China Clinical Research Network Development

Introduction of China Tuberculosis Clinical Trial Consortium (CTCTC)

4th Annual RePORT International Meeting
Sep 12-14 2018  Suzhou, China

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Coordinator, China Tuberculosis Clinical Trial Consortium (CTCTC)
Co-PI, RePORT
Background:
- Rapid development on TB drug and regimen globally.
- High quality clinical trial sites in high burden countries are urgently needed.

CTCTC established in Sep, 2013 with first 12 CFDA certificated GCP sites.

The leadership and management of the Consortium is located at Beijing Chest Hospital.

FHI 360 was selected to work with NIAID/DAIDS to support CTCTC network.

**CTCTC Vision:** Leading China’s effort in conducting high standard clinical research on TB treatment, diagnostics and vaccine, to support evidence based response to TB epidemic.
Beijing Chest Hospital, Capital Medical University
Beijing TB & Thoracic Tumor Research Institute
Clinical Center on Tuberculosis, China CDC (CCTB)
WHO Collaborating Centre for Research and Training on TB

- Grade IIIA hospital with 612 bed, 200 for TB
- TB and lung cancer
- 12000 inpatients/year
- 28000 outpatients/year

- 8 research departments
- CFDA certificated GCP sites for TB & lung cancer
- Leading national TB clinical trial network (CTCTC)
- Leading China TB hospital Consortium (101 hospitals)

- National training workshop/year
- National web-based TB consultation & training Platform
- WHO CC for TB Research and Training

- National clinical center supporting NTP
CTCTC Development Phases

**Established**
- Sep 2013
- 12 sites
  - Regulation
  - Mechanism
  - Structure

**Developed**
- 16 sites
  - Site assessment
  - Extensive training
  - CTCTC SOP development

**Expansion**
- 20 sites
  - CTCTC research groups
  - Strengthened assessment, training and cooperation
  - Academic communication
  - Initiate clinical researches

**Current and the future**
- 24 sites (by the end of 2018)
  - Research grants;
  - Focus on quality;
  - Promote international cooperation;
  - Expand influence of CTCTC.
CTCTC member hospitals

<table>
<thead>
<tr>
<th>Participating Study Sites</th>
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Decision Making Mechanism

Proposal/proposal concept by PI

The submission of written

CTCTC central Office

Submission

CTCTC Scientific Committee

Accept

CTCTC Research Dept. & QC/QA Dept.

Reject

Drop or revision

Feedback

CTCTC Executive Committee

Accept

Reject
Communication mechanism

- **Face to face meeting:**
  - Managerial: 1/year, at China National TB Hospital annual meeting
  - Academic: 1/year, at China CMA-TB annual meeting
  - Training workshop: 3-4/year in the beginning, and current 1/year with specific focus

- **Webinar meeting/training:** 1/month

- **CTCTC quarterly update, and annual report**
On-going Studies

NDIP
新药引入和保护项目
New Drug Introduction & Protection

S - E - M - S

Careful Selection
Information Monitoring
Expert Committee
Patient Support

NDIP (BDQ post-market observational Cohort) kick-off Nov, 2017

BDQ Approved by FDA in Dec 2012
BDQ Approved by CFDA Nov 23, 2016
DLM approved by EU in Apr, 2014
DLM approved by CFDA on Mar 12, 2018
NDIP (DLM)

NDIP (BDQ post-market observational Cohort) kick-off Nov, 2017

Careful Selection
Information Monitoring
Expert Committee
Patient Support

NDIP (BDQ post-market observational Cohort) kick-off Nov, 2017

Careful Selection
Information Monitoring
Expert Committee
Patient Support
NDIP (BDQ) Sites and Patients Enrolment
On-going Studies: RePORT-CHINA

- Joined RePORT international in Jan 2017
- 10 selected sites in RePORT-China
- 93 qualified cases enrolled for Cohort A, and 896 specimens collected
- Funded locally from BJ municipal government and IATB
- Key partnerships are NIH and FHI 360
## On-going Studies:
**CTCTC Research Grants for Young Investigators: R1 (2017)**

<table>
<thead>
<tr>
<th>Leading site</th>
<th>Research topic</th>
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<tbody>
<tr>
<td>Chengdu Public Health Clinical Center</td>
<td>Clinical features of tuberculosis complicated with HIV and viral hepatitis: a retrospective study</td>
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<tr>
<td>Ningxia No 4 People’s hospital</td>
<td>The synergy effect of cycloserine (CS) on the therapy of tuberculosis in vitro</td>
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<tr>
<td>Shenyang Chest Hospital</td>
<td>Evaluation of the diagnostic value of GeneXpert MTB/RIF test in urinary tuberculosis of HIV(-) population</td>
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<tr>
<td>Beijing chest hospital</td>
<td>Evaluation of Xpert MTB/Rif test on centrifugal cerebrospinal fluid in the diagnosis of tuberculous meningitis</td>
</tr>
<tr>
<td>Jingzhou Chest Hospital</td>
<td>The synergy effect of cycloserine (CS) on the therapy of tuberculosis in vitro</td>
</tr>
<tr>
<td>Shanghai pulmonary hospital</td>
<td>Effects of isoniazid and rifampicin MIC on therapeutic efficacy of primary MDR-TB</td>
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<tr>
<td>Shanghai Pulmonary hospital</td>
<td>A novel lymphocyte transformation test in the diagnosis and prognosis of anti-TB drug induced hypersensitivity</td>
</tr>
<tr>
<td>Changsha Central hospital</td>
<td>The risk of extensive drug-resistant tuberculosis transmission in China.—Interview and Location of 20 patients with extensive drug-resistant tuberculosis.</td>
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### On-going Studies:

**CTCTC Research Grants for Young Investigators: R2 (2018)**

<table>
<thead>
<tr>
<th>Leading site</th>
<th>Research topic</th>
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<tbody>
<tr>
<td>Shandong Chest Hospital</td>
<td>Effect of empiric anti-tuberculosis therapy on the PZA resistance in newly diagnosed patients</td>
</tr>
<tr>
<td>Beijing Chest Hospital</td>
<td>Application of Real-time Fluorescence Quantitative Nucleic Acid Amplification (Xpert MTB/RIF) in the Diagnosis of Intestinal Tuberculosis</td>
</tr>
<tr>
<td>Shenzhen No.3 Hospital</td>
<td>Correlation between linezolid serum concentration and drug neurotoxicity</td>
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<tr>
<td>Beijing Chest Hospital</td>
<td>Study on ototoxicity associated with anti tuberculosis injections (Am, Cpm) in patients with tuberculosis</td>
</tr>
<tr>
<td>Chongqing Public Health Center</td>
<td>Clinical application of overlapping extension PCR fragment sequencing for detection of drug resistance of three kinds of anti tuberculosis drugs</td>
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<tr>
<td>Tianjin Haihe Hospital</td>
<td>Optimization and evaluation of MALDI-TOF-MS identification method for BactecTM MGITTM 960 liquid culture</td>
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<tr>
<td>The Fifth People's hospital of Suzhou</td>
<td>Effect of fluoroquinolone exposure on detection of Mycobacterium tuberculosis</td>
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On-going Studies: Hospital data Standardization

- Hospital data: large amounts, complicated, isolated and more emphasis on application than analysis
- Standardization: first step for application
- Real World Study (RWS): specific application of hospital data standardization
- By 2018: carried out by 6 hospitals
On-going Studies: Imaging Big Data

- To fill the gap on TB diagnosis at peripheral level: remote medical imaging consultation
- By the end of 2018:
  - to establish a pulmonary TB image center consist of 11 TB hospitals and 100,000 pulmonary image database
  - the design of the AI (Artificial Intelligence) image-reading software will have been finished

AI’s prospect encouraging
On-going Studies: Patient management System

**TB Aid**

**For Patients use**
- Remind drug taking and F-U visits
- Monitor adherence
- Provide patients education and patient incentives
- Allow communication between patients and doctors

**TB Doctor**

**For doctors use**
- Link to TB Aid: monitor patients/answer questions
- Doctors community for technical discussion
- Doctor's education: on-line training
- Share TB related resources
### Planned Studies

<table>
<thead>
<tr>
<th>Area</th>
<th>Description of Study</th>
<th>Sponsor</th>
<th>CTCTC sites evolved</th>
<th>Current Status</th>
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<tbody>
<tr>
<td>MDR Treatment</td>
<td>STREAM 2: 6-9 months treatment with/without BDQ</td>
<td>Union</td>
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<td>Expected start in Nov 2018</td>
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<tr>
<td>MDR Treatment</td>
<td>DLM post-market Observational Cohort</td>
<td>Otsuka</td>
<td>TBD</td>
<td>Expected start in Jun 2019</td>
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Into the future:

➢ Research:
  ▪ New drug & new regimen
  ▪ bio-repository
  ▪ Big-data
➢ Research Team Capacity Building
➢ International cooperation
Acknowledge:

- Strong support from NIAID/NIH, FHI 360
- Joint efforts of CTCTC member hospitals