TBCAB
GLOBAL TB COMMUNITY ADVISORY BOARD

Meeting Report
9th Semi-annual Global TB Community Advisory Board Meeting

29 November – 1 December 2015
Cape Town, South Africa

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TB Preventive Therapy Training

Dr. Gavin Churchyard from the Aurum Institute led a training on latent TB infection (LTBI) and preventive therapy. He discussed the shortcomings of existing diagnostic tools– namely their inability to differentiate between TB infection and disease– and ongoing work to discover markers, and improve our understanding of risk of disease progression. The group discussed preventive therapy regimens and strategies, both existing and under study, and their utility in high vs. low transmission settings. Gavin also highlighted data gaps for the rifapentine-containing short-course regimen (3HP), including the need to characterize 3HP pharmacokinetics when given with dolutegravir or optimized efavirenz (at the reduced dose of 400mg), and in children younger than two years. The TB CAB then discussed the Aurum Institute's planned open label study that will evaluate 3HP given (self-administered therapy) as a single course or on a yearly basis in high TB burden settings, and how the study's findings will be used to inform the World Health Organization's (WHO) policy on the use of 3HP in high TB burden settings. The training session closed with an overview of several planned studies to evaluate preventive therapy in contacts of people with drug-resistant TB (DR-TB) using delamanid or levofloxacin.

TB CAB Business and Governance

Lindsay presented the final TB CAB meeting application scoring rubric on behalf of the Governance and Membership Committee (GMC). In response to a request made at the previous TB CAB meeting in New York, Lindsay also presented the 2015 TB CAB budget broken out by meeting. Next, the TB CAB reviewed key sections of its Terms of Reference (ToR), set to expire at the end of this year and made necessary updates, including those related to its priority research advocacy areas and the process for adding new members and observers. The group then discussed the location and timing of future TB CAB meetings—the group felt attending the Union Conference continued to be important despite the frustrations of the conference. Newer members of the TB CAB expressed the need for several resources/trainings in the future.

Training on TB Pharmacokinetics

Kelly Dooley from Johns Hopkins University led a training on TB and TB/HIV pharmacokinetics (PK) and pharmacodynamics (PD) with specific focus on the pharmacology of TB drugs and HIV/TB co-treatment. The training included an overview of key terms and tools, the role of clinical pharmacology in TB drug and regimen development, the types of research questions that can be answered using PK analyses, and research gaps that might be filled using PK studies. Potential advocacy activities identified during the training for the TB CAB to take forward when engaging with TB researchers and reviewing clinical trials protocols, included advocating for phase II C trials to enable investigators to look at early relapse and using trials data determine the optimal dose to take into phase III studies; and for PK sub-studies to be a part of phase III trials to help tease out the contributors to treatment failure or relapse, specifically if failure is related to drug exposures and to determine if there particular subgroups with low drug exposures for

whom the regimen may not work. Kelly discussed the importance of this information as part of a concept she introduced for getting as many people into the "cure boat" as possible. That is, a regimen that will be introduced globally must be able to also cure the hardest-to-treat patients.

Janssen

The TB CAB met with Chrispin Kambili, Global Medical Affairs Leader, and James Smith-Plenderleith, Director of Communications and Public Affairs in the Asia Pacific region to discuss several bedaquiline-related research and access issues. Chrispin gave an update on Janssen's efforts to register bedaquiline at the country level and the USAID bedaquiline donation program. The TB CAB and Janssen discussed the status of their phase III (STREAM II) and pediatric studies (C211) and barriers to each study's start. The meeting ended with an overview of Janssen's drug-susceptibility test development efforts for bedaquiline and efforts around other potential anti-TB compounds.

TB Alliance

The TB CAB met with Willo Brock, Senior VP of External Affairs, and Dr. Christo van Niekerk, Senior Director, Clinical Development from the TB Alliance. The TB Alliance presented on a wide range of topics, including its early development and discovery programs, its lack of progress securing funds necessary to establish a compassionate use program for pretomanid, the STAND trial hold, Nix-TB, and plans to facilitate future access to pretomanid, assuming the drug is proven safe and effective.

Site Visit to Médecins Sans Frontières (MSF), Khayelitsha

Dr. Jen Furin, covering MSF Khayelitsha clinical lead for Dr. Jennifer Hughes, who was out on maternity leave, facilitated the TB CAB site visit to the MSF offices and clinic in Khayelitsha. While there, TB CAB members heard from TB patients, treatment supporters, and community leaders and were given opportunities to ask questions about their experiences. For the second part of the site visit, the TB CAB heard about the New Start study MSF Khayelitsha is hoping to conduct to evaluate an 18 month, all oral regimen, inclusive of bedaquiline, linezolid, levofloxacin, clofazimine, pyrazinamide, with or without isoniazid under pragmatic conditions for people with rifampicin-resistant TB disease. The TB CAB will review the full study protocol in 2016.

Hain LifeScience

Pia Azarchab, International Business Manager and Nicole Kieser, Product Manager for Hain LifeScience met in person with the TB CAB for the first time. The meeting started with introductions and background about Hain LifeScience as a company. The TB CAB then learned about Hain's existing TB products, including several GenoType technologies, and future development plans to further enhance these tests and increase their capability to identify resistance to first- and second-line TB drugs.

TRUNCATE-TB Update

Nick Paton and Padmasayee Papineni from National University of Singapore joined the TB CAB meeting to present updates on the TRUNCATE-TB study, designed to evaluate whether treatment for drug-sensitive TB can be shortened to just two months using combinations of

first-line, new, and repurposed TB drugs. The investigators identified barriers to accessing certain study drugs and the TB CAB discussed how these might be overcome.

Site Visit to University of Cape Town Lung Institute

Dr. Richard van Zyl-Smit, head of the Lung Clinical Research Unit took the TB CAB on a tour of the University of Cape Town (UCT) facilities. Dr. Ali Esmail, who works closely with Keertan Dheda, head of the Lung Infection and Immunity Unit, then provided the TB CAB with an overview of ongoing research at the UCT Lung Institute, including the South African Medical Research Council-funded NeXT trial, which will evaluate 6–9 months of bedaquiline, linezolid, levofloxacin, with ethionamide or high dose isoniazid, and pyrazinamide for MDR-TB.

Cepheid

The TB CAB met with Philippe Jacon, President, Emerging Markets and Martin Colla, Program Manager, High Burden and Developing Countries to discuss Cepheid products in development. The TB CAB heard about various technologies in Cepheid's TB diagnostics pipeline, including GeneXpert Omni, a smaller, portable, single cartridge version of GeneXpert; Xpert MTB/RIF Ultra, a new cartridge for the GeneXpert system that has improved sensitivity in smear negative samples; and Xpert XDR, a more comprehensive drug-susceptibility test designed to follow a positive Xpert MTB/RIF test. The TB CAB and Cepheid then discussed Xpert access issues, including price and the potential for further reductions.

Otsuka

Dr. Rajesh Gupta, Senior TB Project Director and Marc Destito, Communications Director presented an overview of the four pillars of Otsuka's 20 by 2020 FighTBack Initiative. The four pillars cover patient access, collaborative research efforts, innovative research and development, and optimized patient management. Otsuka presented their efforts to facilitate access to delamanid via compassionate use, in country registrations, and voluntary licensing agreements, and their ongoing and planned research collaborations to evaluate delamanid in children, as a component of new, all-oral shortened regimens, and for preventive therapy among contacts of MDR-TB.