LETTER TO PARTNERS ON XPERT MTB/RIF AND TMC207

By *moderator*
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On 12 November 2010, TAC and partners jointly sent open letters to Cepheid and Tibotec calling for affordable and expanded access to the Xpert® MTB/RIF TB diagnostic test that works on the GeneXpert® diagnostic system and for expanded access to the drug TMC207.

The Xpert MTB/RIF is a TB diagnostic test that detects TB disease and rifampicin resistance within two hours and is much more accurate than the currently available tests at district health centres. TMC207 is an experimental drug for TB that has shown success in patients with drug resistant TB. The addition of TMC207 to standard therapy resulted in a quicker time to sputum-negative conversion for patients with drug resistant TB in a phase II clinical trial.

Attached is an overview of the responses received from Cepheid and Tibotec, as well as, developments in pricing and endorsements.

Letter to partners on follow up on Xpert MTB/RIF and TMC207

12 November 2010 open letters to Cepheid and Tibotec

Response from Cepheid

Response from Tibotec

3 March 2011

Dear partners,

FOLLOW UP ON XPERT MTB/RIF AND TMC207

On 12 November 2010 we jointly sent open letters to Cepheid and Tibotec calling for affordable and expanded access to the Xpert® MTB/RIF TB diagnostic test that works on the GeneXpert® diagnostic system in areas with a high burden of tuberculosis (TB) and for expanded access to the drug TMC207 for compassionate use for patients with drug-resistant TB.

The Xpert MTB/RIF is a TB diagnostic test that detects TB disease and rifampicin resistance within two hours and is much more accurate than the currently available tests at district health centres. We are confident that the implementation of this rapid diagnostic test can prevent tens of thousands of TB deaths annually across the world especially in people with HIV and/or drug resistant TB, two instances in which TB is difficult to diagnose.

The risk of dying from extremely drug resistant (XDR) TB and multi drug resistant (MDR) TB is extremely high. TMC207 is an experimental drug for TB that has shown success in patients with drug resistant TB. The addition of TMC207 to standard therapy resulted in a quicker time to sputum-negative conversion for patients with drug resistant TB in a phase II clinical trial.

Below is an overview of the responses received from Cepheid and Tibotec, as well as, developments in pricing and endorsements.

Campaign for affordable access to the Xpert MTB/RIF diagnostic

On 24 November 2010, we received a response to our letter from Dr Giorgio Roscigno, CEO of the Foundation for Innovative New Diagnostics (FIND), and Mr John L Bishop, CEO of Cepheid. FIND and Cepheid jointly developed this TB diagnostic test. In the letter they indicated that lower prices would be made available for the public sector, non-profit organisations and international funding mechanisms such as the Global Fund for AIDS, TB, and Malaria and UNITAID to roll out the test in high TB burden and low- and middle-income countries. They further indicated that civil society could assist in making a case to policy makers and governments for the rollout of this machine.

On 8 December 2010, the World Health Organisation, endorsed the Xpert MTB/RIF, calling for it ?to be rolled out under clearly defined conditions and as part of national plans for TB and MDR-TB care and control.? The WHO also plans to develop operational guidelines for countries to use the machine in their programmes.

On 15 December, the organisers of the open letter to Cepheid held a teleconference with Cepheid executives and Dr Giorgio Roscigno. The test developers, FIND and Cepheid, indicated again that the price of the machine would be reduced. They also indicated that Cepheid would be able to further reduce the cost of the machine as the volumes ordered increase.

During December, FIND announced that it had negotiated a volume based price reduction agreement with Cepheid, reducing the cost of the GeneXpert machine and the Xpert MTB/RIF test cartridge by 75%. Details of Cepheid's access pricing for the Xpert MTB/RIF are available at:
http://www.finddiagnostics.org/programs/tb/find-negotiated-prices/xpert_mtb_rif.html

The negotiated prices are listed below.

Campaign for accelerated access to TMC207

Tibotec, the producers of TMC207, also responded to our joint letter requesting accelerated access to TMC207 for patients with drug-resistant TB until the drug is approved.

Their response stated that Tibotec is currently working with national regulatory authorities to determine what data is required to submit the product for regulatory approval and has begun to initiate preparations for expanded access and/or compassionate use of TMC207 for patients with extremely drug resistant (XDR) and pre XDR-TB. Civil society organisations have endorsed this process to ensure that patients with least access to effective treatment can potentially benefit from this drug even as it is being studied further. Also through working with eligible multi-drug resistant (MDR) TB programmes, Tibotec aims to eventually provide access to MDR patients through their phase III program. No information was provided about pricing.

On 7 January the organisers of the letter and Tibotec executives held a teleconference. Discussions between Tibotec, US and European regulatory authorities on accelerated access to TMC207 are currently underway. By the end of the first quarter of 2011 (i.e. 31 March), Tibotec indicated that it is likely to be in a position to commence providing accelerated access to TMC207. In countries with regulatory authorities that support such a process (e.g. Section 21 authorisation in South Africa), drugs can be made available on a named-patient basis. In countries where this is not possible (much of Eastern Europe), a large clinical trial evaluating safety will be the means of providing access. Tibotec emphasised that access to the drug will only be made available to sites with appropriate infrastructure for ensuring a consistent drug supply and monitoring patient adherence.

The responses from Cepheid and Tibotec are copied below.

Where to from here?

Gene Xpert

We recommend the following:

? Countries with high TB burdens should begin piloting the Xpert MTB/RIF immediately.
? The prices of the machine and the cartridges must continue to be monitored and pressure must continue to be put on Cepheid and FIND to lower these prices.

TMC207

We recommend the following:
? From 1 April 2011, sites providing treatment to patients with MDR and XDR TB should begin to apply to Tibotec and their regulatory authorities to authorise the use of TMC207 on a patient-named basis.
? In countries where the above is not possible, activists must follow up with Tibotec on the status of the proposed safety trial.

The success of these campaigns depends on continued monitoring and action from civil society organisations in high burden TB countries.

Thank you for your support.

Please contact us if you have further questions.

Kind regards,

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OPEN LETTERS TOCEPHEID AND TIBOTEC
Available here:
http://www.tac.org.za/community/node/2962

RESPONSE FROM CEPHEID
Available here:
http://www.tac.org.za/userfiles/Cepheid.pdf

RESPONSE FROM TIBOTEC

Dear Mr Geffen and other signatories,

RE: Your letter of 11th November 2010 to Dr Paul Stoffels and Mr Glenn Mattes regarding Expanded Access to TMC207.

Firstly thank you for your recognition of the work of Tibotec in the development of TMC207. The people at Tibotec are dedicated to making a difference in the world for patients living with HIV/AIDS and other infectious diseases such as tuberculosis (TB).

This work is tremendously important and we acknowledge the urgent need of TB patients worldwide for TMC207. However as you note in your letter this is potentially the first TB drug in a new class in four decades ? and it is also the first time that a new drug has been studied in multi-drug resistant TB (MDR-TB) patients. These two facts mean that much of the research work we are doing has unique challenges as it is breaking new ground and establishing new processes; not the least in the areas of clinical trial design and regulatory processes. In addition, we recognize the challenges for all of us as TB stakeholders, in protecting this new drug class from inappropriate use, potentially leading to the development of resistance to TMC207 and thereby the loss of the public health benefit of TMC207.

We are working with the regulatory authorities to determine what data is required for regulatory approval. We will have a clearer picture after our end of phase 2 meetings with the authorities in the first quarter of 2011.

Meanwhile as you are aware we have initiated preparations for expanded access and compassionate use for TMC207. We recognize the importance of early access to TMC207, in combination with other active TB drugs, for patients with extensively drug resistant tuberculosis (XDR-TB) and pre-XDR-TB with limited treatment options. However as you note in your letter such access is not without risks.

In order to get community input into our preparations for expanded access/compassionate use of TMC207, we convened a special Advisory Board meeting on 10th November 2010 on this topic prior to the recent IUALTD conference in Berlin. TB advocacy/community representatives from Treatment Action Group, Médecins Sans Frontières and Partners In Health participated in this meeting.

We received broad endorsement for our proposed strategy of a phased roll-out of early access to TMC207. The first phase would comprise either an expanded access program (EAP) clinical trial or compassionate use (CU) (depending on local regulations) for pre-XDR-TB and XDR-TB in countries with a high burden and well-functioning treatment programs. For CU specifically, it was agreed that we should work with ?Eligible MDR-TB Programs? in order to be sure that such hospitals have the capacity to support XDR-TB treatment, have access to quality assured second line drugs, and access to drug susceptibility testing. The phase III program represents an opportunity to provide access to patients with MDR-TB.

We trust that you will agree that we are taking appropriate action to ensure that expanded access/compassionate use of TMC207 is being made to those TB patients in most urgent need of new treatment options. We look forward to working with you in improving access and treatment outcomes for patients with multi-drug resistant TB, while ensuring the appropriate use of TMC207.

Yours sincerely
Johan Van Hoof

Wim Parys
Global Therapeutic Area Head Global Head of Clinical Development
Infectious Diseases and Vaccines Infectious Diseases and Vaccines

cc: Dr Paul Stoffels
Mr Glenn Mattes

n/a
