HPTN 052 2011: A NEW REALITY

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Principal Investigator
HPTN 052: Study Objectives/Goals

- 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

- Phase III, randomized multi-center, controlled clinical trial in HIV serodiscordant couples
- Composite primary endpoint of linked HIV infections in the uninfected partner and clinical events in the infected partner
- 1763 couples enrolled
  - 97% heterosexual
- Median CD4 at entry - 436
- Conducted in Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, United States & Zimbabwe
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!
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 Prasarakkee, Thanyalak Thongphan, Cholticha Ruangyuttikarn (Study-Co), Kanlaya Wongworapat, Wilawan Chaikan, Wipada Cheewawat, Dr. Natthapol Kosashunhanan

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Back Row :  Kittipong Rungruenthanakit, Piyathida Sroysuwan, Sineenart Nimsakul, Rojana Srichan, Niranporn Jaikuar, Saowalak Kunjuya, Napha Ruengtarin, Praphapin Suriyasorpi
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 Prevention Results

- **39 total infections**
  - 28 linked infections
    - 27 delayed arm
    - 1 immediate arm
      - 17 of 27 infections in delayed arm occurred when the index partners’ CD4 was >350
  - 7 unlinked infections
    - 4 delayed arm
    - 3 immediate arm
  - 4 infections still being analyzed (all in delayed arm)
HPTN 052 Results

Viral Load Data
- Median entry of all ppts 4.4 log

- Delayed arm remained at about 4.5 log (until ART initiated)
- Immediate arm rapidly decreased to below 400 copies/ml
- Median VL for transmitting partners at visit prior to seroconversion was 4.91 log
- More detailed analysis to determine if specific VL level is predictive of transmission underway
HPTN 052 Clinical Results

- 105 morbidity and mortality events (trend, but did not meet pre-set criterion of >20% - p=0.07 – however, when analyzed without pre-set then p= 0.01)
  - 65 in delayed arm
  - 40 in immediate arm

- 20 cases of extrapulmonary TB (p= 0.0013)
  - 17 in delayed arm
  - 3 in immediate arm

- 23 deaths (NS)
  - 13 in delayed arm
  - 10 in immediate arm
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
HPTN 052  IDEAS

• Couples Counseling is Important
• Unlinked Transmissions Matter
• Are the WHO Treatment Guidelines Correct?
WHAT DOES HPTN 052 MEAN?

• Why did we observe a transmission event in the ART arm? Stay tuned for further results.
• What do we tell couples?
• Did we observe greater adherence to ART than expected? Is there “altruistic adherence”?
• 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 TNT… “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 avert the transmission of HIV-1.