endTB

Updates from the observational study

Uzma Khan
[On behalf of the endTB consortium]
15 Nov 2018
endTB Observational Study
Largest multi-centric observational study on regimens containing bedaquiline and/or delamanid

17 > 2600 Countries Patients
**Methods**

**Cohort analysis of research-consented patients**
- Receiving MDR-TB treatment regimen including bedaquiline and/or delamanid per WHO recommendations

**Data capture**
- Standardized data collection at project sites
- Electronic medical record (OpenMRS, Bahmni), pharmacovigilance database
- Standardized endpoints
Cohort Description
April 1, 2015 to May 31, 2018

2241 patients
starting Bdq or Dlm

- Kazakhstan: 23%
- Bangladesh: 11%
- Georgia: 12%
- Armenia: 4%
- Peru: 9%
- Pakistan: 12%
- Myanmar: 2%
- Lesotho: 9%
- Kyrgyzstan: 1%
- DPRK: 5%
- Vietnam: 0.6%
- Armenia: 4%
- Bangladesh: 11%
- Belarus: 4%
- Ethiopia: 3%
- Georgia: 12%
- Haiti: 0.5%
- Indonesia: 2%
- Kenya: 0.2%
Use of Bedaquiline Predated Use of Delamanid
Enrolled until May 31 2018

![Graph showing the number of enrollments over time for Bedaquiline (BDQ) and Delamanid (DLM), with cumulative enrollments (Cumu_BDQ and Cumu_DLM) also displayed. The graph indicates a trend where Bedaquiline enrollments increase over the years, and Delamanid enrollments follow a similar pattern.]
## Patient Characteristics

April 1, 2015 – 31 May 2018

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total N (%) N=2241</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age [range]</td>
<td>37 [9 – 88]</td>
</tr>
<tr>
<td>Female</td>
<td>794 (35)</td>
</tr>
<tr>
<td>Body mass index &lt;18.5 (n=2207)</td>
<td>928 (42)</td>
</tr>
<tr>
<td>Resistance (n=2137)</td>
<td></td>
</tr>
<tr>
<td>RR/MDR-TB</td>
<td>697 (31)</td>
</tr>
<tr>
<td>Pre-XDR (FQ)</td>
<td>519 (23)</td>
</tr>
<tr>
<td>Pre-XDR (Inj)</td>
<td>270 (12)</td>
</tr>
<tr>
<td>XDR</td>
<td>651 (29)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>HIV (N=2217)</td>
<td>297 (13)</td>
</tr>
<tr>
<td>Hepatitis C (N=2194)</td>
<td>236 (11)</td>
</tr>
<tr>
<td>Diabetes (N=2107)</td>
<td>266 (13)</td>
</tr>
<tr>
<td>Previously treated w/ SLDs (N=2240)</td>
<td>1638 (73)</td>
</tr>
</tbody>
</table>
Patients Enrolled Early were Chronic & Sicker

- Resistance indications
- Unable to tolerate MDR drugs
Indonesia

**Indonesia**

- **2014**
  - DS-TB Rx at a private clinic, outcome unknown

- **2015**
  - Started treatment at another private clinic. Doctor suggests patient should seek treatment in Malaysia

- **2016**
  - Returned to Jakarta. Got hospitalized at a private hospital. After discharge, did not return to the hospital

- **2017**
  - Patient traveled to Malaysia and stayed there for 2 months without improvement

- **– now –**
  - Patient started treatment again at a private hospital, after a few months patient was asked to go to RS Islam Cempaka Putih

- **– now –**
  - Received MDR TB treatment at RS Islam Cempaka Putih (enrolled on endTB in October 2017)
endTB Interim Analysis

1. What is the evidence for or against the use of delamanid in multidrug regimens for RR/MDR-TB?

2. What is the evidence for or against the use of injectable-sparing regimens for RR/MDR-TB when BDQ &/or DLM are available?

3. What is the range of adverse event (AE) profiles observed in multidrug regimens that include bedaquiline and/or delamanid?
Interim Analysis
Delamanid Efficacy & Toxicity

- ≥ Grade 3 QTc interval prolongation infrequent
- Culture conversion occurs in ~80%, including among XDR and patients with comorbidities
  - Conversion in HIV coinfected lower
- Balance of efficacy and safety supports delamanid use
Important toxicity common among patients receiving SL injectable

- 20% of patients had hearing loss
- 36% had injectable-related AE (hearing loss, acute renal failure, electrolyte imbalance)

Balance of evidence does not support universal use of SL injectable (also supported by the IPD analysis – WHO recommendations)

- Consider treatment options, patient preference
- Effective monitoring

Interim Analysis
Injectable Efficacy & Toxicity
BDQ- and DLM-containing multidrug-regimens achieve excellent interim treatment response without safety concerns

endTB Interim Analysis

http://www.endtb.org/resources/endtb-interim-analysis-july2018