Too little, too late; new anti-TB drugs for patients with complex drug-resistant tuberculosis in Mumbai

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- For all types of TB, treatment should contain > 4 effective drugs
Treating DR-TB

- Current recommended regimen for DR-TB:
  - Lack of clinical trial evidence
  - Toxic
  - Very long (up to 2 years)

- Outcome of DR TB treatment
  - Treatment success in MDR TB: 48%
  - HIV/DR TB co-infected: 38%
since Rifampicin > 50 years ago

Bedaquilline (Bdq) & Delamanid (Dlm)
- validated by WHO with “monitoring of pharmacovigilance”
- The price of new drugs is still high – Bdq: 900 USD/course, Dlm: 1700 USD/course

New drugs are available to only 2% of patients who need them (AC)
- Compassionate Use programs and restrictive protocols for Dlm
- Bdq Conditional Access Programs that is about to start in India
- Provides ambulatory free DR TB and HIV treatment services since 2006
- 1101 HIV and 253 TB/DR TB beneficiaries
- Increasing proportion of complex DR TB cases (PreXDR and XDR)
- Counseling and consent

**Enrolled DR TB patients (2013-2015)**

<table>
<thead>
<tr>
<th>Year</th>
<th>EMP</th>
<th>PDR</th>
<th>MDR</th>
<th>PreXDR</th>
<th>XDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2014</td>
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<tr>
<td>2015</td>
<td></td>
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</table>
Method of study

- Retrospective cohort analysis of
  - 12 patients registered for Bdq
  - 14 patients for Dlm,
  - from Feb 2013 to Feb 2015
- MSF ERB approval
### Characteristic of patients

<table>
<thead>
<tr>
<th></th>
<th>Bedaquiline Group (n=12)</th>
<th>Delamanid Group (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>18-37</td>
<td>17-47</td>
</tr>
<tr>
<td><strong>Gender (M:F)</strong></td>
<td>4 : 8</td>
<td>4 : 10</td>
</tr>
<tr>
<td><strong>HIV co-infected</strong></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Type of DR TB (based on 13 drugs Drug Susceptibility Testing)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre XDR</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>XDR</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td><strong>Prior exposure to 2\textsuperscript{nd} line anti-TB drugs</strong></td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>
No of patients by ≥ 4 and < 4 likely working drugs* including 1 new drug

*likely working drugs arbitrarily defined as

- drugs sensitive in DST-results
- and/ or < 3 month-of-exposure

![Bar chart showing number of patients with ≤ 4 and ≥ 4 drugs for Bdq and Dlm.](chart.png)

- Bdq: 3 patients with ≤ 4 drugs and 9 with ≥ 4 drugs
- Dlm: 2 patients with ≤ 4 drugs and 12 with ≥ 4 drugs
Outcome

12 requests Bdq CU

- 1 died prior to initiation
- 11 started on treatment

- 1 died after Bdq course

- 2 cured / completed
- 8 doing well on treatment

14 requests Dlm CU

- 1 died prior to initiation
- 1 no effective regimen
- 12 started on treatment

- 2 died on treatment

- 10 doing well on treatment
## Results – Major SAE

<table>
<thead>
<tr>
<th></th>
<th>Death during treatment</th>
<th>Severe Cardio-toxicity (QTc &gt; 500ms)</th>
<th>Other severe Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bdq (n=11)</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Dlm (n=12)</td>
<td>2</td>
<td>2*</td>
<td>2*</td>
</tr>
</tbody>
</table>

- 3 deaths = probably not attributable to new drugs
- Dlm - cardio-toxicity triggered by electrolytes imbalance (vomiting) *
- No need for permanent discontinuation
We can offer ambulatory treatment with adequate monitoring (clinical, lab & ECG)

Promising outcomes: sustained culture conversion – 16/20 cases

Limitation: Small cohort (10% of global Dlm cohort at time of analysis)
Discussion

- 21 patients with < 4 likely working drugs,
  - Diagnosed too late
  - Too few drugs ≈ sub-standard regimens

- Started on treatment too late: patients are likely to die before accessing new drugs (2/26) - Complex / restricted access

- 2 patients with no drug exposure ≈ on-going transmission in the community
Conclusions & Programmatic Implications

- Implementation of new treatment implies capacity-building in
  - Pharmacovigilance
  - Intensified treatment monitoring.

- Treat DR-TB promptly and aggressively
  - Urgent need for broader access to combination treatment with Bdq + Dlm

- Need to tackle community transmission of DR TB
Acknowledgements

MSF team in Mumbai/Delhi &
Our Patients on their difficult life-journey with DR TB

Thank You!