THAB0106LB



Low acceptance of early antiretroviral therapy (ART) among post-partum women enrolled in IMPAACT PROMISE studies across the globe

Lynda Stranix-Chibanda, S. Brummel, K. Angelidou, C. Tierney, A. Coletti, K. McCarthy, J. Pilotto, M. Mutambanengwe, V. Chanaiwa, T. Mhembere, M. Kamateeka, G. Masheto, R. Chamanga, M. Maluwa, S. Hanley, E. Joao, G. Theron, A. Chandawale, M. Nyathi, B. Santos, L. Aurpibul, M. Mubiana-Mbewe, R. Oliveira, M. Basar, N. Chakhtoura, R. Browning, J. Currier, M.G. Fowler, PROMISE study team



Promoting Maternal and Infant Survival Everywhere



PROMISE study



- Randomized controlled trial began in 2010
- To determine optimal antiretroviral strategy to prevent vertical transmission of HIV and maintain maternal and infant health
- Across diverse care settings:
 - 1077HS where ART and formula feeding standard
 - 1077FF/BF where other antiretroviral strategies were standard plus formula feeding (FF) or breastfeeding (BF)





Promoting Maternal and Infant Survival Everywhere

1077BF Sites

1077HS Sites

1077BF/FF Sites

Legend:

70 sites in 15 countries



Study Design

- Healthy HIV-infected women
- Did <u>not</u> meet local criteria for ART
- Randomly assigned to different antiretroviral strategies to assess:
 - prevention of vertical transmission during pregnancy and post-delivery
 - infant safety
 - maternal health



1077 HS research question

Among women who did <u>not</u> meet local criteria for ART initiation and were past the period of risk for transmission:

- Is long term health better served by continuing or stopping ART?
 - HIV disease progression
 - ART complications





PROMISE 1077BF/FF Research Questions



ANTEPARTUM: Among women who do not meet criteria for initiation of ART for their own health, *what is the optimal intervention to prevent in utero and intrapartum transmission* of HIV to infants? Specifically, what is the relative safety and effectiveness of a single ARV prophylaxis regimen compared to triple ARV prophylaxis regimen for reducing the risk of transmission?



POSTPARTUM: Among HIV-infected women who do not meet criteria for initiation of ART for their own health, *what is the optimal intervention to prevent transmission of HIV to infants during breastfeeding*? Specifically, what is the relative safety and effectiveness of maternal ARV prophylaxis compared to infant ARV prophylaxis for reducing the risk of transmission?



MATERNAL HEALTH: What is the optimal intervention to preserve maternal health after the period of risk for MTCT? Specifically, among women who do not meet criteria for initiation of ART for their own health, are survival and other health outcomes improved by stopping or continuing a triple ARV regimen after the infant is no longer at risk?

START* study results announced

- ART in those with CD4 count <u>>500 cells/mm³</u> reduces risk of HIV disease progression
 - Inform active participants from June 2015
 - Strongly recommend women <u>not</u> receiving ART at that time to immediately initiate ART to optimise their own health
- Treatment initiation carried no financial cost
- Decision did not determine continued participation in the PROMISE studies

* The INSIGHT START Study Group. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. 27 August 2015 N Engl J Med 2015;373:795-807



Information giving

- Mixed methods approach
- Qualitative/quantitative responses
- Actively contacted participants
- START information giving session:
 - Structured script
 - Language chosen by the participant
 - Assessed comprehension
- Talking points included information about the START trial aims, study location and results



Talking Points provided in PROMISE "These results are important for women in **PROMISE.** One reason why **PROMISE** is being done is to look at whether it is better for women with higher CD4 counts who took ART during pregnancy or breastfeeding to keep taking ART or to stop taking ART after they are no longer pregnant or breastfeeding. Now that the START study has shown that it is better to start ART earlier, we recommend that all women in **PROMISE take ART.**"



Counselling

- Client-centered counselling session
 - Implications of START for the individual woman
 - Those not on ART discussed the offer of early ART with study staff and decided whether or not to accept early ART at that session
- Sessions documented in real time
 - Closed and open-ended questions on a data form
- Primary reasons for accepting or rejecting the offer of ART were recorded and categorized into a list of pre-set options



Early ART Uptake

- 5398 women enrolled
- 4,513 in active follow-up at that time — median 2.8yrs (8mos-6yrs)
- 4192 (93%) women traced and underwent information giving and counselling session
- 1,483 (35%) women <u>not</u> on ART
 - 984 (66%) accepted ART
 - 499 (34%) declined ART



Early ART uptake by country





Reasons given for <u>accepting</u> ART

Reason	1077BF/FF	1077HS
Concerned about health	46%	43%
Understands treatment is now recommended	35%	36%
Concerned about CD4 count	16%	13%
Other reason	2%	7%



Reasons given for <u>declining</u> ART at first

Reason	1077BF/FF	1077HS
Wants more time to consider	44%	33%
Feels well/knows CD4 count is high	13%	28%
Concerned about HIV disclosure	9%	3%
Concerned about commitment to life-long ART	9%	7%
Concerned about potential side effects	8%	8%
Other reason	7%	14%
Knows treatment not indicated per current local guidelines	6%	0%
Too busy with child care or other responsibilities	2%	5%
Concerned about adherence	1%	5%



Conclusion



- Substantial number did not initiate early ART after an <u>initial</u> counselling session
- Despite prior exposure to intense ART education and HIV monitoring within a highlyresourced clinical trial setting
- More time needed to consider the offer to start early ART for their own health
 - Continued to counsel through study exit, the proportion women who remain off ART decreases with each visit
- Of importance for the "Treat All" strategy







Promoting Maternal and Infant Survival Everywhere

The PROMISE protocol team gratefully acknowledges the dedication and commitment of the more than 5,000 women and motherinfant pairs without whom this study would not have been possible.

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network was provided by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) under Award Numbers UM1AI068632 (IMPAACT LOC), UM1AI068616 (IMPAACT SDMC) and UM1AI106716 (IMPAACT LC), with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.



Study Teams 1077BF/FF/HS



Sponsors: US National Institutes of Health (D Gnanashanmugam, K Klingman, L Purdue, G Siberry, LM Mofenson)

Protocol Chairs and Vice Chairs: MG Fowler *BF*: J McIntyre, T Chipato, P Flynn; *HS*: J. Currier, J. Pilotto

Operations Center: M Allen, K George, M Valentine, K McCarthy, V Hardy; Statistical and Data Management Center: D Shapiro, T Fenton, K Butler, M Qin, C Marr, C Tierney, K Angelidou, M Basar, L Marillo, A Manzella, A Zadzilka Laboratory Center: S Fiscus, A Loftis **CMC**: D Bhattacharya, J.Currier R Hoffman, A Gupta, G Theron, B Chi, P Flynn, M Owor **PROMISE Principal Investigators:** : R Bhosale, P Sambarey, B Makanani, M Mallewa, T Taha, F Martinson, D Moodley, R Bobat, S Pillay, G Theron, A Violari, L Fairlie, A Coovadia, P Mlay, M Mbewe, M Losso, E Machado, J de Menezes, G Duarte, R Sperhacke, J Pinto, R Kreitchman, B Santos, L Wei, J Pape, J Sanchez, E Sandoval, K Chokephaibulkit, J Achalapong, G Halue, P Yuthavisuthi, S Prommas, C Bowonwatanuwong, V Sirisanthana, S Riddler, P Kumar, W Shearer, R Yogev, G Scott, S Spector, C Cunningham, M Bamji, E Cooper, A Wiznia, J Hitti, P Emmanuel, R Scott, M Acevedo, S Nachman, T Jones, S Rana, M Keller, A Stek, M Rathore, E McFarland, A Puga, A Agwu, T Chen, R Van Dyke, J Deville, M Purswani, P Tebas, M Fischl

