HPTN 052 2011: A NEW REALITY

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Principal Investigator
The HPTN 052 Timeline: NOT (!) the “Fast Track”

- ART research toward prevention of HIV: 1993
- ART Working Group Presentation to Advisory Board: 1999
  - First choice, pre-exposure prophylaxis, rejected!
- HPTN 052 Protocol development: 2000
- ACTG 5175 Requirement: 2001
- HPTN 052 Drug Procurement: 2002-4
- HPTN 052 Pilot: 2005
- HPTN 052 Enrollment: 2007-10
- HPTN 052 DSMB: (#11) April 28, 2011
Bench to Bedside (SLOWLY)  
“TEST AND TREAT” in Development


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- HPTN 052+ Requirement: 2001 and ACTG 5175
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To evaluate the effectiveness of ART to prevent the sexual transmission of HIV in serodiscordant couples where the infected partner is ART-naïve with CD4 count of 350 – 550.

To evaluate the optimal time to initiate ART (250-200 cells/mm$^3$ vs. between 350 and 550 cells/mm$^3$) in order to reduce morbidity and mortality in people infected with HIV.
HPTN 052 Study Design

HIV+ subjects with CD4 350 to 550 cells/µL
1763 serodiscordant couples

Randomization

Immediate ART
CD4 350-550

HAART

Delayed ART
CD4 ≤250

Endpoints:

i) Transmission Events
ii) OIs, other Clinical Events-WHO 2,3,4 & Death
iii) ART Toxicity
HPTN 052 RECOGNITION
Who Made this Study Possible?

• Thirteen Sites (9 Countries)
• The Network Lab at JHU
• SCHARP/U Wash
• Family Health International
• NIH Program Officers
• HPTN Leadership
• Six pharmaceutical partners
• ACTG Collaborators
• PARTICIPANTS!
IPEC Rio de Janeiro, Brazil
HGNI Rio de Janeiro, Brazil

Jose Pilotto, Ana Claudia Nunes Rodrigues, Tania Brum, Aline Ramalho, Cintia Lopes da Silva, Tatianna Cha, Monica Couto, Natalia Lima, Luciane Viana, Lara Somma Portela, Renata Oliveira, Flavia Duarte, Ana Carolina Alves, Patrícia Duarte, Luciana Pereira
Porto Alegre, Brazil

Front: Andre, Claudio, Rui, Andrea, Karin, Nava
Middle: Ivana, Ivete, Rita, Cristina, Kelin, Elizabeth, Marineide, Yvonne, Caroline, Mariana, Mara
Back: Rosana, Inelva, Cleia, Lourdes, Edmundo, Dimas, Breno, Marcelo, Vicente, Andre B.
Chennai, India
NATIONAL AIDS RESEARCH INSTITUTE, CTU, PUNE, INDIA – HPTN 052 STUDY

- Gadikhana CRS
- Community Staff
- NARI Staff
- Regulatory Staff
- Laboratory Staff
- Community Staff
- Data Management
Above: Dr. Joel Gallant, Prof. David Celentano (CTU PI), Dr. Suwat Chariyalertsak (Site PI/CRS Leader), Louise Walshe

Front Row: Marisa Guptarak, Dr. Taweewat Supindham, Chanidapa Prasaraakee, Thanyalak Thongphan, Cholticha Ruangyuttikarn (Study-Co), Kanlaya Wongworapat, Wilawan Chaikan, Wipada Cheewawat, Dr. Natthapol Kosashunhanan

Second Row: Sontiya Mueanapai, Dr. Voravit Suwanvanichkij, Dr. Kriengkrai Srithanaviboonchay (Co-PI), Rassamee Keawvichit, Dr. Suwat Chariyalertsak, Dr. Nuntisa Chotirotsniramit (Co-PI), Dr. Sunida Thetket, Antika Wongthanee, Boonyarat Puisaeng, Supatra Pookmanee,

Back Row: Kittipong Rungruengthanakit, Piyathida Sroysuwan, Sineenart Nimsakul, Rojana Srichan, Niranporn Jaikuar, Saowalak Kunjuya, Napha Ruengtarin, Praphapin Suriyasorpi
Lilongwe, Malawi

Front: Tiwonge Mtande, Mwayi Chipeta, Hellen Masowo, Ida Shumba, Emma Kachipapa, Lucy Dzama, Dorothy Sichali and Kenneth Kasambara
Not pictured: Francis Martinson, Wiza Kumwenda, Bertha Maseko, Esnath Mkandawire
Seated: Thandiwe Chirenda, Cleopatra Langa, Patience Sibanda, Mary Tichareva, Wilfred Gurupira, Jimjika Batani, James Hakim, Nehemia Nhando, Zvenyika Gomo, Elizabeth Magada, Jester Makwara, Fiona Mutsi, Jessie Musundire, Violet Mandioma
Standing: Memory Chikosha, Monica Nyamuhuka, Nancy Jokonya, Loveness Mugari, Bevelyn Muhwati, Thembelihle Bafana, Collen Pamire, Miriam Njaya, Beauty Nyamayaro, Christina Maluwa, Misai Hukuimwe, Justice Gumbo, Ernest Chimuka, Jacob, Kagona, Mugove Chahwanda, Vernon Murenje, Gilton Kadzyanike
Not pictured: Fadzayi Mandima, Lucia Chirongoma
Gabarone, Botswana
Soweto, South Africa
Kisumu, Kenya

Seated: Elizabeth Rambara, Erica Mimba, Beatrice Nyagol
Front Row: Clement Zeh, Boaz Oyaro, Vitalis Sewe, George Ouma, Lisa Mills, Ray Goldstine, Arthur Ogendo, Victor Mudhune, David Omungi
Back row: Emily Kerubo, Kayla Laserson, Elizabeth Ayuo, Anne Gumbo, Elizabeth Ogutu, Jean Muhanji
In front of rock: Angela Were, Carren Winnie Ouma, Sylvia Odhiambo, Janet Adhiambo
On ladder: Erick Ondieki, Victor Akelo, Hillary Nengo
SCHARP Team

Front: Lei Wang, Xin Li, Sue Tracy-Waisanen, San-San Ou, Jami Moksness
Middle: Leslie Cottle, Stacie Kentop, Debbie Lands
Back: Ying Chen, Maija Anderson
Other team members at FHI

Andrea Jennings, Phaedrea Watkins, Jackie Talley, Rhonda White, Jonathan Lucas
Not pictured: Cheryl Cokley
VERBATIM DSMB Recommendations:

• The Board recommends that the results of the trial be announced as soon as possible.
• The Board congratulates the team for a very well-done trial that definitively shows that immediate ART reduces transmission of HIV.

HPTN 052 HAS NOT BEEN STOPPED – Modifications are underway with input from all parties

The Sponsor and investigators have decided to offer all subjects ART so as to realize the BENEFITS of results to date
HPTN 052 Results

- Immediate ART (350 – 550) reduced transmission to uninfected partner by >96% (27 fold decrease – [HR]= 0.038; 95%CI 0.005 – 0.280)
- Immediate ART conferred a clinical benefit for infected partner
- CD4 level is not a reliable predictor of transmission
HPTN 052 IDEAS (I)

- Couples Counseling and HIV Incidence
  - Are we inspiring unprotected intercourse?
  - Are we inspiring partner risk behaviors?

- Delaying ART till CD4<250>200 and the health of the HIV infected study subjects
  - Are the WHO Guidelines correct?
• At the time of the NIH press briefing (May 12, 2011) recommended as urgent by the DSMB
  – Does ART reduce 96.3% of HIV transmission, or more or less?

• What are the (unpredictable) public health impacts of HPTN052
  – For those committed to “Test and Treat”?
  – For WHO discordant couples Guidelines
  – For the New York Times
THERE is now, for the first time, hard clinical evidence of an effect that AIDS doctors have suspected for years: If you are H.I.V.-positive, being on antiretroviral drugs will probably save not only your life, but also the lives of your sexual partners.

This month, a randomized clinical trial — the gold standard in medical research — showed that the drugs lowered the chances of infecting a partner by 96 percent.

This is good news for the infected and their lovers. But it is a moral dilemma for doctors whose infected patients do not want to start taking drugs immediately, usually because they do not yet feel sick and have heard exaggerated rumors about side effects.

What does a responsible doctor do with a patient who is sexually active and teeming with a fatal and incurable virus? Advise him to use condoms and trust him to act decently? Beg?

Behind each doctor — whose primary duty is to one patient — there is a government public health bureaucracy, whose duty is to protect the whole country. The epidemic has been killing Americans for 30 years now.
HPTN052 IDEAS (III)

- The VERY strange life of ART through HPTN 052
  
  - At inception local IRBs questioned the treatment of HIV-infected people with CD4 >200
  
  - In 2009 WHO indicated best treatment at CD4<350
  
  - NIH and the study investigators are committed to offering ART to all subjects, most of whom have CD4 >350, above WHO or country guidelines
  
  - The industry, country and local IRB responses?
Future Plans for HPTN 052

• Offer ART to all study subjects in delay arm

• Continue study for at least 1 year:
  – Continued durability of prevention benefit?
  – Any differences in prevention benefit in those in delayed arm
  – Clinical events and toxicity in both arms
  – Adherence to ART
WHAT DOES HPTN 052 MEAN?

- Why did we observe a transmission event in the ART arm?
- What do we tell couples?
- Did we observe greater adherence to ART than expected?
- Test and Treat?? HPTN 052 serves as the cornerstone of the TNT strategy since without remarkable transmission suppression the strategy would fail.

HPTN 052 results are “A SINA QUA NON”
WHAT DOES HPTN 052 MEAN?

• But HPTN 052 does NOT mean a TNT strategy will succeed. We must redouble our efforts to explore TNT and at all cost avoid hyperbole toward unrealistic expectations.

• HPTN 052 results must lead to experiments with combination prevention strategies, including TNT, that the HPTN can show will work.