RESIST-TB
Research Excellence to Stop TB Resistance
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RESIST-TB ANNUAL REPORT FOR 2015

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 2015 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 and eNewsletter, developing consensus guidelines on molecular TB diagnostics, and hosting a symposium at the 46th Union World Conference on Lung Health); (2) DR-TB clinical trials development (through our Clinical Trials Progress Report published on www.resistttb.org); (3) influencing public policy (through the RESIST-TB Annual Meeting open to Union World Conference on Lung Health attendees, tracking the rollout of new drugs, and advocating for access to new drugs for MDR-TB by collecting provider experiences with compassionate use).

SCIENTIFIC ADVOCACY

DR-TB RESEARCH AGENDA

Following on our work initiated in 2014 on updating the 2008 research agenda on the programmatic management of drug-resistant tuberculosis (PMDT), the Research Agenda (RA) Working Group continued collaboration with the Global Drug-Resistant TB Initiative (GDI). Data analysis on the 2014 survey was completed and a manuscript was drafted and has been 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. The manuscript has been submitted and is currently under review.

RESIST-TB WEBSITE AND eNEWSLETTER

The RESIST-TB website (www.resisttb.org) remains active and updated often in order to accurately reflect advances in MDR-TB clinical trials and disseminate news, developments and publications. 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 MDR-TB. We began tracking engagement of newsletter recipients and found that approximately 35% more RESIST-TB newsletter recipients opened the newsletter compared to the average in the non-profit industry. Additionally, 80% more RESIST-TB newsletter recipients clicked on web links to blog posts and publications than the average in the non-profit industry. The newsletter had the most engagement from recipients in Japan, Switzerland, the US, and the Netherlands.

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 will provide 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

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 15% are in Phase 1, 50% are in Phase 2, and 35% are in Phase 3. Roughly 45% of trials listed are currently enrolling participants, 25% are not yet open and enrolling, and approximately 30% have completed enrollment and follow up or data analysis is ongoing. This resource is updated regularly.

GLOBAL MDR-TB CLINICAL TRIALS LANDSCAPE MEETING REPORT

The report of the first Global MDR-TB Clinical Trials Landscape meeting was published in *BMC Proceedings* in November 2015. The meeting 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. During the meeting, key MDR-TB trial-related issues were identified, including: standardization of trial definitions; clinical trial capacity building and; regimens optimized to foster compliance, avoidance of emergence of resistance and clinical relevance for special populations, including children and those co-infected with HIV. The full meeting report can be accessed on the *BMC Proceedings* website here. A supplement to the *International Journal for Tuberculosis and Lung Disease* to be published in 2016 is currently being prepared and will address these issues in greater detail.

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* in late 2015 and was published in the March 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 will serve as a forum for updates on pressing issues in MDR-TB and presentations on recent publications. Presentations in the 2015 series had steadily increasing attendance, with the last webinar attracting over 70 international participants. The webinar series has serves 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 expanding the series in 2016. The presentations included in the 2015 series are listed below:

January 15, 2015	Eric Nuermberger	*What have we learned from recent trials of shortening treatment for DS-TB with fluoroquinolones?*
March 19, 2015	Molly Franke	*Counting pyrazinamide in regimens for MDR-TB*
July 16, 2015	Lawrence Geiter	*Update on the Otsuka FightTBack Initative*

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. This year we conducted a survey of providers and other relevant stakeholders to determine perceptions, barriers, and successes of obtaining new drugs through compassionate use or other pre-approval mechanisms. We invited approximately 100 participants and received 57 responses representing 37 countries. We shared results from this investigation at the 46th Union World Conference on Lung Health in Cape Town, South Africa in December 2015 during a symposium entitled "Pre-approval access to new TB drugs: What, where, and how." The symposium featured speakers from civil society, industry, and programs that have successfully utilized compassionate use to increase access to bedaquiline and delamanid. We plan to disseminate a report of our investigation into pre-approval access of new TB drugs through publication on our website or peer-reviewed journal.

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.

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. The RESIST-TB annual meeting at the 46th Union World Conference on Lung Health in Cape Town, South Africa drew an audience of over 50 people interested in hearing about the newest developments in MDR-TB. The annual meeting featured a summary of RESIST-TB's efforts of 2015. Robert Horsburgh, Chair of the RESIST-TB Steering Committee, led a presentation summarizing RESIST-TB work in 2015 and clinical trials for MDR-TB. The meeting also featured a panel discussion, "Access to bedaquiline and other new drugs – Getting new drugs into patients who need them." The panel spotlighted a variety of perspectives on the topic and included representation from providers and national TB programs in South Africa, Namibia, Germany, Latvia, Belarus, and Swaziland. Additionally, the panel included policy makers from USAID and the Global Drug Facility. The annual meeting and the symposium "Pre-approval access to new TB drugs: What, where, and how" brought attention to the critical need for increased access to promising new TB drugs.

GOALS FOR 2015 AND BEYOND

RESIST-TB released a new strategic plan in early-2015, 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 new strategic goals are available 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 the research agenda on the programmatic management of DR-TB, 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. Potential webinar topics include an update on the clofazimine MDR-TB trial from Novartis, advances in preventive therapy trials for MDR-TB from ACTG, IMPAACT and the Australian/Vietnamese collaboration and discussions with authors of important new publications.
- Publication of a report "Barriers to compassionate use for new TB drugs," with support from the Firland Foundation
- Establishment of a Scientific Working Group on MDR-TB in the Union Against Tuberculosis and Lung Disease.
- Plan and co-host the Second Global MDR-TB Clinical Trials meeting in mid-2016.

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.