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

Tuberculosis Trials Consortium

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Clinical Research Branch
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

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

*Results of site survey, April 2010; capacity decreased since, due to (1) loss of Manila site and (2) diminished funding*
**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 feasibility shown)
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)
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4-Key Subgroups

- **HIV-TB** -- increasingly engaged by 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