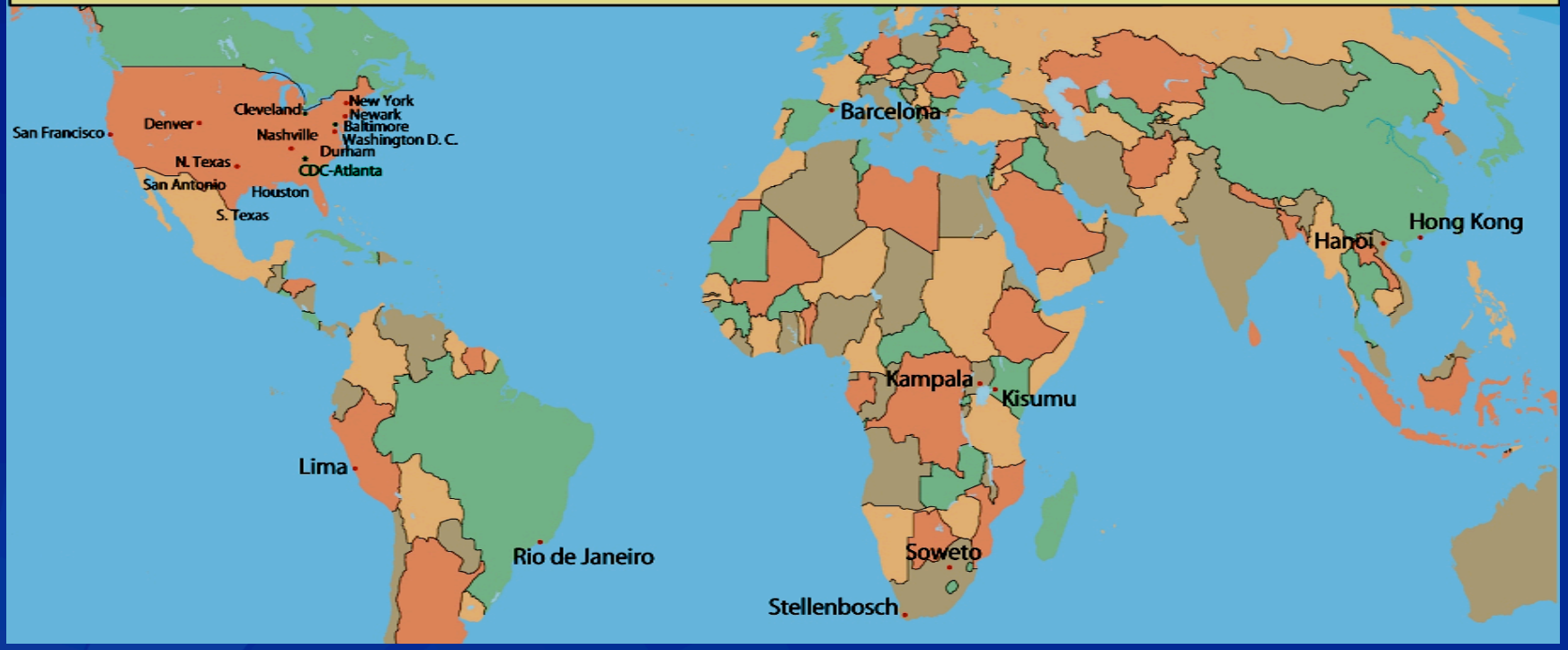
Stop TB Working Group on New Drugs
Annual Meeting
October 26, 2011

Tuberculosis Trials Consortium

Andrew Vernon, MD, MHS
Clinical Research Branch

National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention
Division of Tuberculosis Elimination

TB Trials Consortium 2010-2020



9 International and 11 domestic sites

https://www.tbtrialsnetwork.org/tbtc/
http://www.cdc.gov/tb/topic/research/tbtc/introduction.htm

Estimated TBTC Capacity

Subject Type	Estimated Yearly Enrollment
Smear-positive pulmonary	1842
Smear-negative pulmonary	1723
Extrapulmonary	761
Drug-resistant, non-MDR	344
MDR/XDR	163
TB/HIV co-infected	855
Children	370
LTBI, presumed drug-susceptible	3719
LTBI, presumed drug-resistant	319

*Results of site survey, April 2010; capacity decreased since, due to (1) loss of Manila site and (2) diminished fundiing

TBTC Priorities

1) **Treatment of LTBI:** shorter, safer, better tolerated, fewer interactions, and (ideally) active against MDR LTBI also
2) **Treatment of DS disease:** shorter, safer, better tolerated, fewer interactions, effective for high risk patients
3) **Treatment of DR disease:** shorter, safer, better tolerated, more effective, less costly
4) **Key subgroups:** HIV-infected; children & mothers
5) **Trial design:** surrogate endpoint for relapse
6) **Collaborations :** effective partnerships

1-Treatment of LTBI

- **TBTC Study 26 -3 mos. once weekly INH/RPT vs 9 mos daily INH for LTBI; f/u continues for added HIV+ and children 2-12**
- ***TBTC Study 29X****- randomized trial comparing RPT(10)HRZ, RPT(15)HRZ, RPT(20)HRZ & RIF (10)HRZ; Primary endpoint=tolerability*
- ***TBTC Study 31*** *– Treatment-shortening based on daily RPT*
- ***TBTC Study 32*** *– Opti-Q (optimal dose of levofloxacin for MDR); compares 4 doses of levofloxacin; 20 patients per arm; enroll mid-2012 if co-funded by NIH*
- **TBTC Study 33: Directly observed vs. self-administered weekly RPT/INH; enrollment – 1st quarter 2012**
- **ACTG 5295/TBTC Study 34** *– Evaluation of Gene Xpert in low-incidence setting; collaborative study with ACTG; sample size=1634 patients; at least 1144 from U.S. sites; 25% AFB smear +; TBTC will enroll patients from U.S. sites*
- **ACTG 5300/TBTC Study 35 – TMC207 for HH-contacts to MDR; collaborative study with ACTG; sample size 6000+ patients (pilot 1000 patients, with completion if**

2-Treatment of DS disease

- ***TBTC Study 26*** *-3 mos. once weekly INH/RPT vs 9 mos daily INH for LTBI; f/u continues for added HIV+ and children 2-12*
- **TBTC Study 29X- randomized placebo-controlled comparison RPT(10)HRZ-- RPT(15)HRZ-- RPT(20)HRZ -- RIF (10)HRZ; Primary endpoint=tolerability; secondary endpoints=efficacy, PK; enrollment Oct 2011**
- **TBTC Study 31 – Treatment-shortening daily RPT (S29-29B-29X-A5311-Riomar-CapeTown)**
- ***TBTC Study 32*** *– Opti-Q (optimal dose of levofloxacin for MDR-TB); compares 4 doses of levofloxacin; sample size – 20 patients per arm; enroll mid-2012 if co-funded by NIH*
- ***TBTC Study 33:*** *Directly observed vs. self-administered weekly RPT/INH; enrollment – 1st quarter 2012*
- **ACTG 5295/TBTC Study 34** *– Evaluation of Gene Xpert in low-incidence setting; collaborative study with ACTG; sample size=1634 patients; at least 1144 from U.S. sites; 25% AFB smear +; TBTC will enroll patients from U.S. sites*
- ***ACTG 5300/TBTC Study 35*** *– TMC207 for MDR-contacts; collaborative study with ACTG; sample size – 6000 patients (2000 households); Pilot phase of 1000 patients, with completion if feasibility shown*

3-Treatment of DR disease

- ***TBTC Study 26*** *-3 mos. once weekly INH/RPT vs 9 mos daily INH for LTBI; f/u continues for added HIV+ and children 2-12*
- ***TBTC Study 29X-*** *randomized placebo-ctrl comparison RPT(10)HRZ-- RPT(15)HRZ-- RPT(20)HRZ -- RIF (10)HRZ Primary endpoint=tolerability; key secondary endpoints=efficacy, PK; enrollment Oct 2011*
- ***TBTC Study 31*** *– Treatment-shortening daily RPT (S29-29B-29X-A5311-Riomar-CapeTown)*
- **TBTC Study 32 – Opti-Q (optimal dose of levofloxacin for MDR-TB); compares 4 doses of levofloxacin; sample size – 20 patients per arm; enroll mid-2012 if co-funded by NIH**
- ***TBTC Study 33:*** *Directly observed vs. self-administered weekly RPT/INH; enrollment – 1st quarter 2012*
- **ACTG 5295/TBTC Study 34** *– Evaluation of Gene Xpert in low-incidence setting; collaborative study with ACTG; sample size=1634 patients; at least 1144 from U.S. sites; 25% AFB smear +; TBTC will enroll patients from U.S. sites*
- ***ACTG 5300/TBTC Study 35*** *– TMC207 for MDR-contacts; collaborative study with ACTG; sample size – 6000 patients (2000 households); Pilot phase of 1000 patients, with completion if feasibility shown*

4-Key Subgroups

- **HIV-TB --** *increasingly engaged b y ACTG, IMPAACT, HPTN;* ***TBTC will continue to enroll and evaluate HIV+ patients; S26 assessing HIV+***

- **Children and mothers –** *Pediatric Interest Group proposing new studies; S26 assessing young children 2-12 and S26PK to evaluate children 0-10; interest in pediatric PK for bedaquiline (TMC207)*

5- Trial Design

- **Surrogate endpoints and Biomarkers –**
  - *S29X assessing time to positivity in MGIT at all sites*
  - *Sub-study will compare TTD in MGIT and GeneXpert*
  - *Multiple biomarker sub-studies underway with collaborating investigators*

Thank You