 6736)
C 24hr ng/ml	56 (<10 – 181)	81 (<10 – 299)
<10th centile AUC 0-24	2/28 (7%)	3/28 (11%)

Cord /Maternal blood ratio 0.55

One subject had <LDL at C24 despite observed dosing – either poor absorption or increased clearance

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HIV PERSISTENCE AND REACTIVATION

VIRAL CONTROL INDUCED BY HIVCONSV VACCINES & ROMIDEPSIN IN EARLY TREATED INDIVIDUALS

Beatriz Mothe

IrsiCaixa-HIVACAT, Hospital Germans Trias i Pujol, Badalona, Spain

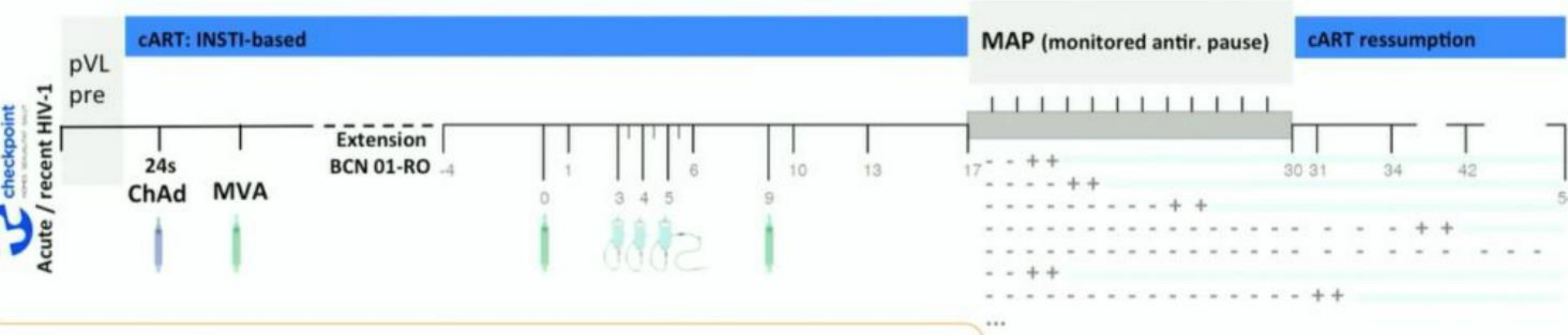
Background

- Early_cART during PHI has shown benefits in immune recovery[1,2] and in limiting latent reservoir size[3,4].
- Conserved therapeutic vaccines may help to tackle HIV-1 viral diversity in the viral reservoir driven by immune escape[5,6,7]
- BCN 01 trial (NCT01712425) refocused T cells towards highly conserved regions of HIV-1 in early treated individuals but did not impact the viral reservoir size[8].
- Combination of vaccines with drugs that reactivate latent virus (Kick & Kill) may be required to clear the viral reservoir[9].

[1]Le, 2013; [2]Fidler, 2013, [3]Ananworanich, 2014; [4]Hocqueloux, 2013
[5]Rolland, 2007; [6]Letourneau, 2007; [7]Deng, 2015; [8]Mothe, CROI 2016, PO 320;
[9]Shan, 2012.

Mothe B. et al, BCN 02

Methods



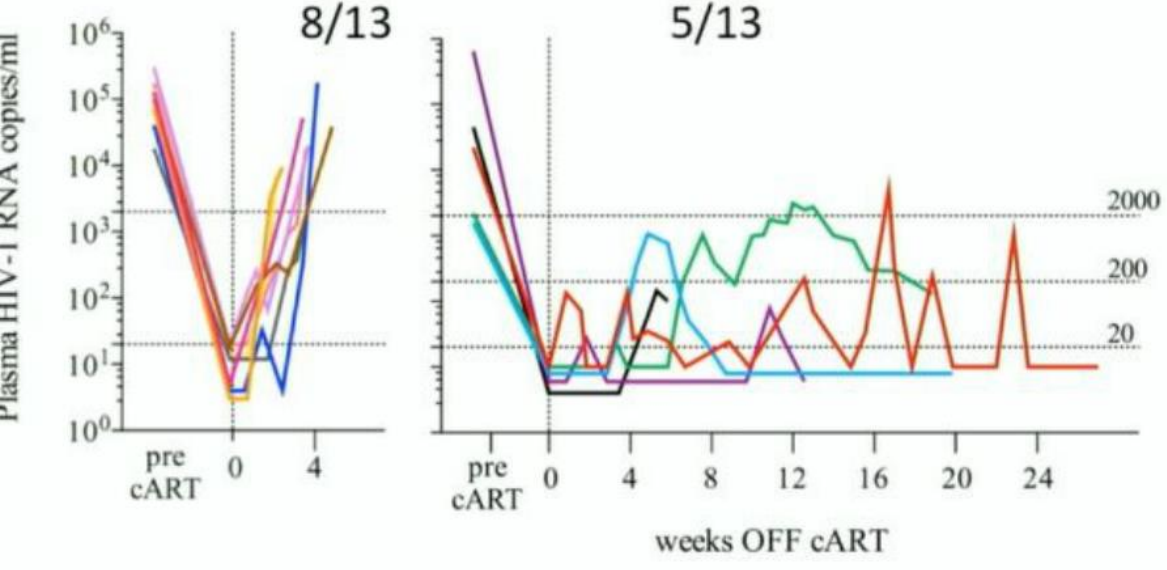
Effect on viral rebound

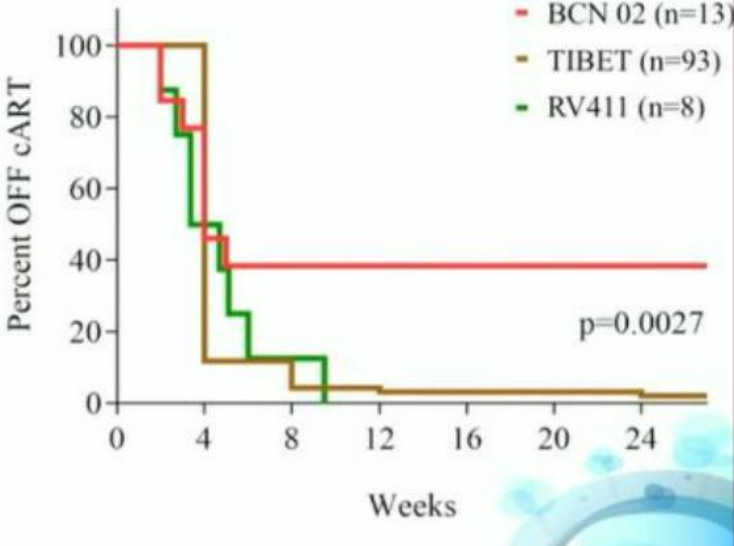
Mothe B. et al, BCN 02

Monitored Antiretroviral Pause (MAP)

n=13
Feb 15th

- 13 participants have interrupted cART to date.

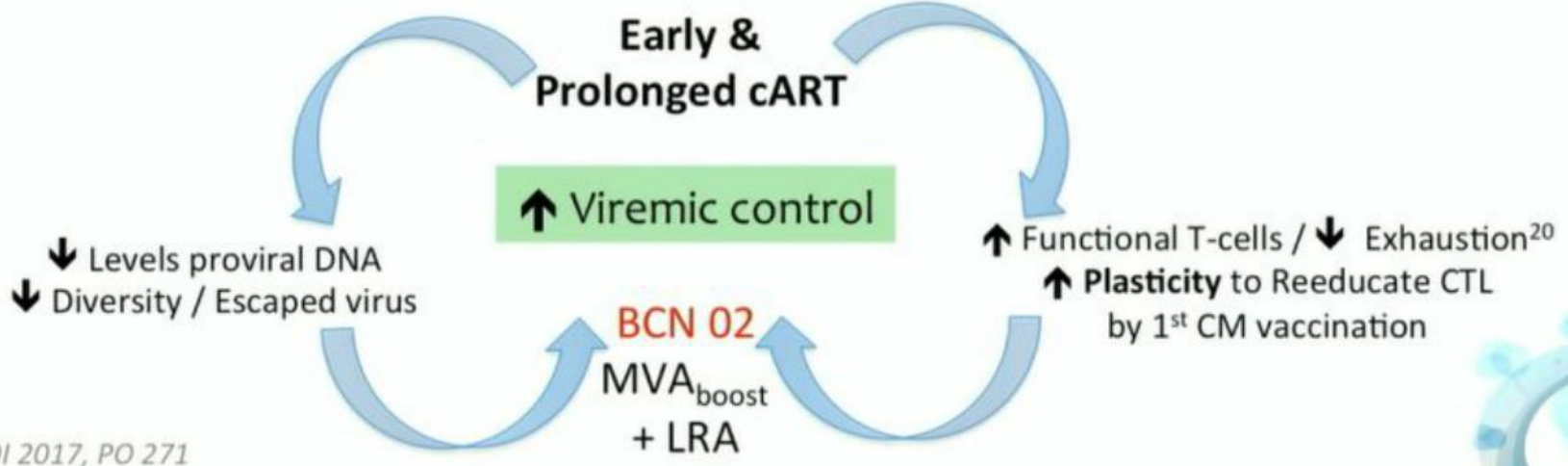




[15]Ruiz, 2007; [16]Colby, #124; [16]Leal, #336; [17]Genevieve, 2017; [18]Saez-Cirion, 2013; [19]Rosenberg, 2010; [20]Cockerhan, 2016

Conclusions

- This is the first therapeutic vaccine trial reporting a durable control of HIV-1 after cART cessation in a substantial proportion of patients (≈35-38%, so far >12-24wks).
- BCN 02 data suggest that viral control can be achieved by an effective redirection of CTL towards conserved regions in the context of a limited viral reservoir.



[20]Rosas, CROI 2017, PO 271

Mothe B. et al, BCN 02

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Dr Sanjay Bhagani
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