

# RESIST-TB

*Research Excellence to Stop TB Resistance*

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## STEERING COMMITTEE

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## RESIST-TB ANNUAL REPORT FOR 2014

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 2014 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, Médecins Sans Frontières, the KNCV Tuberculosis Foundation, and the Firland Foundation.

Our 2014 activities centered on (1) DR-TB scientific advocacy through continuing the process of updating the 2008 research agenda on the programmatic management of DR-TB, dissemination of information through our website ([www.resisttb.org](http://www.resisttb.org)) and eNewsletter, tracking GeneXpert use, and developing consensus guidelines on molecular TB diagnostics; (2) DR-TB clinical trials development through our Clinical Trials Progress Report published on [www.resistttb.org](http://www.resistttb.org), and cohosting a meeting to address the need for better communication and coordination among MDR-TB; (3) influencing public policy through the annual meeting open to conference attendees, tracking the rollout of new drugs, and advocating for access to new drugs for MDR-TB by acting as signatories on multiple letters.

### SCIENTIFIC ADVOCACY

#### DR-TB RESEARCH AGENDA

Following our work in 2014 on updating the 2008 research agenda on the programmatic management of drug-resistant tuberculosis (PMDT), the Research Agenda (RA) Working Group began collaborating with the Global Drug-Resistant TB Initiative (GDI). The RA WG began data analysis on the 2014 survey and presented preliminary results to GDI during a working meeting at the 2014 Union World Conference on Lung Health in Barcelona, Spain. The RA WG and GDI have begun drafting a manuscript. We expect publication of the updated research agenda on PMDT in 2015.

### RESIST-TB WEBSITE AND eNEWSLETTER

The RESIST-TB website ([www.resisttb.org](http://www.resisttb.org)) remains active and updated often to accurately reflect new advances in MDR-TB clinical trials and disseminate news, developments and publications. A monthly eNewsletter highlights information about new DR-TB related publications, news updates, and events distributed to over 300 contacts each month. We also added a new feature to our website, the “Clinical Trials Progress Report”, a real-time listing of the status of all registered clinical trials enrolling patients with MDR-TB.

### GENE XPERT WORKING GROUP

The GeneXpert (GE) Working Group is preparing an analysis that will correlate GeneXpert cartridge use with changes in the number of MDR-TB cases diagnosed. This analysis is focusing on the 27 high-burden MDR-TB countries. Analyses will be stratified by the populations targeted for GeneXpert diagnosis and adjusted for increases in other methods of MDR-TB diagnosis (such as increases in culture-based DST capacity).

### MOLECULAR TB DIAGNOSTICS WORKING GROUP

RESIST-TB has been collaborating with TBNET on a manuscript formulating consensus guidelines on the clinical implications of molecular TB drug susceptibility diagnostics. This publication is intended to provide guidance for clinicians on the clinical implications of specific genotype drug resistance mutations.

## **CLINICAL TRIALS**

### CLINICAL TRIALS PROGRESS REPORT

RESIST-TB sought to provide a resource where information and updates on the progress of clinical trials for MDR-TB could be accessed in one place. The Clinical Trials Progress Report was created to meet this need. Included in the Clinical Trials Progress Report are study names, description, status and links to more information on all MDR-TB planned or in progress. This resource is updated regularly.

### GLOBAL MDR-TB CLINICAL TRIALS LANDSCAPE MEETING

RESIST-TB, in collaboration with TREAT-TB, held the “MDR-TB Clinical Trials Landscape Meeting” on December 4-5, 2014. The meeting was held in Washington DC at the Center for Strategic and International Studies, with a videoconference location in Cape Town, South Africa. The goal of the meeting was to address the need for better communication, consensus and coordination among current and future MDR-TB trials. Objectives were to discuss key methodological challenges for MDR-TB trials of new regimens and opportunities for standardization, identify other promising new regimens and combinations for future field evaluations, and consider mechanisms for coordination of research efforts for MDR-TB.

The meeting was met with an overwhelming amount of interest. In total, over 60 researchers, donors, policy makers and other stakeholders convened between the

two locations to listen and participate in presentations and discussion. Attendees included representative from over 15 academic research institutions and organizations such as The World Health Organization, Médecins Sans Frontières, Clinton Health Access Initiative, US Centers for Disease Control, National Institute for Health/ National Institute of Allergy and Infectious Disease, US Food and Drug Administration, United States Agency for International Development, The Union, Janssen, Sequella, KNCV Tuberculosis Foundation, Treatment Action Group, Novartis, Otsuka, and TB Alliance. A report of the meeting will be published in 2015.

## **PUBLIC POLICY**

### ACCESS TO NEW TB DRUGS

Promoting early access to new TB drugs is an important policy priority. In 2014, RESIST-TB was awarded a grant from the Firland Foundation to examine mechanism for pre-approval access to new drugs in the 27 high burden MDR-TB countries, and survey providers on their experiences with compassionate use. In 2014, we completed our review of the legal frameworks for early access to new drugs in each of the 27 high burden MDR-TB countries. We have created the survey that will be sent to providers and other relevant stakeholders to determine perceptions, barriers, and successes of obtaining new drugs through compassionate use or other pre-approval mechanisms in these countries. We expect to present and publish our findings in 2015.

RESIST-TB acted as signatories on two letters in 2014. In March, RESIST TB signed a letter to Otsuka pharmaceuticals entitled “Continued concern over access to Delamanid.” This letter demanded access to delamanid through compassionate use and rapid registration of delamanid in trial site countries and other high burden MDR-TB countries. In September 2014, RESIST-TB signed a letter to Janssen entitled “Open letter: reducing the price of bedaquiline.” This letter focused on the tiered pricing structure for middle-income countries. The letter demanded lowering the price of bedaquiline for all non-high income countries.

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

- Janssen’s preapproval access programs for bedaquiline have granted access to over 600 patients since 2011.
- European approval of delamanid was granted by the EMA in 2013; Otsuka is planning a delamanid expanded access (EA) program for future implementation, and this will be monitored by RESIST-TB
- Although there are currently no plans for CU or EA for the remaining new TB drugs, this is largely because there are not any others that have undergone adequate clinical evaluation. RESIST-TB will watch closely to determine when additional CU/EA programs are justified

## UNION CONFERENCE

RESIST-TB continues to ensure that drug resistant tuberculosis stays in the spotlight at TB scientific meetings. The RESIST-TB annual meeting at the 2014 Union World Conference on Lung Health in Barcelona, Spain, drew an audience of over 50 interested in hearing about the newest developments in MDR-TB trials, as well as RESIST-TB's efforts in promoting those trials. The annual meeting featured a summary of RESIST-TB's efforts of 2014. Robert Horsburgh, Chair of the RESIST-TB Steering Committee, led a presentations entitled "Summary of Phase II and Phase II Clinical Trials Planned and in Progress." Also included was a presentation by Dr. Andrew Nunn of the MDR Clinical Trials Unit entitled "Stage II of the STREAM Study: Details of Two new Bedaquiline-containing Arms and Timeline for Initiation."

## **GOALS FOR 2015 AND BEYOND**

During 2014 RESIST-TB initiated a strategic planning update. Many of the goals of our original strategic plan, covering 2008-14, had been achieved and the Steering Committee felt an updated plan was needed for the coming 5 years. A strategic planning retreat was held in November 2014 and new goals were identified. These new goals will be reviewed and approved, with posting on the RESIST-TB website expected in early 2015. A major new focus is expected to be development of convenient regimens for MDR-TB treatment that can be easily rolled out in programmatic settings.

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. Our objectives for the upcoming year include:

- Continue development of the research agenda on the programmatic management of DR-TB and submit the manuscript for peer-reviewed publication, in collaboration with the Global Drug-Resistant TB Initiative (GDI)
- Demonstrate the effectiveness of GeneXpert in increasing diagnosis of MDR-TB by publishing findings from our analysis on increases in MDR-TB diagnosis through the GeneXpert Diagnostic Roll-out Surveillance Project in collaboration with WHO
- Advocate for increased availability of New TB drugs by publishing a report on access to compassionate use and other pre-approval mechanisms for access to new TB drugs in the 27 high burden MDR-TB countries, with support from the Firland Foundation
- Accelerate progress towards improved DR-TB treatment by increasing communication between ACTG, TBTC, DMID, GATB and other international partners and by convening working groups to standardize outcome definitions and initiate an international prospective MDR-TB observational cohort study

- Increase awareness of utility of molecular diagnostics for rapid tailoring of MDR-TB treatment regimens by publishing consensus guidelines on molecular diagnostics for MDR-TB, in collaboration with TBNet
- Advance cooperation between trial networks investigating MDR-TB treatment by publishing the meeting report from the Global MDR-TB Clinical Trials Landscape Meeting
- Advocate for programmatically-friendly MDR-TB regimens by organizing a follow-up to the Landscape Meeting

RESIST-TB continues to fill an important and unmet need. By addressing the existing gaps in the treatment and prevention of MDR-TB, the organization draws attention to needed research and takes on important projects that are not currently 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 the continued progress of research and advocacy on MDR-TB, ultimately resulting in more effective and better-tolerated treatment for MDR-TB and XDR-TB