TBCAB
GLOBAL TB COMMUNITY ADVISORY BOARD

Meeting Report
7th Semi-annual Global TB Community Advisory Board Meeting

26–27 October 2014
Barcelona, Spain

Basic science training on TB drug mechanisms of action

Dr. Eric Nuermberger from Johns Hopkins University trained the TB CAB on the various mechanisms of action for new and existing tuberculosis (TB) drugs and their resulting contributions to TB treatment regimens. Dr. Nuermberger also detailed mechanisms through which drugs develop resistance, the implications for new regimens, and ways that these might be overcome.

US Government appropriations and TB funding

Treatment Action Group's Policy Director, Kenyon Farrow walked the TB CAB through the United States Government's budget and appropriations processes. This information is relevant to the TB CAB given its work to promote increased investments in TB research and development, especially considering that the United States Government is the leading global funder of TB research and development.

TB CAB discussions

TB CAB members Polly Clayden and Marcus Low facilitated an internal discussion regarding the potential benefits of clinical access programs compared to full registration in the absence of high quality phase III data. The TB CAB then discussed the potential need for a TB CAB statement of expectations for phase III trial designs for multidrug-resistant TB (MDR-TB).

Bedaquiline: progress of clinical access program in South Africa

Dr. Francesca Conradie from Right to Care and Wits Health gave the TB CAB an overview of South Africa's clinical access program for bedaquiline. At the time of presentation 160 patients were enrolled in the clinical access program, including people with HIV. A discussion of challenges experienced thus far in implementing the clinical access program in South Africa included inconsistent availability of linezolid and cost.

Regulatory and registration processes

Dr. Jen Furin – who has been consulting for WHO on facilitating access to new and repurposed drugs, TB CAB member Jonathan Stillo – who has been working on access to second-line and new TB drugs in Romania, and Dr. Jennifer Hughes – from MSF in Khayelitsha, spoke to the TB CAB about their experiences working to advance in-country access to new and repurposed TB drugs. Their presentations outlined regulatory and other access barriers, and offered solutions for how these might be overcome. The TB CAB discussed then discussed the potential utility of building patient demand, encouraging the use of import waivers, promoting registration of generics, advocating for price reductions, pursing litigation, and reforming country patent laws for promoting access to TB drugs.

TB Alliance

Carl Mendel, Dan Everitt, Stephanie Seidel, and Willo Brock presented on the TB Alliance's TB drug and regimen development pipeline, including STAND (Pa824, moxfloxacin, and pyrazinamide), NC005 (bedaquiline, Pa824, and pyrazinamide),

and Nix TB (bedaquiline, Pa824, and linezolid). The TB Alliance also presented ongoing efforts to explore the establishment of a future compassionate use program for Pa-824 and to expand its community engagement program to include site-specific activities in Brazil, Peru, and the Philippines.

MSF & PIH: endTB

Carole Mitnick from Harvard Medical School, Michael Rich from Partners In Health (PIH), and Francis Veraine from Medécins Sans Frontières (MSF) presented plans for a UNITAID-funded phase III study evaluating several shortened, injectable-free combinations of new and repurposed drugs, including bedaquiline, delamanid, clofazimine, and linezolid, for the treatment of MDR-TB. They shared an overview of the clinical trial protocol in development and described the programmatic component of the endTB project, which aims to expand access to new and repurposed TB drugs in several countries in which MSF and PIH have operations. The TB CAB advocated for the investigators to explore expanding the study's inclusion criteria to include adolescents.

Novartis: clofazimine

David McNeely and David Hughes from Novartis provided background information on clofazimine, a drug originally developed for leprosy and now used as an off-label component of MDR-TB treatment regimens. Following a brief history of clofazimine's development for leprosy and an overview of its profile and potential for TB treatment, David McNeely briefly described ongoing and planned efforts by Novartis and other research networks to fill pre-clinical and toxicity data gaps, to optimize dosing, and to evaluate clofazimine-containing regimens for the treatment of MDR-TB and establish the benefit-risk profile for people with limited other therapeutic options. Particular challenges noted are the several months of clofazimine dosing it takes to build to steady-state levels. Novartis indicated plans to examine clofazimine as an addition to an optimized background regimen compared with optimized background regimen alone in an open-label, randomized trial to determine its independent contributions to MDR-TB treatment.

Medicines Patent Pool

Esteban Burrone provided an overview of the history of the UNITAID Medicines Patent Pool (MPP) and its achievements in HIV, including signed licenses and manufacturing agreements and completed technology transfers for ARVs, the launch of the Pediatric HIV Treatment Initiative, and establishment of a patent status database. Esteban then shared information about a planned feasibility study to explore a possible future role for the MPP in TB. Esteban solicited TB CAB feedback about where the MPP might fit in and have a meaningful impact in TB drug and regimen development. The TB CAB expressed support for MPP's involvement in TB.

Otsuka: delamanid

Larry Geiter, Patrizia Carlevaro, and Marc Destito updated the TB CAB on Otsuka's research and access plans for delamanid. This update included information about Otsuka's phase III and pediatric pharmacokinetic and safety studies. Otsuka also

discussed its progress advancing A5343– a planned AIDS Clinical Trials Group (ACTG) study to evaluate the safety of co-administering bedaquiline and delamanid– and initiating a global compassionate use program. Otsuka revealed little information regarding its access plans or progress.

Bedaquiline

Chrispin Kambili, Tine De Marez and Daniel De Schryver from Janssen; ID Rusen from the Union; Mukadi YaDiul from the United States Agency for International Development (USAID); and Andrew Nunn from the United Kingdom Medical Research Council (UK MRC) updated the TB CAB about STREAM-II– a phase III trial to evaluate shortened bedaquiline-containing regimens for MDR-TB. Updates included protocol status and regulatory approvals for STREAM stage II, and ongoing efforts to engage communities around the trial.

Following STREAM-related discussions, Chrispin Kambili, Tine De Marez and Daniel De Schryver from Janssen stayed on to discuss bedaquiline research, pricing, and access with the TB CAB. The discussion included an update on approved, pending, and planned country registrations, ongoing discussions with the Global Drug Facility (GDF), numbers of patients enrolled in Janssen's compassionate use program, and barriers to implementation of the registry required as a condition of bedaquiline's accelerated approval by the U.S. Food and Drug Administration (FDA).