

RESIST-TB

Research Excellence to Stop TB Resistance

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RESIST-TB ANNUAL REPORT FOR 2016

RESIST-TB is an organization of concerned patients, physicians, research scientists and stakeholders. Its mission is to promote and conduct clinical research to cure and prevent drug-resistant tuberculosis. RESIST-TB is committed to addressing the substantial existing gaps in knowledge and to helping provide access to effective curative and preventive treatment for drug-resistant tuberculosis (DR-TB). Efforts in 2016 were sponsored by the World Health Organization, the Stop TB Partnership, the International Union Against Tuberculosis and Lung Disease, Treatment Action Group, Partners in Health, the U. S. Centers for Disease Control & Prevention, Vital Strategies, Médecins Sans Frontières, the KNCV Tuberculosis Foundation, and the Firland Foundation.

Our 2016 activities centered on:

(1) DR-TB scientific advocacy, through updating the 2008 research agenda on the programmatic management of DR-TB, dissemination of information through our website, including promoting and arranging a series of webinars and an eNewsletter, developing consensus guidelines on molecular TB diagnostics;

(2) DR-TB clinical trials development, through our Clinical Trials Progress Report published on www.resisttb.org);

and

(3) influencing public policy, through the RESIST-TB Pediatric Landscape Meeting, the the creation of a working group at the 47th Union World Conference on Lung Health, tracking the rollout of new drugs, and advocating for access to new drugs for MDR-TB by collecting provider experiences with compassionate use.

Details about these activities are provided below.

SCIENTIFIC ADVOCACY

DR-TB RESEARCH AGENDA

Following on our work initiated in 2014 to update the 2008 research agenda on the programmatic management of drug-resistant tuberculosis (PMDT), the Research Agenda (RA) Working Group continued its collaboration with the Global Drug Resistant TB Initiative (GDI). Data analysis on the new survey was completed and a manuscript was drafted and reviewed by all authors. In the manuscript we detail the process undertaken and results of the survey on priorities in PMDT. These include new diagnostics and their effect on improving treatment outcomes, improved diagnosis of paucibacillary and extrapulmonary TB, and development of shorter, effective regimens. Interruption of nosocomial transmission and treatment for latent TB infection in contacts of known MDR-TB patients were also top priorities in their respective categories.

In May 2016, PLoS One published our research. Results from both the survey and other resources showed that there was continuity around the priorities for research in PMDT that could help fill longstanding evidence gaps barring expanded treatment access. Identified priorities specifically highlighted the importance of increased coordinated efforts to address questions regarding: shorter treatment regimens; knowledge of disease burden without representative data; and treatment for latent TB infection in household contacts of known DR-TB patients. The open access article can be found on the PLoS website [here](#).

RESIST-TB WEBSITE AND eNEWSLETTER

The RESIST-TB website (www.resisttb.org) remains active and updated often in order to accurately reflect advances in DR-TB clinical trials and disseminate news, developments and publications to over 200 subscribers. In 2015 we launched a newly designed monthly eNewsletter, which highlights information about new DR-TB related publications, news updates, and events. Topics covered in our news articles included trial status updates, announcements of publications, symposia, and webinars of interest, and global headlines related to DR-TB.

MOLECULAR TB DIAGNOSTICS WORKING GROUP

During 2015, RESIST-TB collaborated with TBNet on a manuscript formulating consensus guidelines for the clinical application of molecular TB drug susceptibility testing. This document provides the first comprehensive guidance for clinicians on the clinical implications of specific genotype drug resistance mutations. The consensus guidelines, entitled “Clinical implications of molecular drug resistance testing for Mycobacterium tuberculosis: a TBNET/RESIST-TB consensus statement” were accepted in the International Journal of Tuberculosis and Lung Disease in late- 2015 and published in the January 2016 issue of the journal. The article is available open access [here](#).

CLINICAL TRIALS

PEDIATRIC MDR-TB CLINICAL TRIALS LANDSCAPE MEETING

On June 17, 2016, RESIST-TB, IMPAACT, Vital Strategies, and New Ventures jointly hosted the Pediatric Multidrug Resistant Tuberculosis Clinical Trials Landscape Meeting in Arlington, VA. The meeting provided updates on current multidrug-resistant tuberculosis (MDR-TB) trials targeting pediatric populations and adult trials that included pediatric patients. A series of

presentations were given that discussed site capacity needs, community engagement, and additional interventions necessary for clinical trials to improve the treatment of pediatric MDR-TB. Specific topics included current pediatric MDR-TB trials (ongoing and planned), the global burden of MDR-TB in children, current regimens for MDR-TB treatment in children, pharmacokinetics of second-line anti-tuberculosis medications in children, design, sample size, and statistical considerations for MDR-TB trials in children, selection of study population, design, and treatment arms for a trial of novel pediatric MDR-TB regimens, practical aspects of pediatric MDR-TB treatment trials and strategies for integrating children into adult tuberculosis trials. These discussions elucidated barriers to pediatric MDR-TB clinical trials and provided insight into necessary next steps for progress in this field.

The conference proceedings are in press and a supplement of individual articles on the topics above is in preparation. The meeting concluded with a brainstorming session for a proposed pediatric MDR-TB clinical trial and a proposal for funding has been submitted. A follow-up meeting is planned in 18-24 months.

CLINICAL TRIALS PROGRESS REPORT

RESIST-TB continues to be the source for up-to-date information on clinical trials for MDR-TB. The Clinical Trials Progress Report gathers information on clinical trials underway and in development, including study names, description, status, study enrollment size, and links to more information on all MDR-TB trials planned or in progress. Of over 20 trials listed on the Clinical Trials Progress Report, approximately 5% are in Phase 1, 45% are in Phase 2, and 60% are in Phase 3. Roughly 55% of trials listed are currently enrolling participants, 20% are not yet open and enrolling, and approximately 20% have completed enrollment and follow up or data analysis is ongoing. This resource is updated regularly.

GLOBAL MDR-TB CLINICAL TRIALS LANDSCAPE MEETING SUPPLEMENT

The Global MDR-TB Clinical Trials Landscape Meeting Supplement was published online in the International Journal for Tuberculosis and Lung Disease (IJTLD) in December 2016. The first global MDR-TB Clinical Trials Landscape meeting held in December 2014 convened sixty international experts who met in Washington D.C. and Cape Town, South Africa to strategize coordination of research and development of new treatment regimens for MDR-TB. This supplement includes a collection of manuscripts that address key topics from the Landscape meeting, including both methodological issues and agent-specific reports. These articles provide an in-depth discussion of the rationale behind current MDR-TB clinical trials as well as important insights to drive future research. The full supplemental report including links to all manuscripts can be accessed online through the IJTLD website [here](#).

DRUG-RESISTANT TUBERCULOSIS CLINICAL TRIALS: PROPOSED RESEARCH DEFINITIONS IN ADULTS

During the Global MDR-TB Clinical Trials Landscape Meeting in 2014, a critical need to standardize research definitions for adults in clinical trials arose. An effort to draft and publish a manuscript detailing these definitions was led by RESIST-TB and collaborators. The manuscript entitled “Drug-Resistant Tuberculosis Clinical Trials: Proposed Research Definitions in Adults” was accepted by the International Journal for Tuberculosis and Lung Disease was published in the March 2016 issue of the journal. The full manuscript can be accessed on the International Journal for Tuberculosis and Lung Disease website [here](#).

WEBINAR AND CONFERENCE CALL SERIES

In 2015 we initiated a webinar series in collaboration with the CDC TBTC MDR/XDR-TB Working Group. This webinar series serves as a forum for updates on pressing issues in MDR-TB and presentations on recent publications. The webinar series helps fill a critical and otherwise unmet role in disseminating newly published advances in MDR-TB care and treatment, and providing an update or elucidating on a topic's status where little is known. We look forward to continuing to expand the series in 2017. The presentations that took place during the 2016 series are listed below:

- January 29, 2016 **Roxana Drake (Novartis)**: *Clofazimine – Repurpose & Strategy*
- March 16, 2016 **Marilyn Bonnet (MSF)**: *Identification of Patients Who Could Benefit from Bedaquiline or Delamanid*
- June 25, 2016 **Carole Mitnick (Harvard Medical School)**: *endTB Clinical Trial: Evaluating Newly Approved Drugs for Multidrug-Resistant TB*
- September 13, 2016 **Kelly Dooley (Johns Hopkins)**: *ACTG A5343, the “DELIBERATE” Trial*
- November 3, 2016 **Greg Fox (University of Sydney)**: *V-QUIN MDR Trial Overview*

PUBLIC POLICY

ACCESS TO NEW TB DRUGS

Promoting early access to new TB drugs is an important policy priority. RESIST-TB continues to build on its work examining mechanisms for pre-access to new TB drugs, with support from the Firland Foundation.

Additionally, RESIST-TB is committed to surveillance of the following activities to examine opportunities for advocacy:

- Monitoring the rollout of Otsuka's expanded access program for delamanid to ensure that it meets expectations and provides access to important patient populations
- Monitoring progress of new investigational antimycobacterial agents to assure that their developers plan for CU/EA when trial results are promising.

MONITORING COMPASSIONATE USE OF NEW DRUGS FOR TUBERCULOSIS

With support from the Firland Foundation, RESIST-TB investigated mechanisms for accessing drugs prior to regulatory approval and surveyed key providers and advocates on their experience attempting to gain access to new TB drugs through compassionate use or similar pre-approval mechanisms. The findings from this project are detailed in this report, which was published in 2016. The full report can be found on RESIST-TB's website [here](#).

UNION WORLD CONFERENCE ON LUNG HEALTH

RESIST-TB continues to strive to ensure that drug resistant tuberculosis remains a focus at scientific meetings and conferences. This year, RESIST-TB proposed creation of a Drug-

Resistant Tuberculosis Working Group (DR-TB WG) within the IUATLD; the proposal was accepted and the WG is being chaired by Bob Horsburgh, Arnaud Trebucq and C-Y Chiang. The DR-TB WG will address a series of objectives focused on DR-TB and will collaborate with GDI to track progress towards End TB Global Plan DR-TB goals. The first meeting of the DR-TB WG was held at the 47th Union World Conference on Lung Health held in Liverpool.

LEADERSHIP TRANSITIONS

Two members of the Steering Committee, ID Rusen and Deron Burton, stepped down from their positions this year. We would like to extend our sincere thanks to both Dr. Rusen and Dr. Burton for their contributions to RESIST-TB and the organization's cause.

RESIST-TB would also like to welcome its two newest members to the Steering Committee, Francesca Conradie and Susan van den Hof.

GOALS FOR 2017 AND BEYOND

RESIST-TB updated its strategic plan in 2016, focusing on accelerating the update of effective, scalable regimens for MDR-TB; Advocating for clinical trials of preventive therapy for MDR-TB; Optimizing communication between stakeholders in the MDR-TB community. These strategic goals are posted on the RESIST-TB website [here](#).

In the coming year, RESIST-TB will continue to provide leadership in scientific advocacy, MDR-TB clinical trials design and preparation, and public policy development. Activities for the upcoming year include:

- Publication of a supplement in the IJTLD of papers presented at the the research agenda on the programmatic management of DRTB, in collaboration with the Global Drug-Resistant TB Initiative (GDI).
- Continuation of the bi-monthly webinar series, and updating and development of the Clinical Trials Progress Report. Upcoming webinar topics include the PHOENiX household contact study of Delamanid by the ACTG and the TB-CHAMP study by the IMPAACT network.
- Monitoring roll-out of the 9-month MDR-TB regimen, in collaboration with the IUATLD DR0TB Workign Group and DR-STAT.
- Continuing to provide up-to date information about MDR-TB clinical trials through the RESIST-TB eNewsletter and Clinical Trials Progress Report

RESIST-TB continues to fill an important and unmet need. By addressing research and implementation gaps in the treatment and prevention of MDR-TB, we draw attention to needed research. We also under take important research projects that are not currently being addressed by the global tuberculosis community. Moreover, focusing on development and demonstration of efficacy of scalable regimens will facilitate rapid translation of these advances into practice. The successful continuation of these activities is recognized as critical to continued improvement in treatment and prevention of MDR-TB and XDR-TB.