Patients and TB: Improving treatment outcomes through a patient centred approach and access to new treatments

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Beyond XDR-TB: which other patients could benefit from new drugs?

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MEDECINS SANS FRONTIERES

MINISTRY OF LABOUR, HEALTH AND SOCIAL AFFAIRS OF GEORGIA

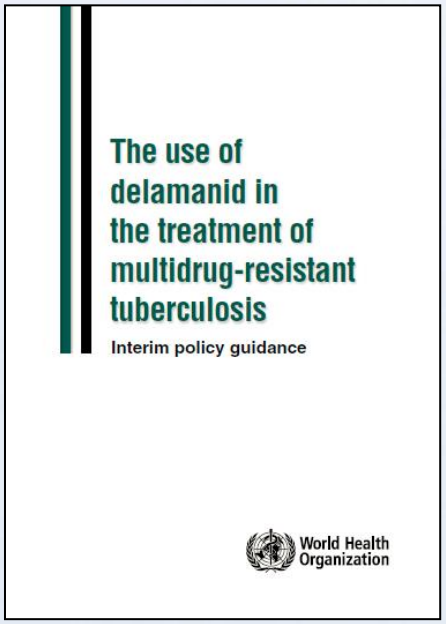
Eligibility criteria for new drugs

1. Drug resistance-related criteria: patients with XDR-TB, MDR-TB with additional resistance to fluoroquinolones or second-line injectable drugs or other advanced drug resistance patterns

2. Patient-related criteria: patients with increased risk of poor outcome

Delamanid patient-related indications : WHO guidance

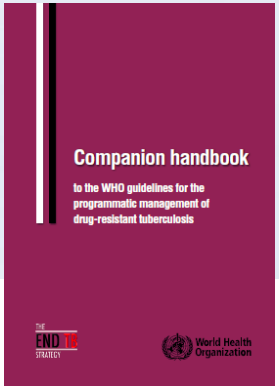
MDR-TB patients at higher risk of poor outcomes (e.g. drug intolerance or contraindication, extensive or advanced disease)



Delamanid patient-related indications : WHO companion handbook

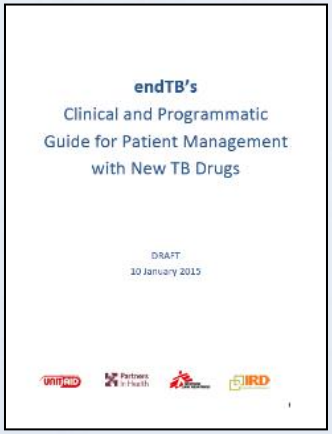
MDR-TB plus evidence of (or unknown) susceptibility to Groups 2 and 3 agents and with risk of poor treatment outcome (acquired resistance, treatment failure or death) (scenario 0)

Use of delamanid in adult patients with MDR-TB may be considered by programs with low treatment success rates despite good programmatic conditions because of decreased mortality associated with delamanid use and its good safety profile.



Elligibility criteria for new drugs: endTB guidance

1. **Patients for whom the construction of a regimen with four likely effective second-line drugs (from Groups 2 to 4) including a fluoroquinolone and an injectable is not possible**
   a) XDR-TB
   b) Pre-XDR-TB
   c) Patients with two or more Group 4 drugs (Eto/Pto, Cs, PAS) compromised.
   d) Patients unable to tolerate MDR-TB drugs necessary for construction of the regimen.
   e) Patients who are a "failure" of an MDR-TB regimen by WHO 2013 definitions.
   f) ….



endTB

Elligibility criteria for delamanid: endTB guidance

2. Patients with other risks of poor outcome

a. Patients with extensive or advanced disease (multiple cavities, bilateral lesions, or extensive parenchymal damage or multiple system involvement)

b. Patients with increased likelihood of treatment failure, or death (patients with low body mass index, HIV, diabetes, etc.)

c. Patients coming from catchment areas that have poor MDR-TB treatment outcomes despite good programmatic conditions (e.g. sites with extensive second-line drug resistance background)

Assessing the needs for new drugs

Identification of patients who could benefit from bedaquiline or delamanid: a multisite MDR-TB cohort study

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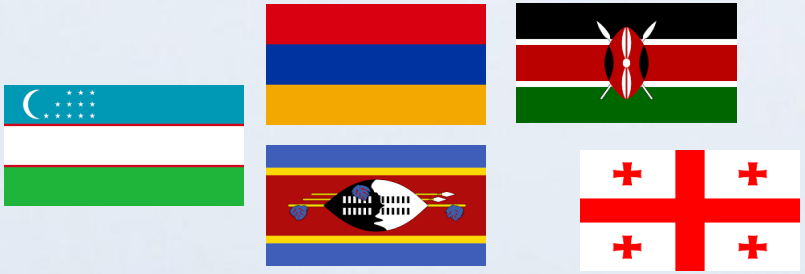
Main Objective:

to identify patients at risk of unfavourable outcomes who could benefit from the addition of the new drugs

Methods

- Multisite, retrospective cohort study of outcomes of treatment in programmes supported by MSF in Uzbekistan, Georgia, Armenia, Swaziland and Kenya
- ≥18 years old MDR-TB patients
- Enrolled from 2001 to 2009
- 2008 WHO outcome definitions
- Univariate and multivariate analysis



Results

- 1433 patients enrolled
- Simple MDR-TB: 66%, pre-XDR: 31%, XDR-TB: 3%
- Known HIV-positive: 2%
- Treatment outcomes:
  - Success (cure + completed): 56%
  - Death: 9%
  - Failure 11%
  - Lost to follow-up: 23%

Patients characteristics

Patients related factors	Resistance related factors
Sex	DST
Age	First-line resistance only
History of incarceration	Pre-XDR-TB 1 injectable agent
Alcohol consumption	Pre-XDR-TB 2 injectable agents
Contact with an MDR-TB patient	Pre-XDR-TB OFX
Anti-TB treatment history	XDR-TB
First-line drugs	Resistance to ETH
Second-line drugs	Resistance to PZA
Diabetes	Resistance to EMB
HIV	
Cavity on X-Ray	Treatment
Low BMI	Number of drugs
AFB grade at initiation	Prescription of FQ
	Prescription of injectable
	Prescrition of thioamides

Factors associated with unfavorable outcomes Multivariate analysis

Factors	aOR (95%CI)
• XDR-TB.....	8.16 (3.22-20.64)
• Resistance to two injectables.....	1.90 (1.00-3.62)
• Resistance to ofloxacin.....	5.56 (2.15-14.37)
• Previous TB treatment	
– 1° line.....	1.97 (1.14-3.42)
– 2° line.....	3.24 (1.53-6.85)
• Past imprisonment.....	2.22 (1.56-3.12)
• Low BMI.....	1.64 (1.07-2.52)
• High bacillary load (2+/3+).....	2.32 (1.15-4.67)

Findings from other studies

Factors associated with poor outcomes

- Lung cavitations[1,3,4]
- Age >40 years[1,2,3] or older age[6,7]
- Comorbidities[1,5,7]
- Weight < 40 kg[1] or low BMI[7]
- Smear positivity[3] and smear +++[6]
- HIV infection[3,7]

1. Ahmad et al, IJTLD 2015
2. Chiang et al, ERJ 2006
3. Balabanova et al, BMJ Open 2011
4. Yew et al, Chest 2000
5. Anderson et al, Eurosurv 2011
6. Velazquez, CID 2014
7. Mitnick et al, Plos One 2013

Conclusions

- Patient characteristics such as low BMI and high-grade smear sputum positivity are consistently associated with poor outcomes in literature
- HIV-positive patients were too few in our cohort to draw any conclusion but could be another risk group
- Comorbidities (i.e. diabetes), cavitary disease and older age are often found as risk factors in literature but not in our cohort

Conclusions

- The proportion of patients at high risk of poor outcome and who could benefit from the prescription of DLM was high in our cohort
  - 48.5% of patients with BMI < 18.5Kg/m^2
  - 72.9% of patients with high bacillary load at treatment initiation
- Other risk factors for poor outcome exist in other settings and need to be considered in the indication of DLM

- Actual indication for delamanid may be much broader than expected

Thank you!