Not deaf or dead!

The seven-year journey of bedaquiline as a third choice for all South Africans with MDR-TB, as told by one fortunate MDR-TB survivor.

Arne von Delft, TB Proof  
SA HIV Clinicians Society Conference, 25 October
Results of clinical trial – 24 weeks

- Significantly reduced time to culture conversion over 24 weeks (hazard ratio 2.253; 95% CI: 1.08 to 4.71; P = 0.031)

McNeely, et al. 41st IUATLD 2010. Oral presentation
18 – 61.5% ototoxicity but differing methodology

Table 1. Studies that have examined ototoxicity amongst patients on treatment for drug-resistant tuberculosis, assessed using a standardised testing and classification methodology (alphabetical order)

<table>
<thead>
<tr>
<th>First author</th>
<th>Year of study</th>
<th>Country</th>
<th>Type to testing and classification of hearing loss</th>
<th>Number of subjects tested</th>
<th>Number with ototoxicity (%)</th>
<th>Age Range</th>
<th>Number known to be HIV-infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Jager[23]</td>
<td>1995-2000</td>
<td>The Netherlands</td>
<td>15dB at two adjacent frequencies or 20dB at one frequency. Testing frequencies 250-8000Hz</td>
<td>61</td>
<td>11 (18.0)</td>
<td>10-83</td>
<td>NS</td>
</tr>
<tr>
<td>Duggal[25]</td>
<td>2000-2006</td>
<td>India</td>
<td>10dB at two adjacent frequencies, 20dB at any one frequency or loss of response at three consecutive frequencies where responses were previously obtained. Testing frequencies 250-8000Hz</td>
<td>64</td>
<td>12 (18.8)</td>
<td>17-65</td>
<td>NS</td>
</tr>
<tr>
<td>Kennedy[45]</td>
<td>2004-2009</td>
<td>Ireland</td>
<td>Audiograms every six weeks. Classification based on article by Brummett[46]</td>
<td>13</td>
<td>8 (61.5)</td>
<td>24-82</td>
<td>1/7 (14.3)</td>
</tr>
<tr>
<td>Pelouquin[22]</td>
<td>1991-1998</td>
<td>USA</td>
<td>20dB at any frequency and 15dB at two adjacent frequencies both assessed. Audiometry tested at 250-8000Hz</td>
<td>87</td>
<td>32.28* (36.8-32.2)</td>
<td>19-79</td>
<td>NS</td>
</tr>
<tr>
<td>Sturdy[24]</td>
<td>2004-2009</td>
<td>UK</td>
<td>10dB at two adjacent frequencies, 20dB at any one frequency or clinical symptoms of hearing loss. Frequencies not specified</td>
<td>50</td>
<td>9 (18.0)</td>
<td>34.6 (12.8)**</td>
<td>5 (10)</td>
</tr>
</tbody>
</table>

*Unclear from the article
**Median and standard deviation presented as age range unavailable

QTcB changes following loading with TMC 207 over two weeks

Time to 50% surface conversion: 12 weeks in the TMC207 group.
Time to 80% surface conversion: 18 weeks in the placebo group.

Baseline
Upper normal
Prolonged
Patient
The case for pre-approval access to bedaquiline

PRESS RELEASE: Bedaquiline is an anti-tuberculosis drug that is still being tested in clinical trials. It is not yet approved anywhere in the world, though it is steadily making progress towards approval in Europe and the United States.

Several organisations, including the Treatment Action Campaign, the Treatment Action Group, HIV i-Base, the Global Tuberculosis Community Advisory Board, Medecins Sans Frontieres and the Southern African HIV Clinicians Society have called for the drug to be made available to patients with drug-resistant tuberculosis (TB) before it is approved. This demand was made as far back as the World Lung Conference in Mexico in 2009. Yet little progress towards pre-approval access has been made in South Africa. The South African medicines regulatory authority, the Medicines Control Council (MCC), has responded sceptically.

We make the case for pre-approval access in this article. Although worked with...
F.D.A. Approves Drug for Resistant Tuberculosis

By KATIE THOMAS
Published: December 31, 2012

The Food and Drug Administration announced on Monday that it had approved a new treatment for multidrug-resistant tuberculosis that can be used as an alternative when other drugs fail.

The drug, to be called Sirturo, was discovered by scientists at Janssen, the pharmaceuticals unit of Johnson & Johnson, and is the first in a new class of drugs that aims to treat the drug-resistant strain of the disease.
NEWLY APPROVED TB DRUG STIRS CONTROVERSY

The local medical industry is divided over the new drug, bedaquiline. The low-cost, single-dose, single-drug therapy is controversial because there is limited data on its safety and there is some evidence that it raises the risk of potentially fatal heart problems.

Dr. Denise van Duin, pictured, tested bedaquiline in South Africa in 2010 and it was only approved in 2012. Her trial suffered from a lack of patients infected with strains of drug-resistant TB.

With the threat of life-long deafness from the current TB treatment and an inpatient and in-hospital cure, Van Duin was ready to try anything.

Access to bedaquiline in South Africa has been extremely limited, with access only granted to the patients in clinical trials.

"As a doctor, I knew the possible risks of the new treatment, but... I had to take the chance," said Van Duin.

Dr. Claudia Manci of the TB Project SA says, "It brings hope to people. People like this drug. It is more toxic than the one we are currently using.

Manci believes the benefits of bedaquiline far outweigh the risks.

"I had a choice between going deaf or death from heart attack."

"This was the difficult choice for Van Duin."

After catching multidrug-resistant TB, doctor faced a stark choice.
Why drug-resistant tuberculosis threatens us all
The use of bedaquiline in the treatment of multidrug-resistant tuberculosis

Interim policy guidance
TB PROOF
XDR-TB Treatment Success Rate

<table>
<thead>
<tr>
<th>Year</th>
<th>Treatment success rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>12</td>
</tr>
<tr>
<td>2008</td>
<td>11</td>
</tr>
<tr>
<td>2009</td>
<td>9</td>
</tr>
<tr>
<td>2010</td>
<td>6</td>
</tr>
<tr>
<td>2011</td>
<td>14</td>
</tr>
<tr>
<td>2012</td>
<td>19</td>
</tr>
<tr>
<td>2013</td>
<td>25</td>
</tr>
<tr>
<td>2014</td>
<td>28</td>
</tr>
<tr>
<td>2015</td>
<td>49</td>
</tr>
</tbody>
</table>

(Chart shows an increasing trend in treatment success rates from 2007 to 2015.)
Phumeza Tisile was cured of XDR-TB with the help of MSF-sponsored linezolid.

True Life: “I will never get used to not hearing”

Activist and extensively drug-resistant tuberculosis (XDR-TB) survivor Phumeza Tisile writes about how a misdiagnosis cost her hearing and what life has been like since.
My patient's choice – the Jolene Samuels MDR-TB Pledge

A carer’s pledge to offer patients an informed choice between a novel drug or an injectable drug for the treatment of MDR-TB

~ In loving memory of nurse Jolene Samuels, MDR-TB Champion & Cochlear Implant recipient ~

F.D.A. Approves Drug for Resistant Tuberculosis

The South African Health News Service

The case for pre-approval access to bedaquiline

True Life: “I will never get used to not hearing”
Rapid Communication: Key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB)

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WHO

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Major improvement in treatment outcomes and quality of life of patients with multidrug-resistant tuberculosis (MDR-TB) are expected, following key changes in MDR-TB treatment announced by WHO in the Rapid Communication.
02. Cumulative Delamanid and Bedaquiline Use Over Time Compared with Conservative Estimated Need, August 2015 - Present

- Estimated Need
- BDQ
- DLM

*calculation of global estimated need for new drugs adjusted in 2016 based on the WHO Report and in 2017 based on cumulative number of patients needing new drugs
Selected references (1)

- Slide 4:
  - http://uwclh.conference2web.com/content/187/details?from_view=all&view_address=search%3Dmcneeley
- 6: http://erj.ersjournals.com/content/40/5/1277
- 10: http://science.sciencemag.org/content/307/5707/223.long
- 11: https://www.health-e.org.za/2012/11/26/the-case-for-pre-approval-access-to-bedaquiline/
- 12: https://www.nytimes.com/2013/01/01/business/fda-approves-new-tuberculosis-drug.html
- 14: http://content.time.com/time/subscriber/article/0,33009,2136819,00.html
- 17: http://www.tbproof.org/areyoutbproof/
- 18: https://sciencespeaksblog.org/2013/03/19/tb-week-survivors-recount-illness-treatment-and-loss/
Selected references (2)

- 21: https://www.health-e.org.za/2015/01/16/true-life-will-never-get-used-hearing/
- 23: http://www.tbproof.org/pledge/
- 27: http://drtb-stat.org/country-updates/ (Downloaded: 2018/10/24)
- 28: http://www.tbproof.org/who-we-are/our-team/
- 29: Excellent overview and advocacy resource developed by TAG and partners (updated in October 2018):
  - Regarding pricing: http://www.treatmentactiongroup.org/content/reality-check-price-of-bedaquiline