Not deaf or dead!

‘I chose risk of death over going deaf’

After catching multidrug-resistant TB, doctor faced a stark choice

BIANCA CAPAZORIO

DEAF or dead. Those were the two options offered to doctor Delene von Delft when she was diagnosed with multidrug-resistant tuberculosis three years ago.

Her existing regimen of seven drugs was causing hearing loss. Then there was the option of a new drug – the first new TB drug developed in 42 years to get Food and Drug Administration (FDA) approval in the US – but the clinical trial was already full.

But the new drug came with serious side-effects, including sudden cardiac arrest, and death.

That was the difficult choice for Von Delft, a doctor working at a public hospital in the Western Cape and

> “I had a choice between going deaf or death from heart attack”

be sold while further clinical trials continue. Phase three trials are still required.

Bedaquiline is not available in South Africa, but the Medicines Control Council has called for a fast-track review of the drug, and has allowed for a clinical access programme which will collect further clinical data. It will be given to patients at four sites as part of a clinical trial.

In April last year Von Delft applied for compassionate access to the drug. This allows patients to access unregistered drugs in the testing phase, to save their lives.

At the time however, the only people accessing it were those in a clinical trial, which was already closed.

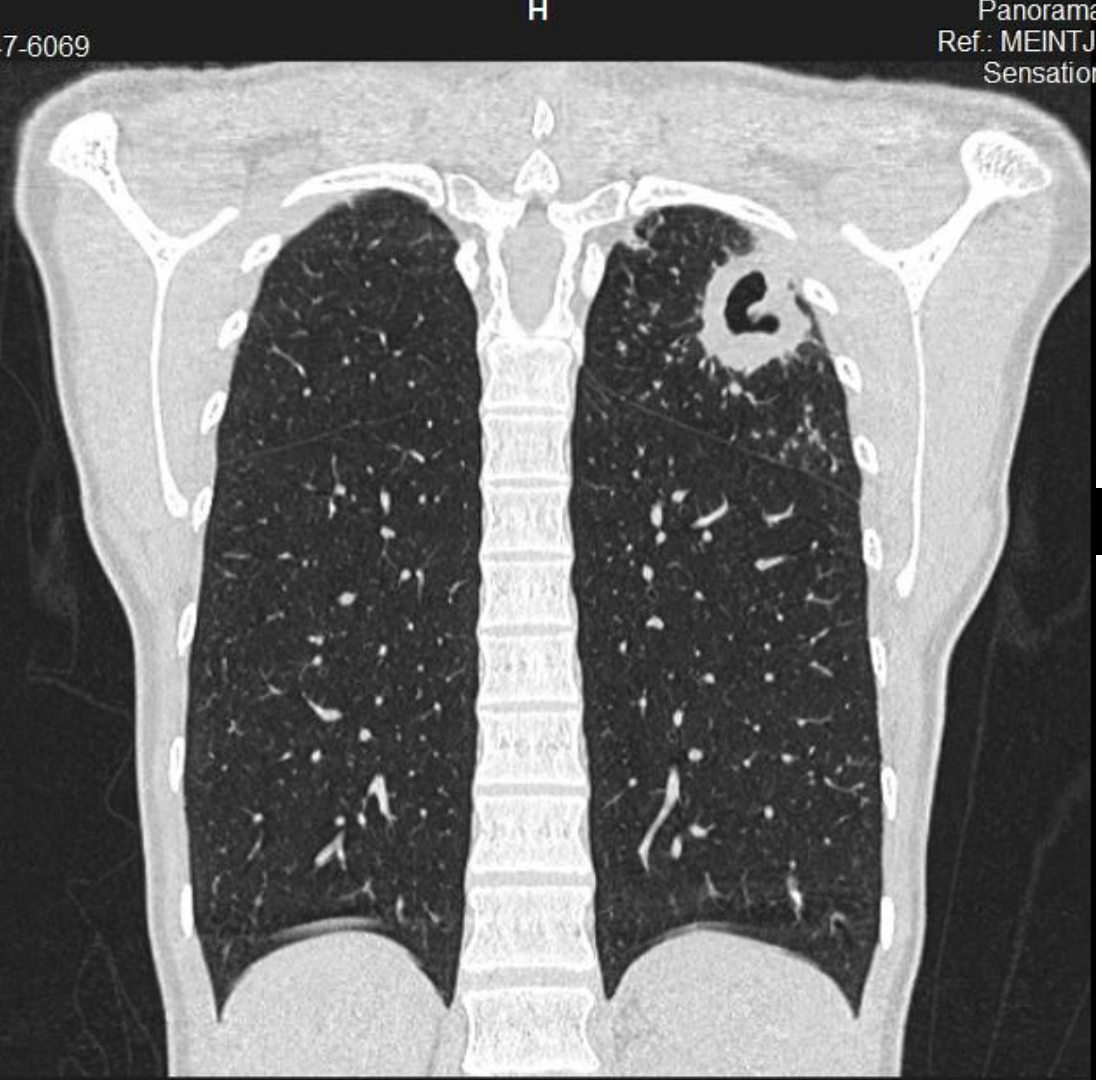
They had all been diagnosed as having extremely drug-resistant (XDR)

SURVIVOR: Somerset West doctor Delene von Delft and her husband Arne. She was one of the first South Africans to take a new new TB drug, the first to get FDA approval in 42 years, which she credits with saving her life. PICTURE: LEON LESTRADE

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.

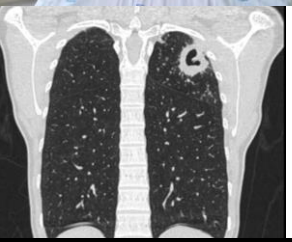
Arne von Delft, TB Proof

SA HIV Clinicians Society Conference, 25 October

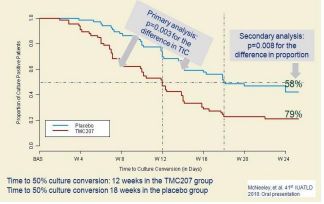


2016 2018

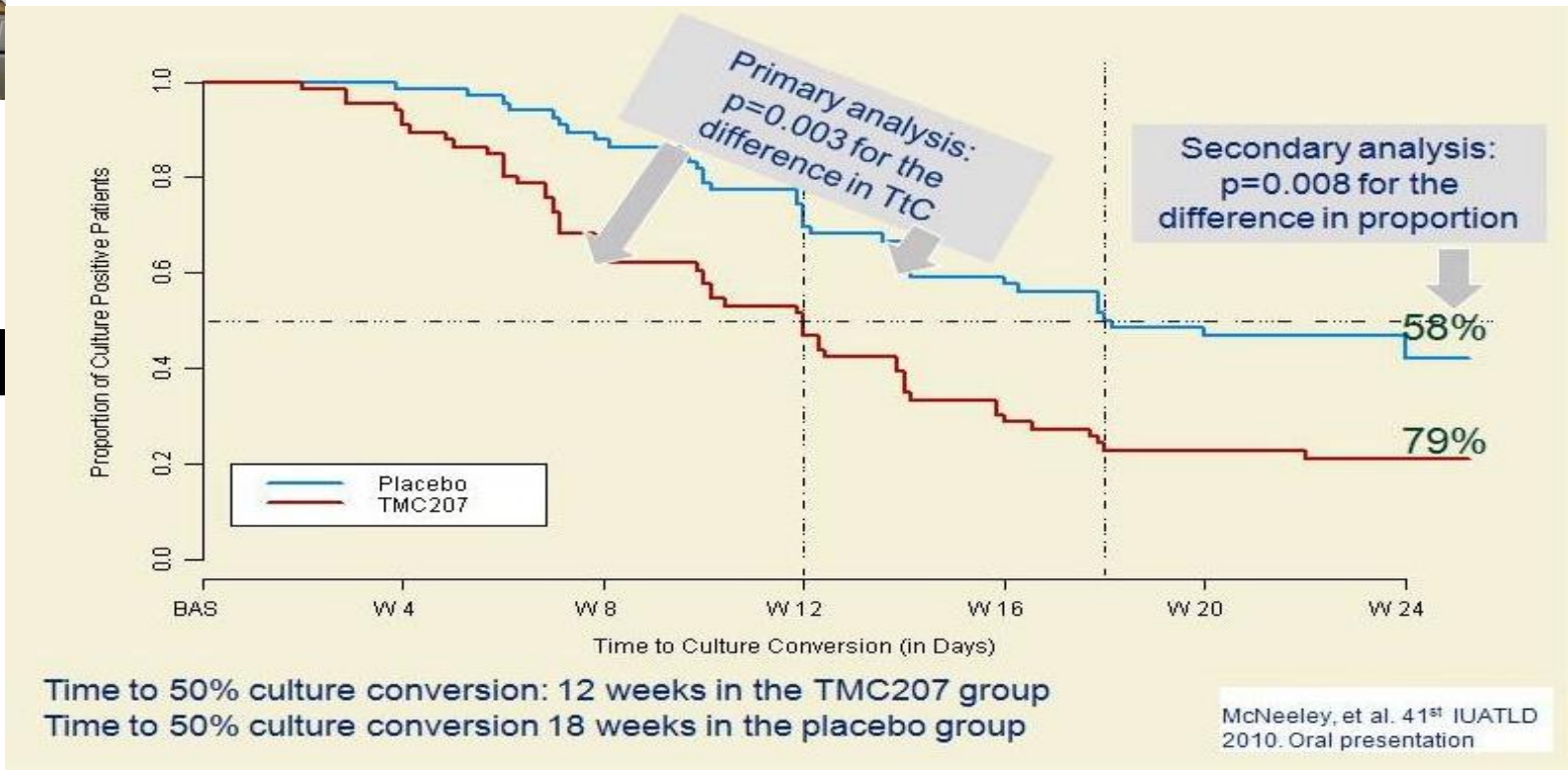
2018



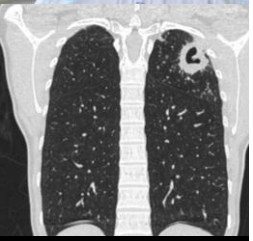
2010



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)



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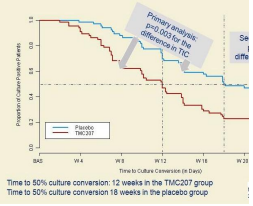
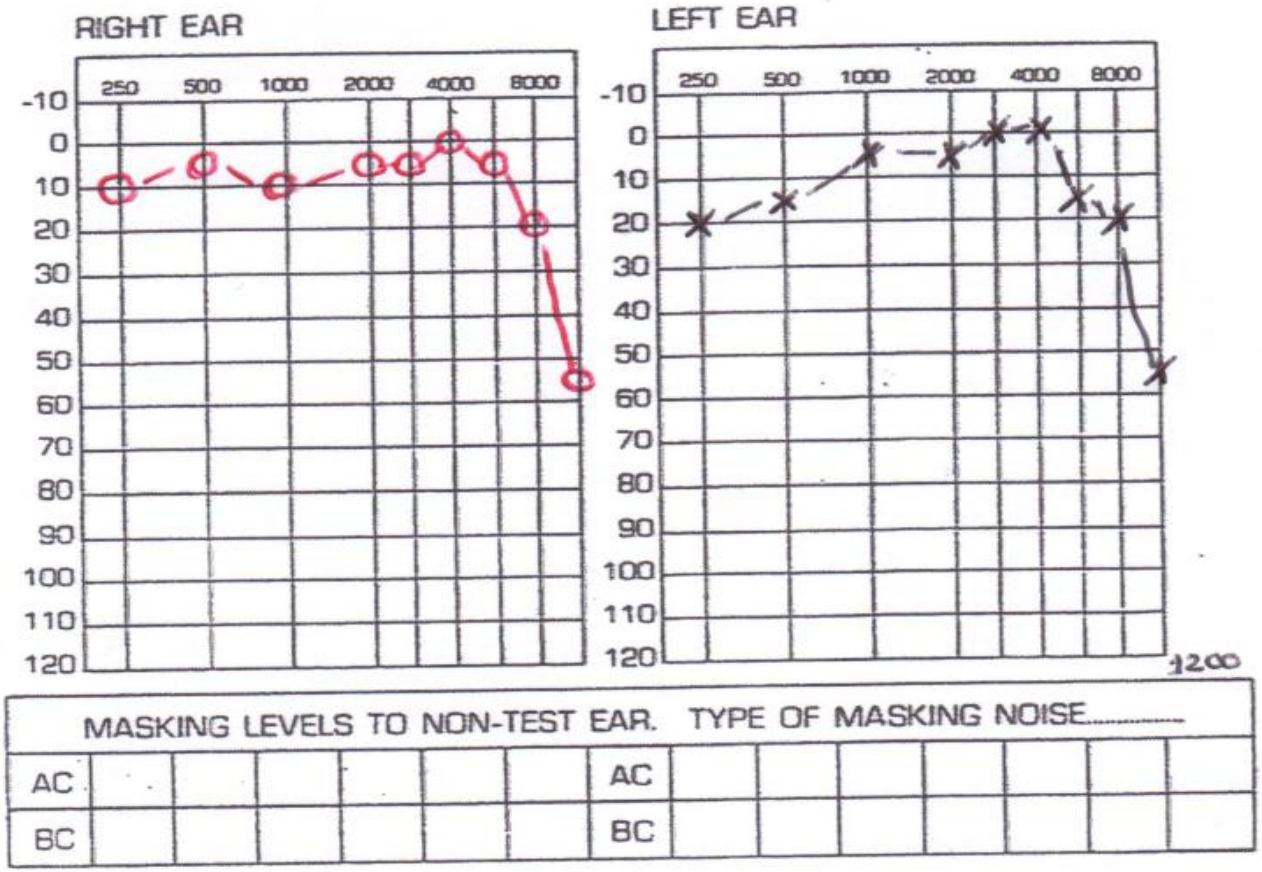

Primary analysis: p=0.003 for the difference in TTC
Placebo
TMC207
Time to Culture Conversion (in Days)
Time to 50% culture conversion: 12 weeks in the TMC207 group
Time to 50% culture conversion 18 weeks in the placebo group


RIGHT EAR
LEFT EAR
250 500 1000 2000 4000 8000
-10 0 10 20 30 40 50 60 70 80 90 100 110 120
12:00
MASKING LEVELS TO NON-TEST EAR. TYPE OF MASKING NOISE.....
AC
BC
AC
BC

2018

18 – 61.5 % ototoxicity but differing methodology

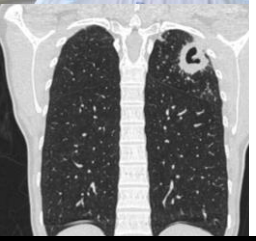
Table 1. Studies that have examined ototoxicity amongst patients on treatment for drug-resistant tuberculosis, assessed using a standardised testing and classification methodology (alphabetical order)

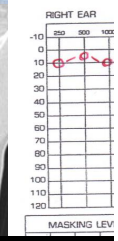
First author	Year of study	Country	Type to testing and classification of hearing loss	Number of subjects tested	Number with ototoxicity (%)	Age Range	Number known to be HIV-infected (%)
de Jager[23]	1995-2000	The Netherlands	15dB at two adjacent frequencies or 20dB at one frequency. Testing frequencies 250-8000Hz	61	11 (18.0)	10-83	NS
Duggal[25]	2000-2006	India	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	64	12 (18.8)	17-65	NS
Kennedy[45]	2004-2009	Ireland	Audiograms every six weeks. Classification based on article by Brummett[46]	13	8 (61.5)	24-82	1/7 (14.3)
Peloquin[22]	1991-1998	USA	20dB at any frequency and 15dB at two adjacent frequencies both assessed. Audiometry tested at 250-8000Hz	87	32-28* (36.8-32.2)	19-79	NS
Sturdy[24]	2004-2009	UK	10dB at two adjacent frequencies, 20dB at any one frequency or clinical symptoms of hearing loss. Frequencies not specified	50	9 (18.0)	34.6 (12.8)**	5 (10)

*Unclear from the article

**Median and standard deviation presented as age range unavailable

Seddon and Schaaf et al. **Hearing loss in patients on treatment for drug-resistant tuberculosis.** ***ERJ Express. June 2012***





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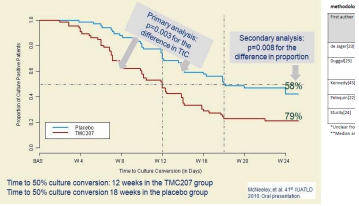
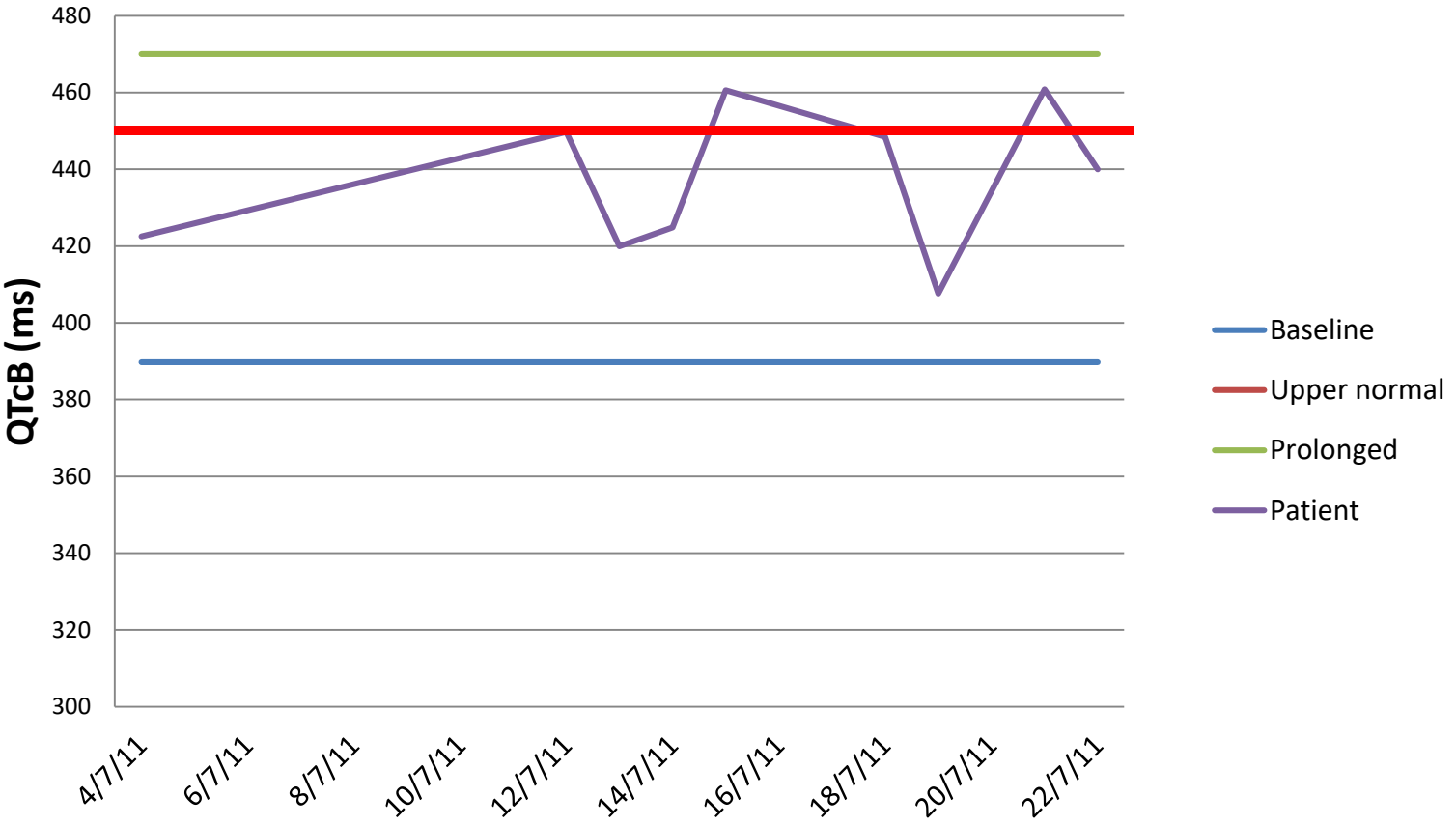
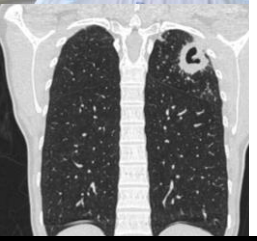


QTcB changes following loading with TMC 207 over two weeks





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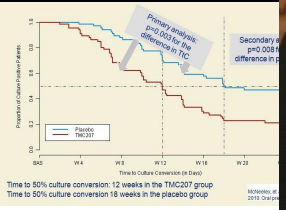
Primary analysis:
Secondary
Placebo
TMC207
BAS
W 4
W 8
W 12
W 16
W 20
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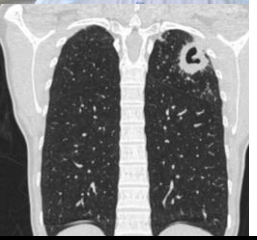
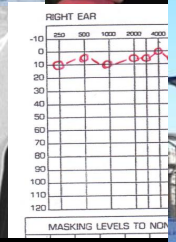
2018





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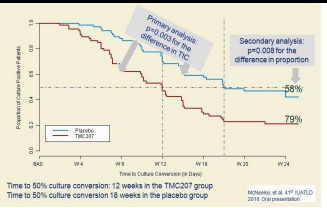

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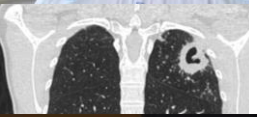
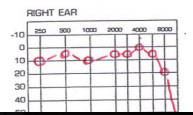
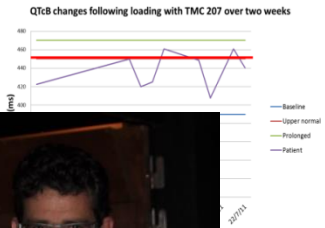
Time to 50% culture conversion 18 weeks in the placebo group

McNeeley, et al. 41st IUATLD 2010. Oral presentation

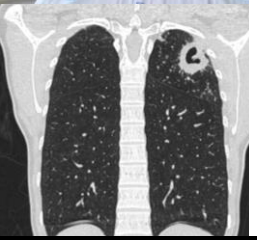






.2 2016 2018

	Number known to be HIV-infected (%)
	NA
	NS
	1/7 (14.3)
	NS
	4 (4%)



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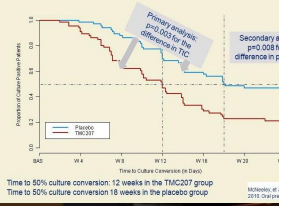


HEALTH-E NEWS

The South African Health News Service

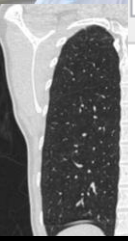
The case for pre-approval access to bedaquiline

November 26, 2012

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.

2018



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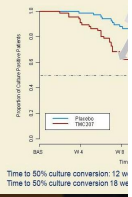

The New York Times

Business Day

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.

Enlarge This Image

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.

2018

WHY SA BANKER LEAPT TO HIS DEATH

PAGE 2

I RISKED DEATH FOR TREATMENT

PAGE 7

SATURDAY Star

R8,50 outside Gauteng
R7,44 for subscribers

SOUTH AFRICA'S BIGGEST-SELLING SATURDA

January 1

MATHS TEACHERS CELE

LOCAL MEDICINE

Newly approved TB drug stirs controversy

Sisi Lwandle
STAFF REPORTER

THE LOCAL medical industry is abuzz with the recent approval of the controversial new TB drug, bedaquiline. The little-tested drug recently received the nod of approval from the Medicine Control Council and may be the last hope for many.

Johnson & Johnson subsidiary Janssen Pharmaceutica's bedaquiline 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 Dalene von Delft, pictured, contracted multidrug resistant TB in 2010 after caring for patients infected with strains of drug resistant TB.

With the threat of lifelong deafness from the current TB treatment and an imminent end to her medical career, Von Delft was ready to try anything.

Access to bedaquiline in South Africa has so far 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 Von Delft. She is now cured of TB.

Dr Claudio Marra of the TB Project SA says: "All drugs... have side effects. People die. This drug is less toxic than the one we are currently using."

Marra believes the benefits of bedaquiline far outweigh the risks.

sibusisiwe.lwandle@inl.co.za

'I chose risk of death over going deaf'

After catching multidrug-resistant TB, doctor faced a stark choice

BIANCA CAPAZORIO

DEAF or dead. Those were the two options offered to doctor Delene von Delft when she was diagnosed with multidrug-resistant tuberculosis three years ago.

Her existing regimen of seven drugs was causing hearing loss. Then there was the option of a new drug – the first new TB drug developed in 42 years to get Food and Drug Administration (FDA) approval in the US – but the clinical trial was already full.

But the new drug came with serious side-effects, including sudden cardiac arrest, and death.

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

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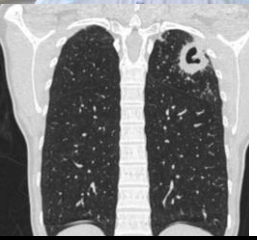
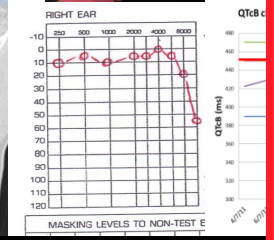
At the time however, the only people accessing it were those in a clinical trial, which was already closed.

They had all





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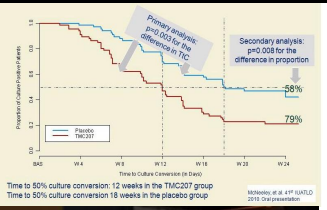
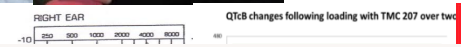


The case for pre-
bedaquiline

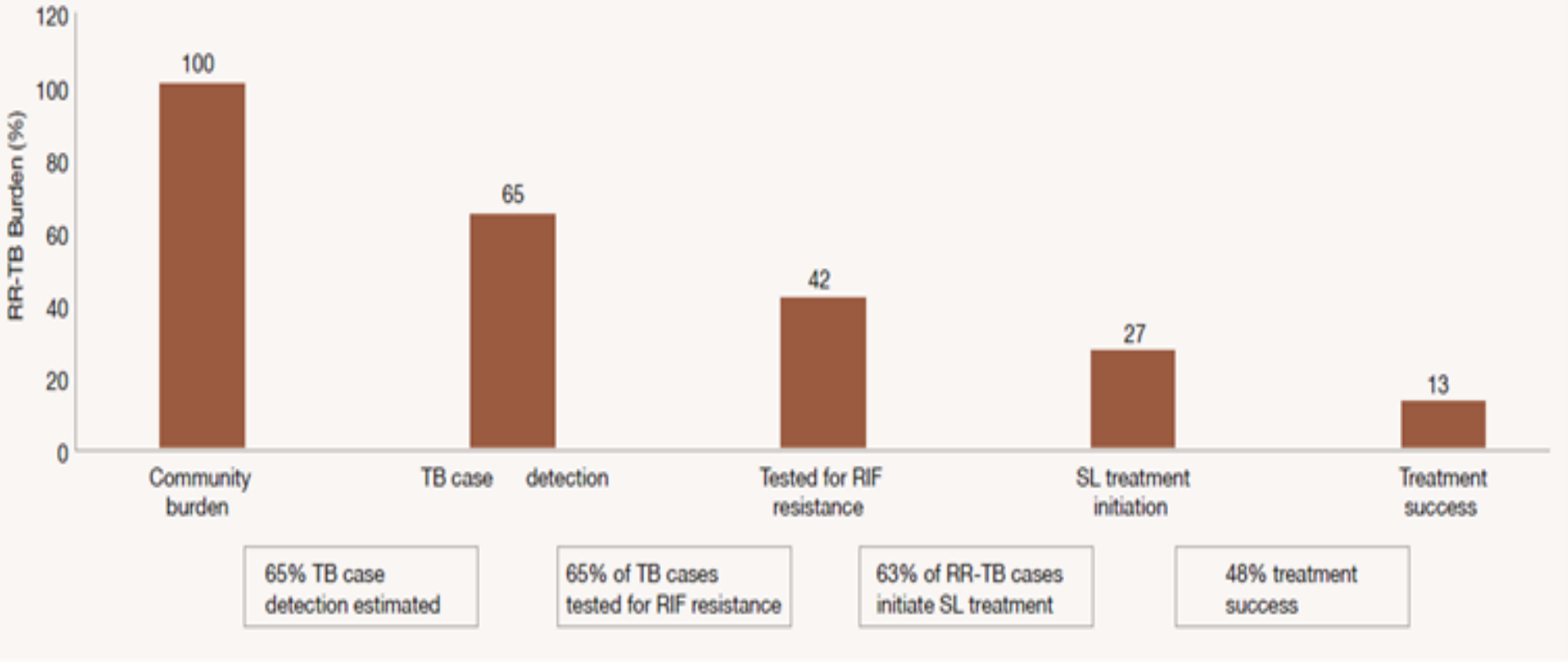
2018

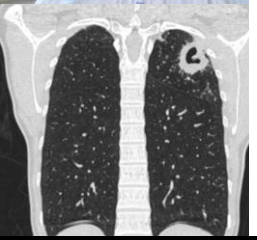
Why drug-resistant tuberculosis threatens us all

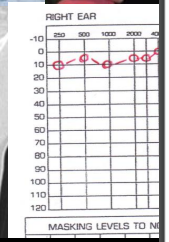

RIGHT EAR

QTcB changes following loading with TMC 207 over two

The Next Pelé / China's Hackers / The World's Hardest Job


RR-TB Burden (%)
120
100
80
60
40
20
0
100
65
42
27
13
Community burden
TB case detection
Tested for RIF resistance
SL treatment initiation
Treatment success
65% TB case detection estimated
65% of TB cases tested for RIF resistance
63% of RR-TB cases initiate SL treatment
48% treatment success





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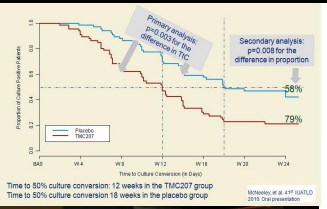
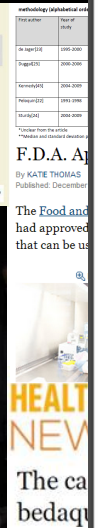




The use of bedaquiline in the treatment of multidrug-resistant tuberculosis

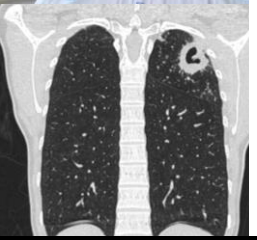
Interim policy guidance

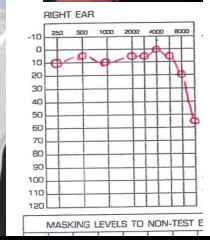
World Health Organization

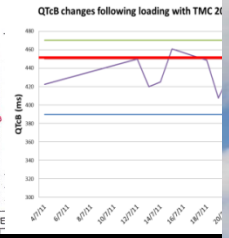
2016

2018


AGENTS OF CHANGE
TB PROOF



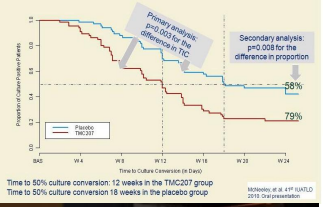


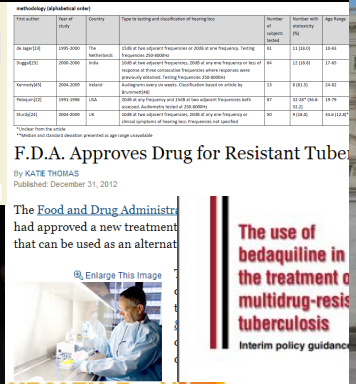


2010

201

2018





methodology (alphabetical order)

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Kennedy[30]	2004-2009	Ireland	Audiograms every six weeks. Classification based on criteria by Brummett[40]	15	9 (81.3)	24-82
Peloquin[115]	1991-1998	USA	2500 at any frequency and 1540 at two adjacent frequencies both assessed. Audiometry tested at 250-8000Hz	97	33 (34* (35.8 - 51.2)	19-79
Sturdy[24]	2002-2009	UK	2000 at two adjacent frequencies, 2500 at any one frequency or clinical symptoms of hearing loss, frequencies not specified	90	9 (16.8)	34.8 (12.8)**

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

F.D.A. Approves Drug for Resistant Tube

By KATIE THOMAS
Published: December 31, 2012

The Food and Drug Administr
had approved a new treatment
that can be used as an alternat

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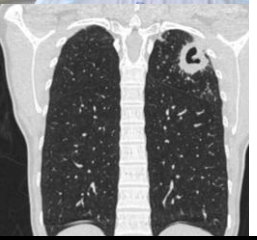
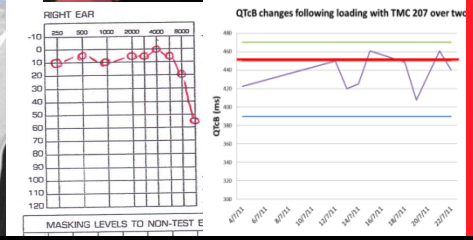
HEALTH-E NEWS

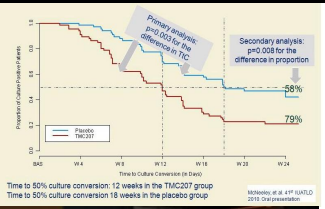
The South
Health Nev

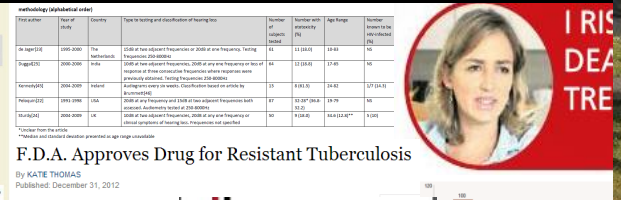
The case for pre-approval acces
bedaquiline

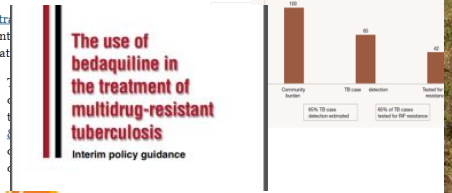


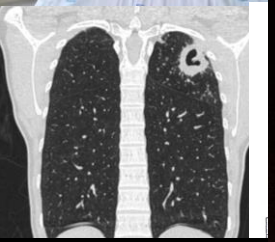


2010 2012 2018









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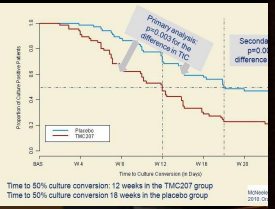
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Placebo
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Time to 50% culture conversion: 12 weeks in the TMC207 group
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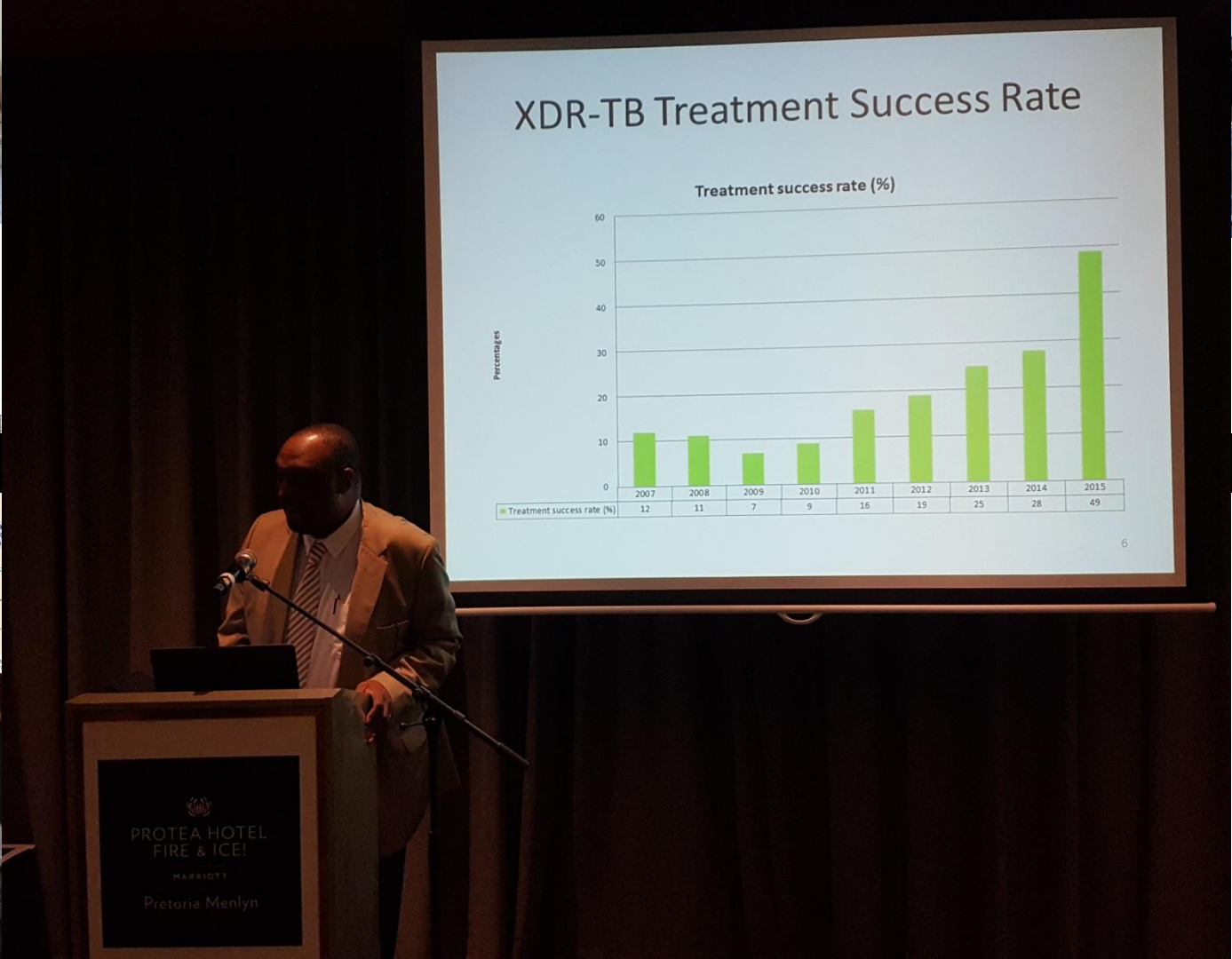
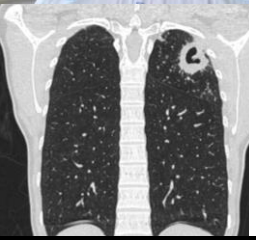
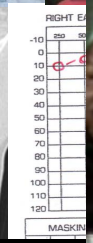

XDR-TB Treatment Success Rate
Treatment success rate (%)
Percentages
60
50
40
30
20
10
0
2007 2008 2009 2010 2011 2012 2013 2014 2015
Treatment success rate (%) 12 11 7 9 16 19 25 28 49
6
PROTEA HOTEL
FIRE & ICE!
MARRIOTT
Pretoria Menlyn

2018





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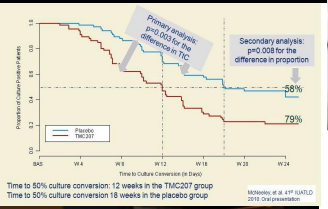


Phumeza Tisile was cured of XDR-TB with the help os MSF-sponsored linezolid.

2018

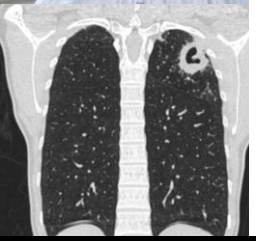
True Life: “I will never get used to not hearing”

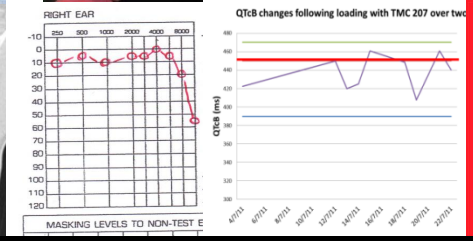
Guest Author

January 16, 2015

News

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.





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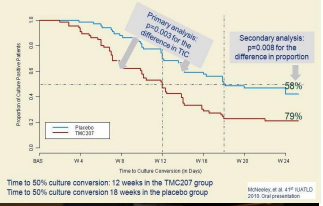

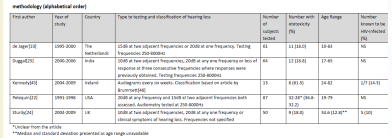

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By KATIE THOMAS
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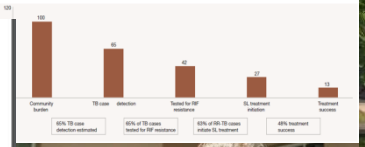

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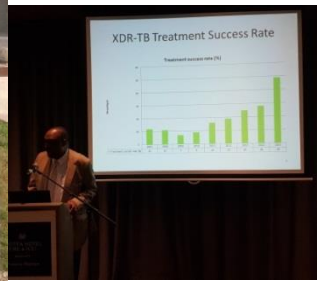
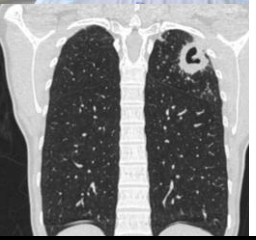
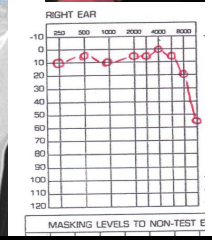
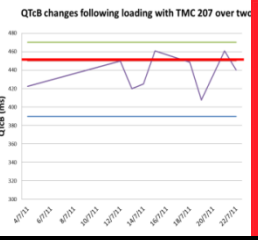
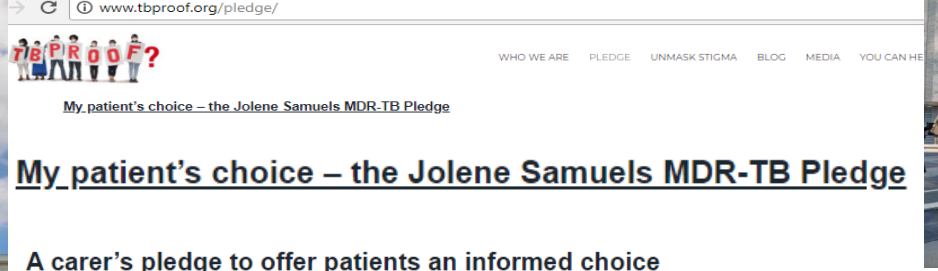
The case for pre-approval access to bedaquiline











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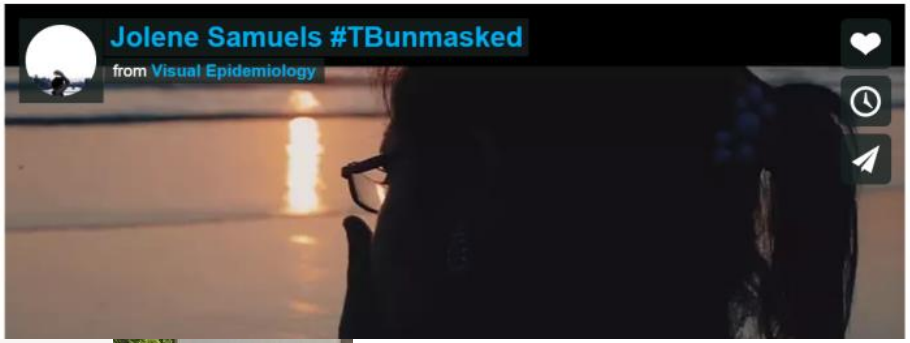

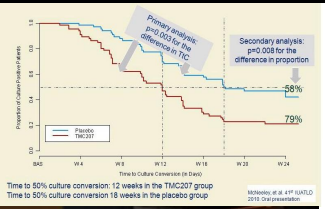

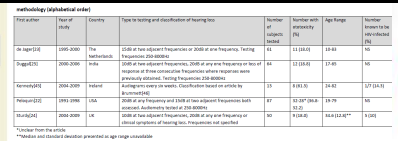

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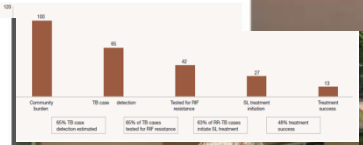

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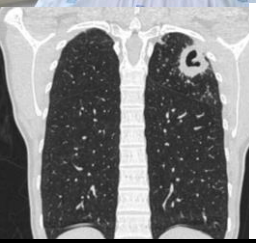

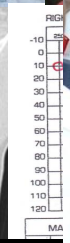

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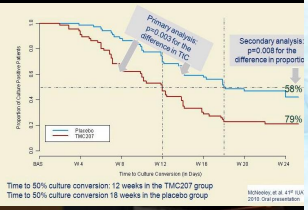

Time to 50% culture conversion: 12 weeks in the TMC207 group
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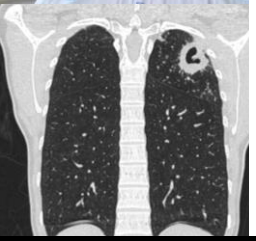
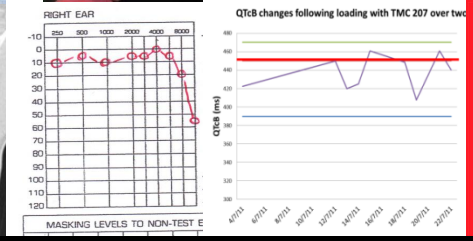
McNeeley, et al. 41st IUA 2010. Oral presentation





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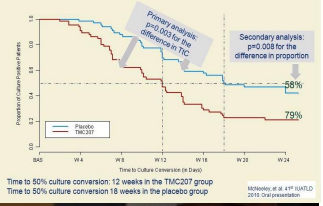
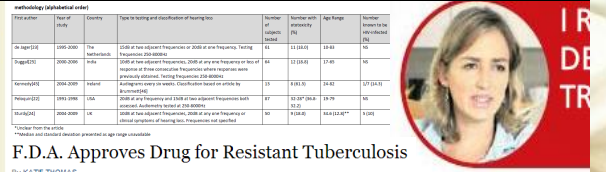
2012





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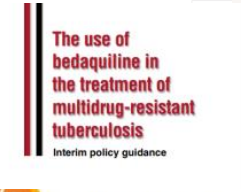

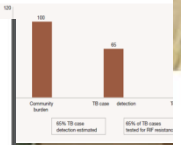

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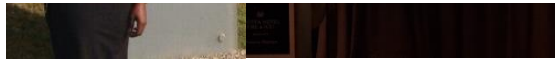
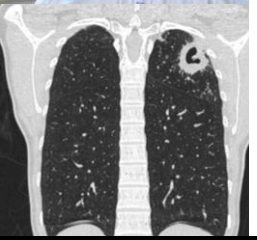
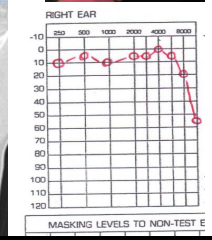
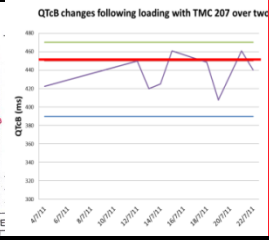
Bedaquiline is one of a handful of new TB drugs used to treat drug-resistant strains. Pediatric TB patient. (Credit: The Global Fund to Fight AIDS, TB and Malaria)

World first for SA: All-access for blockbuster TB drug









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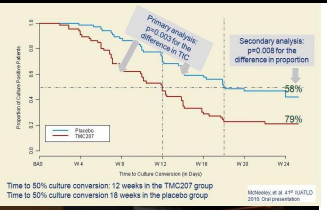

methodology (alphabetical order)

First author	Year of study	Country	Type hr testing and classification of hearing loss	Number of subjects tested	Number with ototoxicity (%)	Age Range	Number known to be HIV-infected (%)
de Jager[114]	1995-2000	The Netherlands	15dB at two adjacent frequencies or 20dB at one frequency. Testing frequencies 250-8000Hz	61	11 (18.0)	18-61	NS
Duggal[25]	2000-2006	India	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	64	12 (18.8)	17-45	NS
Kennedy[30]	2004-2009	Ireland	Audiograms every six weeks. Classification based on article by Brummett[40]	15	9 (81.5)	24-42	1/7 (14.3)
Peloquin[115]	1991-1998	USA	20dB at any frequency and 15dB at two adjacent frequencies both accessed. Audiometry tested at 250-8000Hz	87	53 (61* (56.8-91.2)	19-79	NS
Sturdy[24]	2002-2009	UK	20dB at two adjacent frequencies; 20dB at any one frequency or clinical symptoms of hearing loss. Frequencies not specified	90	9 (16.8)	34.8 (12.8)**	9 (10)

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

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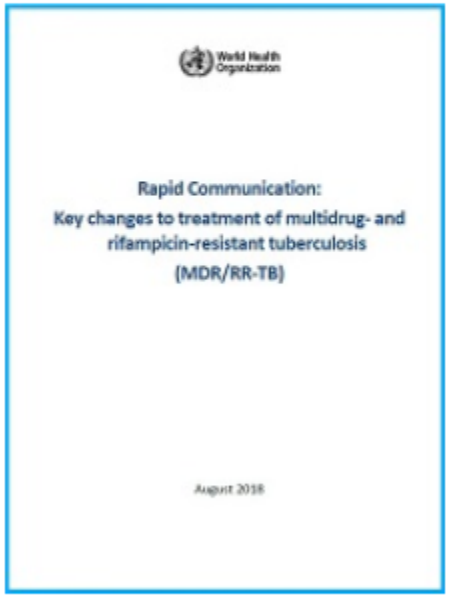
Rapid Communication: Key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB)

Authors:
WHO


World Health Organization

Rapid Communication:
Key changes to treatment of multidrug- and rifampicin-resistant tuberculosis
(MDR/RR-TB)

August 2018

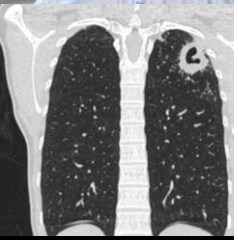
Publication details

Number of pages: 7
Publication date: 2018
Languages: English
WHO reference number:
WHO/CDS/TB/2018.18

Downloads

– Download the Rapid Communication
pdf, 834kb

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.



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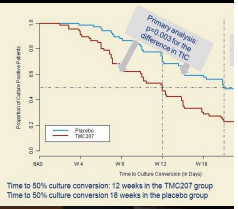

DR-TB STAT

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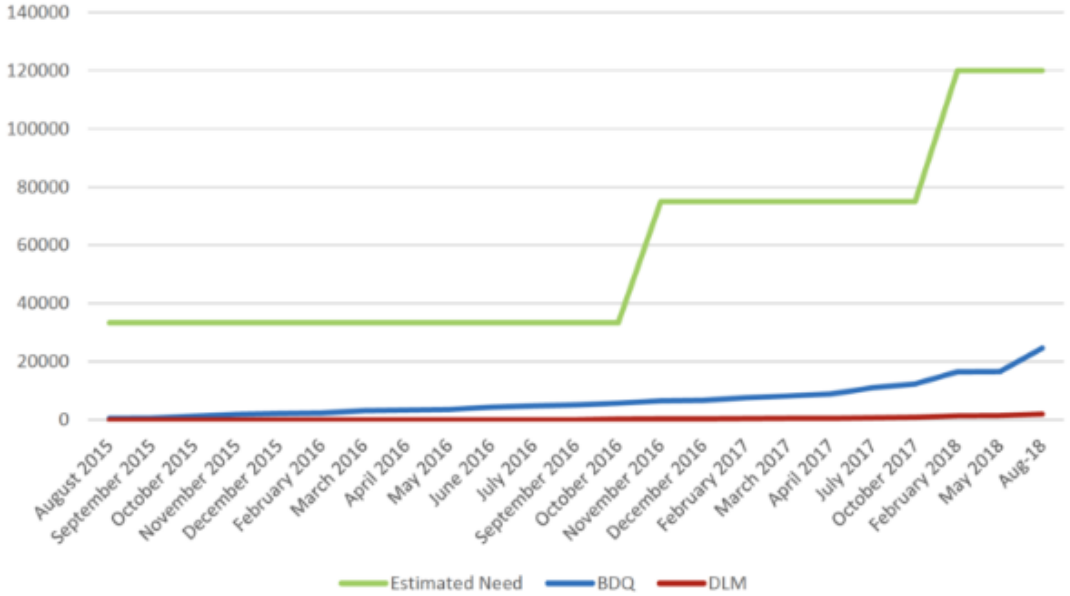
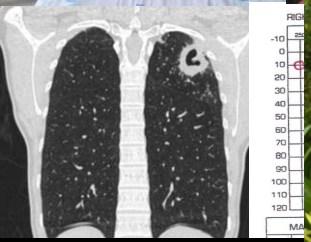
02. Cumulative Delamanid and Bedaquiline Use Over Time Compared with Conservative Estimated Need, August 2015 – Present



*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



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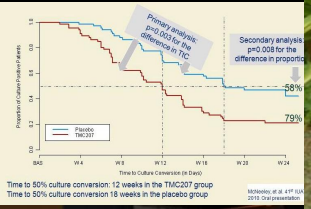
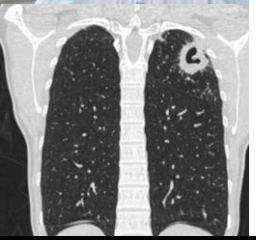
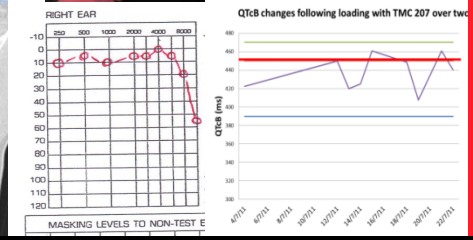
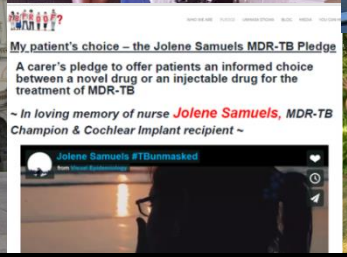

Primary analysis: p=0.003 for the difference in TTC
Secondary analysis: p=0.008 for the difference in proportio
58%
79%
Placebo
TMC207
BAS
W4
W8
W12
W16
W20
W24
Time to Culture Conversion (in Days)
Time to 50% culture conversion: 12 weeks in the TMC207 group
Time to 50% culture conversion 18 weeks in the placebo group

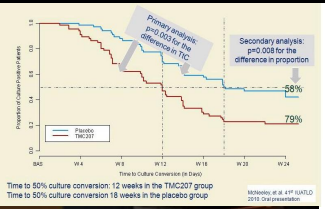

ZERO STIGMA
Together we can
#EndTB







2010 2012 *QUESTIONS?* 2016 2018



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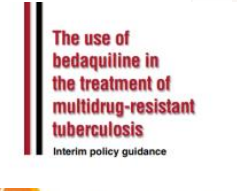
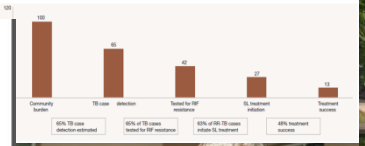
that can be used as an alternat

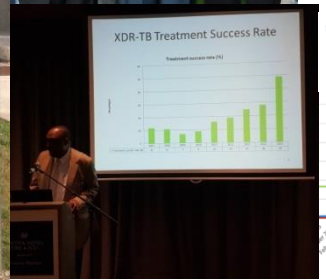




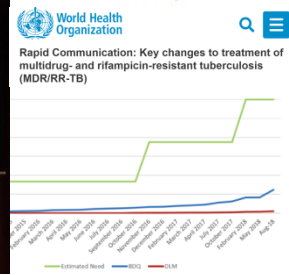
HEALTH-E NEWS
The South African Health News Service

The case for pre-approval access to bedaquiline

True Life: "I will never get used to not hearing"



World first for SA: All-access for blockbuster TB drug



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