

Impact of Triple-ARV Prophylaxis during Pregnancy and Breastfeeding Compared with Short-ARV Prophylaxis for MTCT Prevention on Maternal Disease Progression:

Kesho Bora Study Group

Interim results - July 2010

(Trial registration number ISRCTN71468401)

Presented International AIDS Conference, Vienna, 22 July 2010

Refce: ThLBB105

Study Outline – Intervention Mother

Disease status	Intervention mother
CD4 < 200 or HIV stage 4	PROSPECTIVE COHORT ZDV+3TC+NVP (<i>continued ART from 16 wks</i>)
200 ≤ CD4 ≤ 500 and HIV stage < 4	RANDOMIZATION at 28-36 weeks pregnancy ZDV+3TC+LPV/r (<i>until 6 months post partum</i>) OR ZDV (<i>until labour</i>) + sdNVP (+ ZDV+3TC for one week after delivery)*
CD4 > 500 and HIV stage < 4	PROSPECTIVE COHORT ZDV (<i>until labour</i>) + sd-NVP

• **Amendment introduced during the course of study**

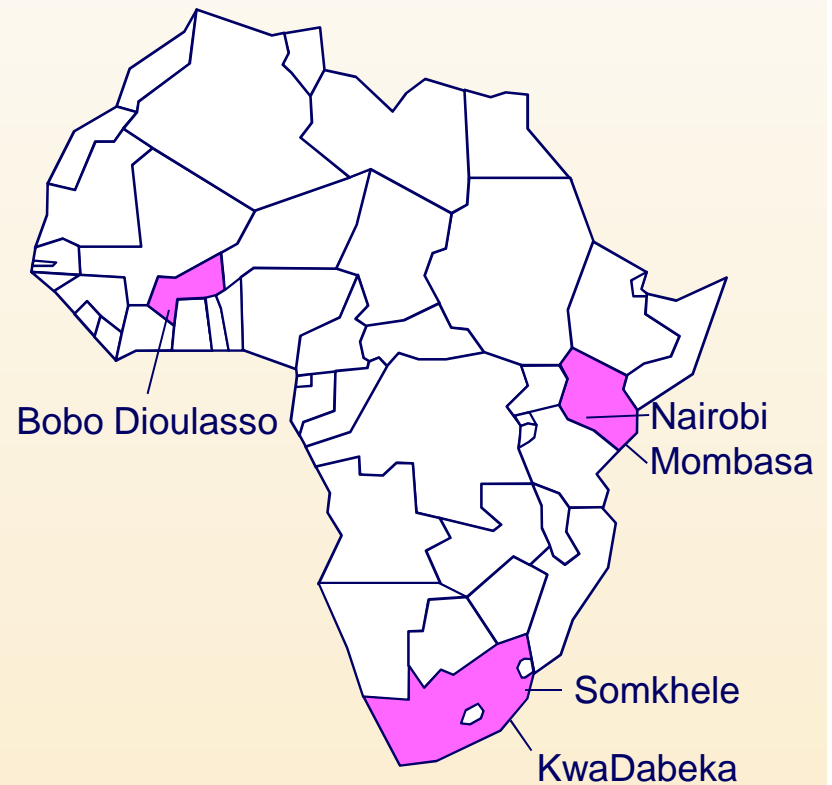
Primary objectives

Compare efficacy and safety of triple-ARV and short-ARV MTCT-prophylaxis with regard to:

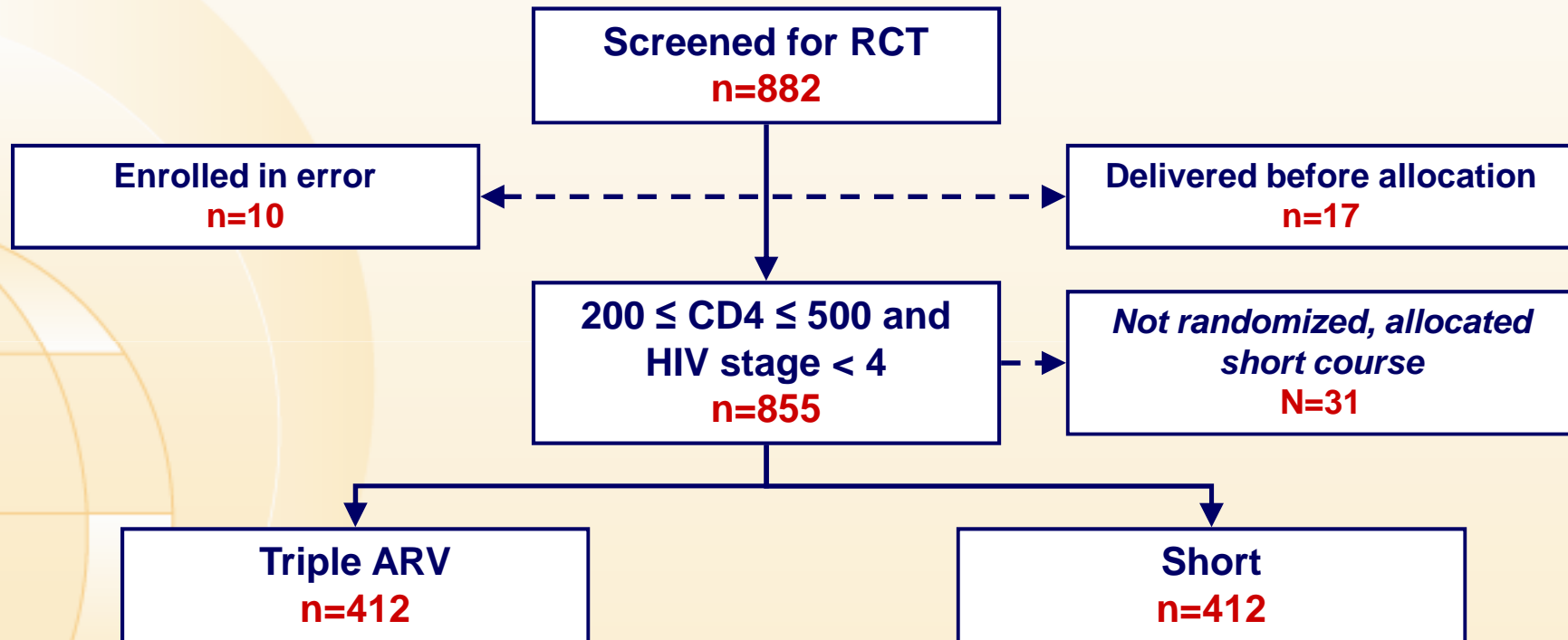
- **Efficacy:** HIV-transmission and infant mortality (IAS 2009)
- **Safety:** Incidence of severe adverse events in mothers and children (IAS 2009)
- **Safety:** AIDS-free survival of mothers at 18 months following delivery

Study sites

- **Bobo Dioulasso, Burkina Faso:**
Centre Muraz – Nicolas Meda
- **Mombasa, Kenya:**
International Centre for Reproductive Health – Stanley Luchters/Marcel Reyners
- **Nairobi, Kenya:**
University of Nairobi – Ruth Nduati
- **KwaDabeka, South Africa:**
University of KwaZulu-Natal – Nigel Rollins/Kevi Naidu
- **Somkhele, South Africa:**
Africa Centre (AFC) – Marie-Louise Newell



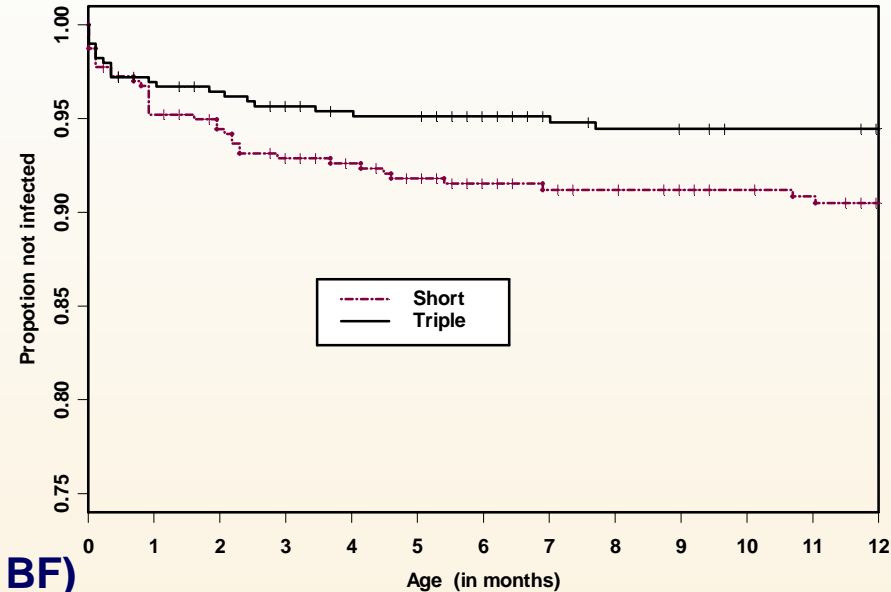
Flowchart – Randomized Controlled Trial



All infants: HIV infections


Log rank test $p = 0.029$
(stratified on centre and intention to BF)

Infant HIV-free rates to 12 months of age.RCT, by study stratum



	Triple		Short		Reduction
	Events (cum) / at risk	Rate (95% CI)	Events (cum) / at risk	Rate (95% CI)	
Birth	7/394	1.8 (0.9, 3.7)	10/402	2.5 (1.3, 4.6)	28%
6 weeks	13/375	3.3 (1.9, 5.6)	20/374	5.0 (3.3, 7.7)	34%
6 months	19/349	4.9 (3.1, 7.6)	33/339	8.4 (6.0, 11.6)	42%
12 months	21/333	5.4 (3.6, 8.1)	37/305	9.5 (7.0, 12.9)	43%

No major safety concerns up to 12 months post-delivery



Maternal disease progression to 18 months post delivery

Definitions

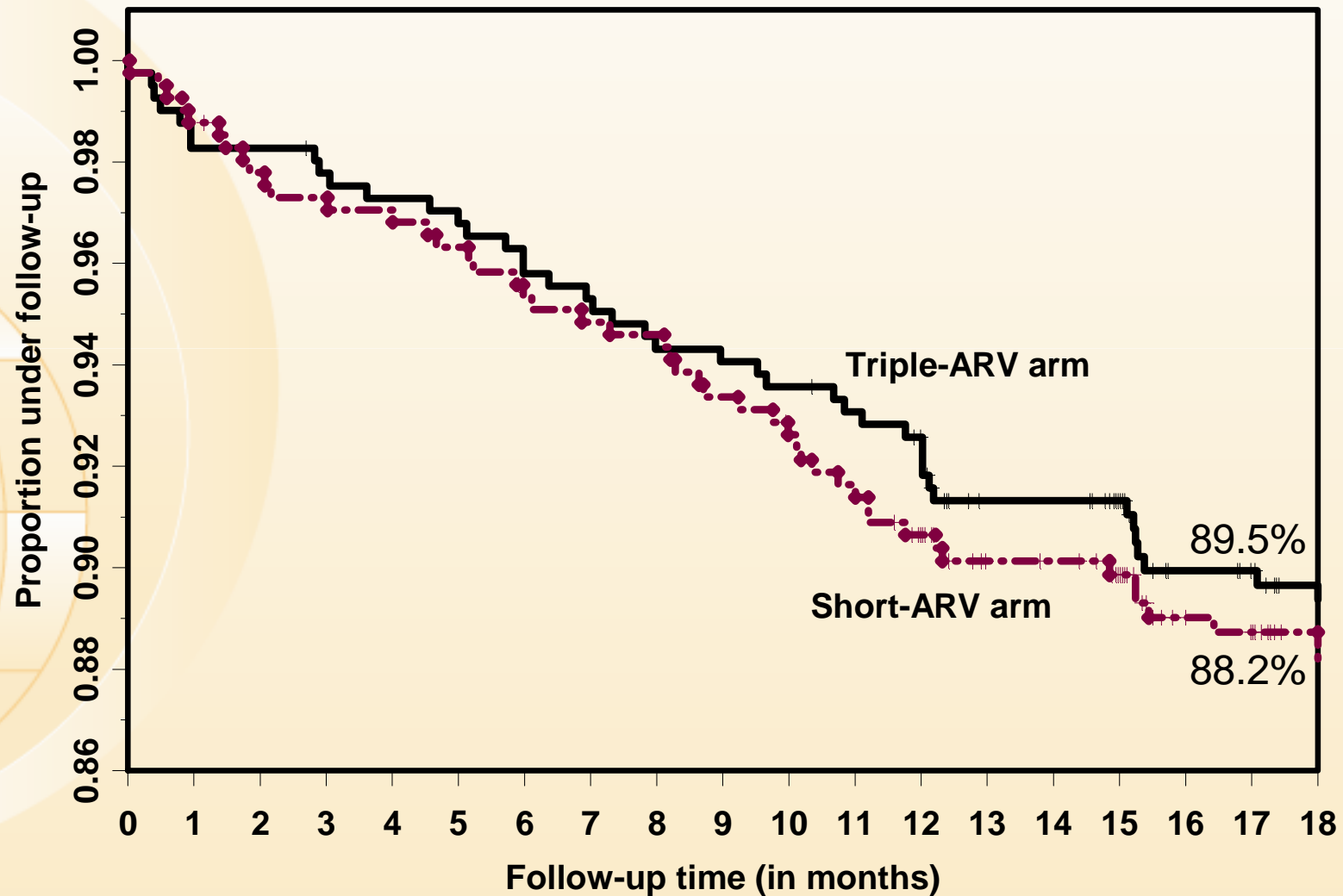
- Progression

- Stage 4 or CD4<200 (indication for ART as per previous guidelines)
 - Women censored if ART initiated before stage 4 or CD4<200
 - All women included
- Stage 3 or CD4<350 (indication for ART as per current guidelines)
 - Women censored if ART initiated before Stage 3 or CD4<350
 - Only women enrolled with Stage 1-2 and CD4>350 included

- Time Origin

- From date of delivery
- From date of cessation of ARV prophylaxis

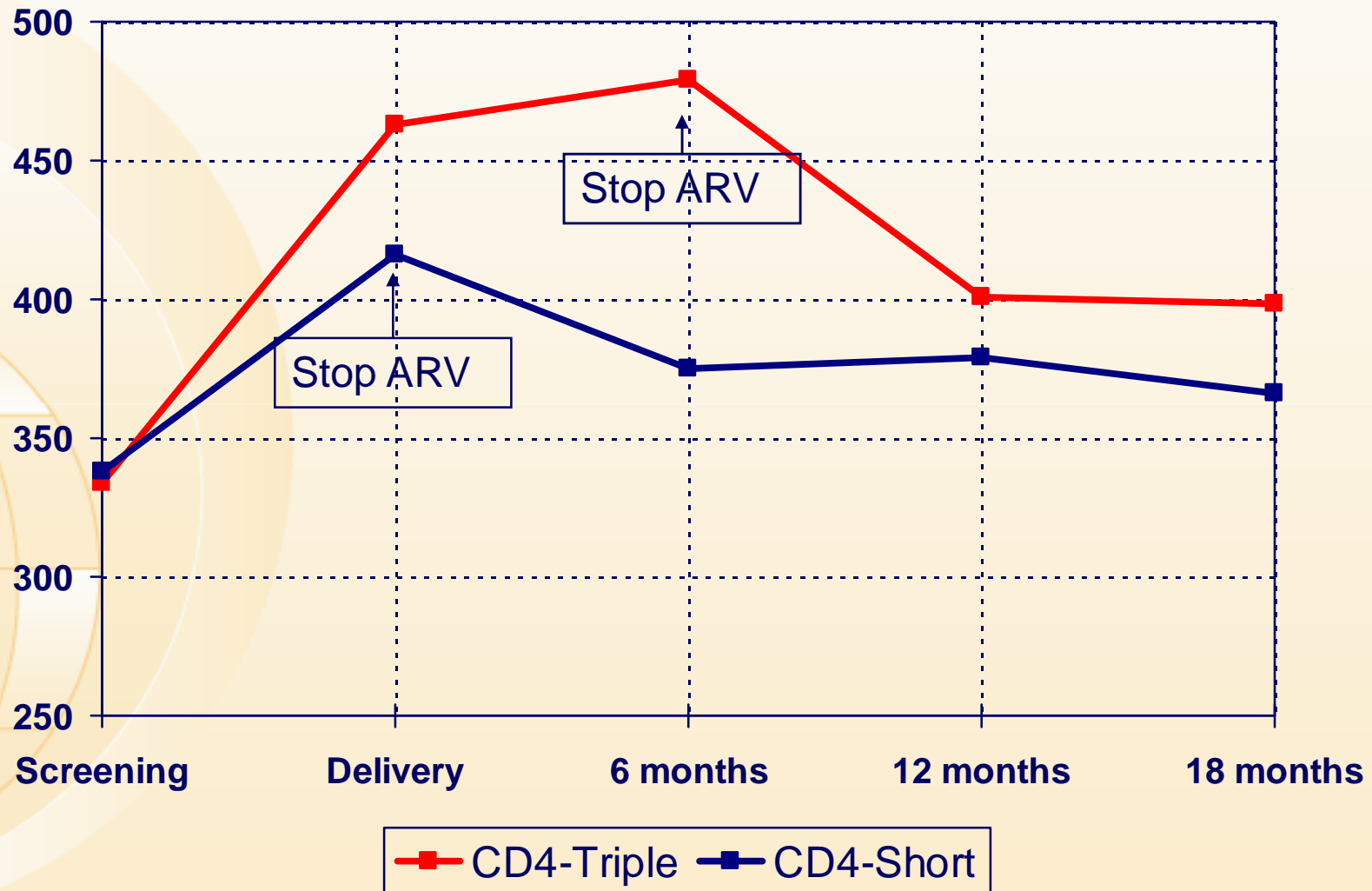
Rates of follow-up of mothers to 18 months postpartum



Mothers' Characteristics

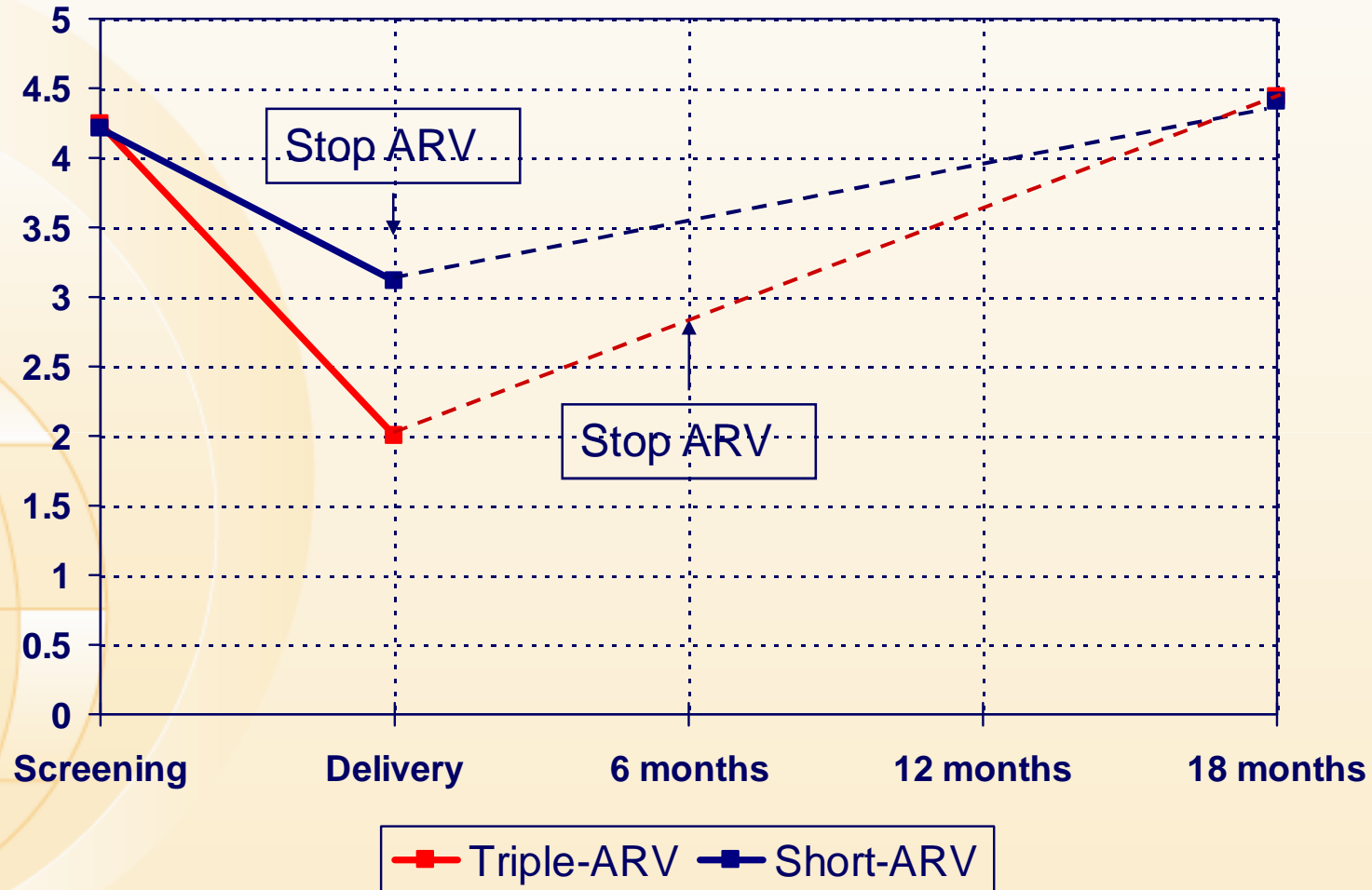
	Triple n=412	Short n=412
Age (mean years)	27	27
Primigravid (%)	18.0	18.0
At least primary education (%)	85.4	84.7
Working (%)	32.8	27.7
Married/regular partner (%)	95.2	97.1
Enrolment CD4 (median cells/mm ³)	336	339
Enrolment viral load (log ₁₀ copies/ml)	4.23	4.21
Duration of ARV prophylaxis (median weeks)		
- before delivery	6.0	6.4
- after delivery	19.0	NA

Median CD4 changes over time per study arm*



* Data censored at ART initiation

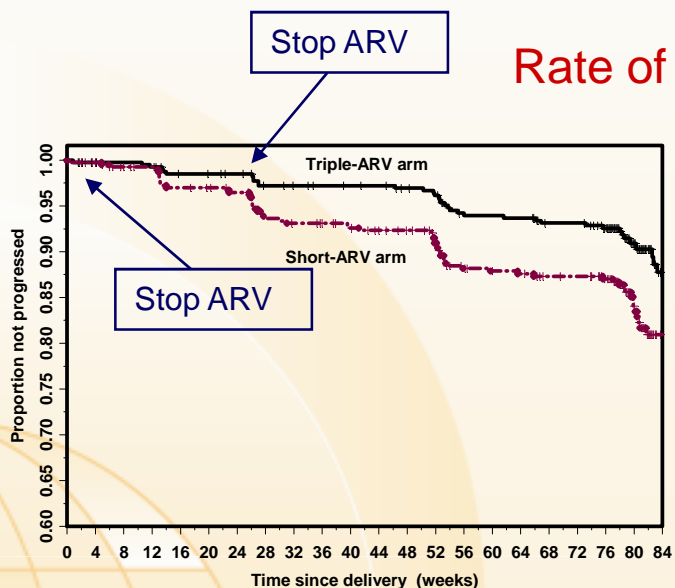
Median Log₁₀ Viral Load Changes over time per study arm*



* Data censored at ART initiation

Rates of Progression to Stage 4 or CD4<200 - All women

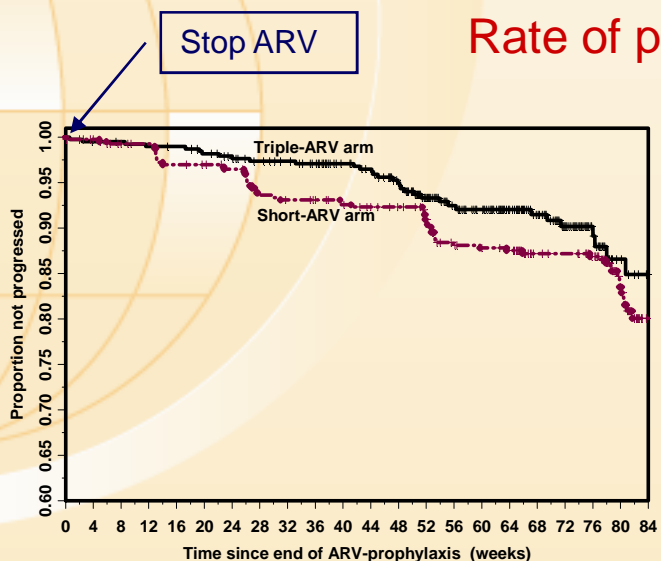
Rate of progression from delivery



	6 months	12 months	18 months
Short-ARV	(408) 6.4%	(362) 11.8%	(303) 19.6%
Triple-ARV	(405) 2.8%	(376) 6.1%	(332) 12.4%

P=0.003

Rate of progression from stopping ARV-prophylaxis

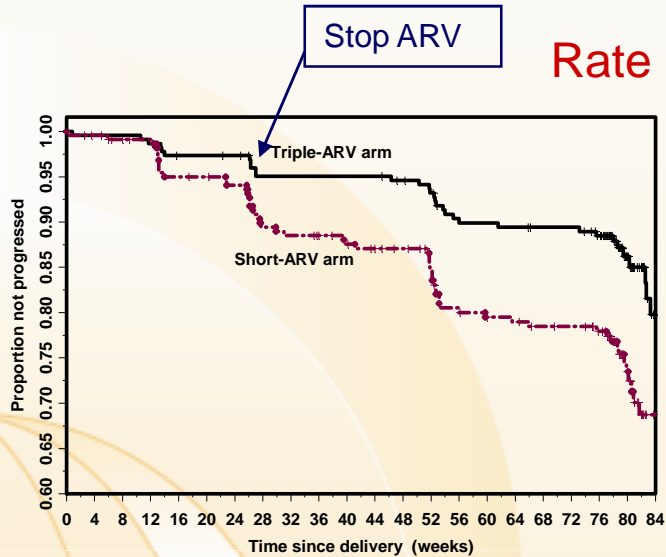


	6 months	12 months	18 months
Short-ARV	6.4%	11.8%	19.6%
Triple-ARV	(386) 2.6%	(358) 7.9%	(213) 14.7%

P=0.159

Rates of Progression to Stage 4 or CD4<200 Women CD4<350 at entry

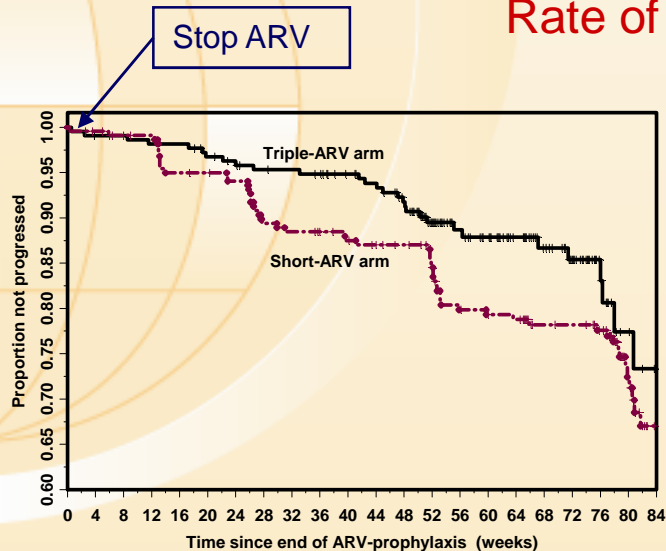
Rate of progression from delivery



	6 months	12 months	18 months
Short-ARV	(226) 10.6%	(192) 20.0%	(152) 32.4%
Triple-ARV	(226) 4.9%	(209) 10.1%	(186) 20.4%

P=0.002

Rate of progression from stopping ARV-prophylaxis

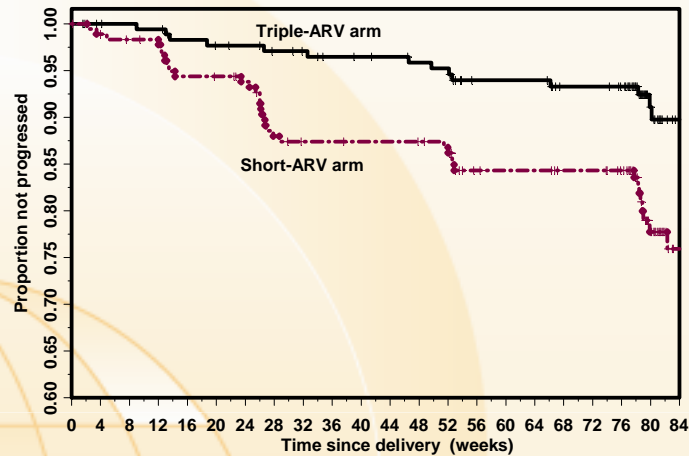


	6 months	12 months	18 months
Short-ARV	(226) 10.6%	(192) 20.0%	(152) 32.4%
Triple-ARV	(217) 4.7%	(199) 12.0%	(107) 25.9%

P=0.107

Rates of Progression to Stage 3 or CD4<350 Women with CD4>=350 at entry

Rate of progression from delivery

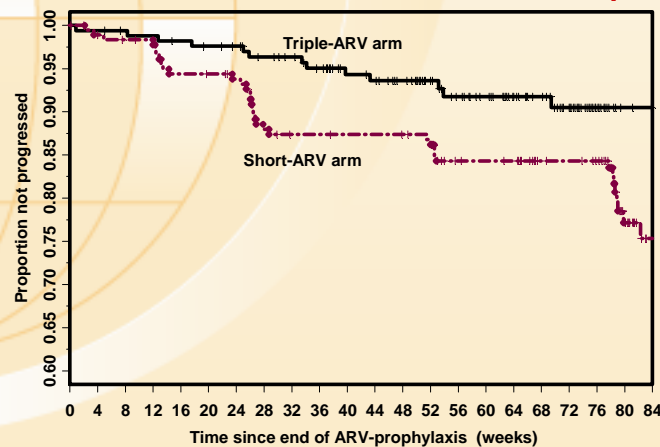


6 months 12 months 18 months

Short-ARV	(182) 12.0%	(151) 15.7%	(129) 24.1%
Triple-ARV	(179) 2.9%	(162) 6.1%	(138) 10.4%

P=0.002

Rate of progression from stopping ARV-prophylaxis



6 months 12 months 18 months

Short-ARV	(182) 12.0%	(151) 15.7%	(129) 24.1%
Triple-ARV	(168) 3.7%	(152) 8.2%	(98) 9.5%

P=0.013

Conclusions

- Balance of Benefits and Risks of Triple-ARV Prophylaxis:



- High rate of progression to CD4<200 (both arms) if CD4 at entry <350
 - Reinforces WHO recommendations to treat from 350
- High rate of progression to CD4<350 (both arms) if CD4 at entry >350
- Stresses importance of early initiation of therapy in pregnant women, or women desiring pregnancy

Participating Institutions



UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE



The Kesho Bora Team

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- Ndema Habib – Statistician
- Sihem Landoulsi – Data Management

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- Francois Rouet – Site Laboratory Coordination and Quality Assurance

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