China Tuberculosis Clinical Trial Consortium (CTCTC) and its RePORT International Potential

Zhang Yao, FHI 360 Beijing Office
Liu Yuhong, CTCTC Central Office
Sun Zhaogang, Beijing Chest Hospital
CTCTC Beginnings: 2013

• High quality clinical trial sites in high burden countries are urgently needed

• NIAID developing collaborations with lead funding agencies in various countries so they may conduct high quality clinical research in TB.

• China’s TB hospital leaders announced formation of the China TB Clinical Trials Consortium (CTCTC) in Harbin, China in September.

• FHI 360 was selected to work with NIAID/DAIDS to support CTCTC network leaders at the China Clinical Center on TB, located at the Beijing Chest Hospital

• The Consortium vision is to lead China’s effort in conducting high standard clinical research of TB treatment, diagnostics and vaccine.
Strengthened international partnership
CTCTC Study Sites

19 Sites in China

- CTCTC Study Sites
- Participating Study Sites
  1. Shenyang Chest Hospital, Shenyang
  2. Beijing Chest Hospital, Beijing
  3. Tianjin Haihe Hospital, Tianjin
  4. Shandong Provincial Chest Hospital, Jinan
  5. Shaanxi Provincial Tuberculosis Institute, Xi’an (not a CFDA certified site)
  6. Xinxiang No. 1 People’s Hospital, Xinxiang
  7. Henan Provincial Infectious Disease Hospital, Zhengzhou
  8. Wuxi No. 5 People’s Hospital, Wuxi
  9. Zhejiang No. 3 People’s Hospital, Zhenjiang
  10. Shanghai Pulmonary Hospital, Shanghai
  11. Shanghai Public Health Clinical Center, Shanghai
  12. Chengdu Public Health Clinical Center, Chengdu (not a CFDA certified site)
  13. Chongqing Tuberculosis Institute, Chongqing
  14. Wuhan Institute for TB Control, Wuhan
  15. Changsha Central Hospital, Changsha
  16. Fuzhou Pulmonary Hospital, Fuzhou
  17. The 1st Affiliated Hospital of Xiamen University, Xiamen
  18. Guangzhou Chest Hospital, Guangzhou (not a CFDA certified site)
  19. Shenzhen Donghu Hospital, Shenzhen
<table>
<thead>
<tr>
<th>Site</th>
<th>No. of 1st-visit pulmonary TB cases</th>
<th>MDR among admitted patients</th>
<th>Children among admitted patients</th>
<th>Patients living in nearby districts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shanghai PH</td>
<td>2,500</td>
<td>8%</td>
<td>30%</td>
<td>40%</td>
</tr>
<tr>
<td>Shanghai pulmonary</td>
<td>6,190</td>
<td>15%</td>
<td>5%</td>
<td>60%</td>
</tr>
<tr>
<td>Guangzhou</td>
<td>5,198</td>
<td>6%</td>
<td>4%</td>
<td>35%</td>
</tr>
<tr>
<td>Tianjin</td>
<td>2,543</td>
<td>12%</td>
<td>0</td>
<td>85%</td>
</tr>
<tr>
<td>Shandong</td>
<td>6,432</td>
<td>7%</td>
<td>6%</td>
<td>58%</td>
</tr>
<tr>
<td>Beijing</td>
<td>6,432</td>
<td>5%</td>
<td>2%</td>
<td>24%</td>
</tr>
<tr>
<td>Chongqing</td>
<td>NA</td>
<td>8%</td>
<td>5%</td>
<td>70%</td>
</tr>
<tr>
<td>Chengdu</td>
<td>7,484</td>
<td>13%</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>Fuzhou</td>
<td>2,963</td>
<td>4%</td>
<td>1%</td>
<td>44%</td>
</tr>
<tr>
<td>Wuhan</td>
<td>6,387</td>
<td>3%</td>
<td>1%</td>
<td>78%</td>
</tr>
</tbody>
</table>
• Topics covered:
  ✔ ICH GCP
  ✔ Research ethics
  ✔ Data management
  ✔ QC/QA
  ✔ GCLP
  ✔ On-site lab training (Kathy Eisenach)
CTCTC Management Structure

- CTCTC Director Board
- Coordinating Center
- FHI (with bi-weekly report to NIH)
- Ethics Unit
- Training
- Scientific Panel
- Lab Unit
- QC, M&E Unit

Connections:
- Advising
- Co-managing
- Hands-on support
Standards and documentation established

China Tuberculosis Clinical Trial Consortium (CTCTC)
Clinical Trial Standard Operating Procedures (SOPs)

CTCTC Network Minimum Standards for TB Clinical Trials

<table>
<thead>
<tr>
<th>Protocol Title</th>
<th>Trial Phase</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The lead institution is responsible for ensuring below items meet minimum standards:

Clinical Trial Protocol
- The protocol has been reviewed and approved by the CTCTC Scientific Review Committee.
- The protocol, informed consent, and other trial participant-related documents have been reviewed and approved by the Central Institutional Review Board/Committee (IRB/EC).
- The IRB/EC have established policies and standard operating procedures (SOPs).
- The clinical trial has been approved by CFDA (if applicable).

Principal Investigator (Lead PI and site PI)
- Qualifications and experience, must have the following credentials:
  - A minimum of two (2) years of relevant TB research experience - including significant involvement as a clinical study investigator, experience in the design analysis, dissemination, and management of research pertaining to TB interventions.
  - Responsible for the proper conduct of the trial throughout all stages of the trial.

Appendix 1

CTCTC Network Minimum Standards for TB Clinical Trials, Version 1.0, June 2016
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THE SCIENCE OF IMPROVING LIVES
<table>
<thead>
<tr>
<th>Area</th>
<th>Description of Study</th>
<th>Enrollment target</th>
<th>Sponsor</th>
<th>Start date</th>
<th>Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic</td>
<td>Validation study of a new TB skin test that uses ESAT-6 and CFP-10</td>
<td>1,500</td>
<td>Longcom Biopharma</td>
<td>August 2015</td>
<td>Enrolling</td>
</tr>
<tr>
<td>DS Treatment</td>
<td>18-week with PZA Prolongation and adding Lfx</td>
<td>3,900</td>
<td>China Ministry of Science and Technology (MOST)</td>
<td>July 2016</td>
<td>About to enroll</td>
</tr>
<tr>
<td>DS Treatment</td>
<td>TRUNCATE-TB: several 2-month DS regimens with multi-arm-multi-stage design</td>
<td>200</td>
<td>Singapore and UK gov.</td>
<td>TBD</td>
<td>Feasibility discussion</td>
</tr>
<tr>
<td>MDR Treatment</td>
<td>STREAM 2: 6-9 months treatment with/without bedaquiline</td>
<td>175</td>
<td>Union</td>
<td>December 2016</td>
<td>Planning</td>
</tr>
<tr>
<td>MDR Treatment</td>
<td>Bedaquiline post-market Observational Cohort</td>
<td>800</td>
<td>Janssen</td>
<td>March 2017</td>
<td>Planning</td>
</tr>
</tbody>
</table>
RePORT International Potential

- Strong interest from Consortium leadership to join RePORT International
  - Fast learning track to improve research quality
- Common protocol has been shared and discussed with member sites
- Meetings held to discuss feasibility and plans
  - Committed to data sharing concept
  - May be challenging for sample exportation given tight MOST policy
Current capacity

- Storage facility in place at all sites.
- All but one sites routinely store TB isolates.
- Three sites have experience in bio-repository establishment (plasma and cells).
- Beijing Chest Hospital receives funding from municipal government and is most experienced.
Beijing Chest Hospital

Facilities

- Space 150 m²
- -80°C fridge 20; liquid nitrogen container
- Temperature monitor
- Lab security
- Electronic info system
Plan

• Pilot project in planning with technical support from DAIDS/Westat/FHI 360.
  – MOST funded DS trial as the parent project
  – Start from 5 sites, with minimal target enrollment of 100 / sites
  – Common protocol is being modified to accommodate shorter treatment
  – Westat consultant to visit pilot site
• Long-term goal to build bio-repository capacity in all sites
• Potential go beyond CTCTC, as several non-CTCTC sites also expressed interest to join.
Thank You!