New Frontiers: Innovation and Access

Rapid implementation of WHO guidelines

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RSPC for Pulmonology and TB, Belarus

February 28th - March 1st 2019
Belarus challenges $M/XDR-TB$

### TB indicator

<table>
<thead>
<tr>
<th>Indicator</th>
<th>No. of patients</th>
<th>Per 100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>1916</td>
<td>20,2</td>
</tr>
<tr>
<td>Prevalence</td>
<td>4035</td>
<td>42,5</td>
</tr>
<tr>
<td>Mortality</td>
<td>242</td>
<td>2,6</td>
</tr>
</tbody>
</table>

### MDR-TB

- **Previously treated**:
  - 1916
  - 20,2

- **New cases**:
  - 1454
  - 2018

- **Incidence**:
  - 2011: 59.2
  - 2012: 66.4
  - 2013: 69.4
  - 2014: 66.7
  - 2015: 65.8
  - 2016: 67.6
  - 2017: 65.6
  - 2018: 64

- **Prevalence**:
  - 2011: 27
  - 2012: 32.9
  - 2013: 33.8
  - 2014: 33.2
  - 2015: 34.3
  - 2016: 35.7
  - 2017: 36
  - 2018: 32
Belarus challenges

**MDR-TB treatment outcomes**

### MDR-TB + HIV

- 2016 n=145
- 2015 n=157
- 2014 n=163
- 2013 n=141

### MDR-TB without HIV

- 2016 n=1349
- 2015 n=1590
- 2014 n=1666
- 2013 n=1272

*Legend:*
- Success
- Failure
- LTFU
- Death
- N/E
Key strategic directions of NSP

1. Scale up of case finding and prophylaxis
2. Full scale-up of rapid molecular diagnostics
3. Rapid uptake of new drugs and regimens
4. Expanding people-centered models of care
5. Scale up TB research

Bedaquiline (June 2015)
Delamanid (June 2016)
Linezolid Clofazimine (2015)
Carbapenems, Amoxicillin/clavulonat
## M/XDR-TB patients on new drugs

<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Sex</th>
<th>DST</th>
<th>Treatment Regimen</th>
<th>Date of Treatment initiation</th>
<th>Baseline</th>
<th>Follow-up Month 1</th>
<th>Follow-up Month 2</th>
<th>Follow-up Month 3</th>
<th>Follow-up Month 4</th>
<th>Follow-up Month 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSF007</td>
<td>56</td>
<td>F</td>
<td>XDR</td>
<td>Bdq-Imp/Cln-Amx/Clv-Cfz-Lzd-Mfx</td>
<td>17-Nov-15</td>
<td>1+ P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSF008</td>
<td>45</td>
<td>F</td>
<td>XDR</td>
<td>Bdq-Imp/Cln-Amx/Clv-Cfz-Lzd-Mfx</td>
<td>19-Nov-15</td>
<td>N P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Total no. of patients (1 Jan 2019)

**1225**

Incl. children and adolescents **37**

### Regimes containing

<table>
<thead>
<tr>
<th>BDQ</th>
<th>DLM</th>
<th>BDQ + DLM</th>
</tr>
</thead>
<tbody>
<tr>
<td>763</td>
<td>314</td>
<td>148</td>
</tr>
</tbody>
</table>

**BDQ, DLM, BDQ+DLM given for more than 24 weeks**

<table>
<thead>
<tr>
<th>BDQ</th>
<th>DLM</th>
<th>BDQ + DLM</th>
</tr>
</thead>
<tbody>
<tr>
<td>58%</td>
<td>46%</td>
<td>43%</td>
</tr>
</tbody>
</table>
# Treatment results *(Jan 1, 2019)*

<table>
<thead>
<tr>
<th></th>
<th>BDQ</th>
<th>DLM</th>
<th>BDQ+DLM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Final treatment outcomes</strong></td>
<td>275</td>
<td>44</td>
<td>11</td>
</tr>
<tr>
<td>Cure + treatment completed</td>
<td>231</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Treatment failed</td>
<td>8</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Lost to follow up (LTFU)</td>
<td>20</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Death</td>
<td>16</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td><strong>Still on treatment</strong></td>
<td>488</td>
<td>270</td>
<td>137</td>
</tr>
</tbody>
</table>

**Age, years, median (range)**

| Gender m/f | 902 / 323 |

**DR profile**

<table>
<thead>
<tr>
<th>DR profile</th>
<th>MDR-TB</th>
<th>MDR-TB+FQ</th>
<th>MDR-TB+SLI</th>
<th>XDR-TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>14%</td>
<td>11%</td>
<td>21%</td>
<td>53%</td>
<td></td>
</tr>
</tbody>
</table>

**TB History**

| New cases | 43% |
| Previously treated | 57% |

**HIV co-infection**

| 9% |

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**Children on new drugs**

| 37 |

| BDQ since Sep. 2015 | 18 |
| DLM since Dec. 2016 | 19 |

**Interim results**

| Failed | 0 |
| LTFU   | 0 |
| Died   | 0 |

| Cured + Treatment completed | 22 (18 BDQ) |
| Treatment continuing       | 15 |
Treatment outcomes

BDQ (n=275)

Treatment success – 84%

- Treatment success
- Treatment failure
- Death
- LTFU
MDR-TB Consilium

- Careful patient selection
- Designing treatment regimen in line with WHO recommendations
- Management of co-morbidities (e.g. HIV, DM)
- Treatment monitoring
- Active Drug Safety Monitoring and Management of Adverse Events (aDSM)
- Adherence issues
  - DOT, VOT
  - Alcohol and drug abuse
  - Mental health problems
  - Social support issues
- Surgery issues
Full scale-up of rapid molecular diagnostics

Acceptable time for DST
Active TB drug safety monitoring and management (aDSM)

Vigibase
National database of ADR

Analysis Report Recommendations

Data analysis and database input

1 m 2 m 3 m 4 m 5 m 6 m 9 m 12 m 15 m 18 m 21, 24 m
**Adverse Events**  
*BDQ (n=275)*

### Serious AE – 21
- 6 - ↑ QT, arrhythmia
- 4 – K+, Mg++, ↓, Ca++↓
- 4 – seizures, cerebrovascular accident
- 3 - toxic nephropathy
- 2 - toxic hepatitis
- 1 – angioedema
- 1 - psychosis
Expanding patient-centered models of care. Treatment adherence improvement (1)

- VOT (GF) = 695, 30% on new drug

- Food packages since 2015 (national budget)
- Payment for public transport (GF)
- Additional payment to DOT nurses (national budget)
- Implantated central venous access port system = 176 (GF)
Expanding patient-centered models of care.

Treatment adherence improvement (2)

**Best Practice: MSF activity in Belarus**

123 patients started treatment with new TB drugs in 2015-2019

- 76.4% - XDR TB
- 88.6% - previously treated with 2nd line drugs
- 33% - with past prison history
- 67% - unemployed
- 40% - in Forced hospitalization center
- 65% - with AUD

- MSF provided hepatitis C treatment to 30 patients
- 25 patients started treatment with new TB drugs in prison
- Implementing Patient Centered Care in collaboration with NTP
Treatment coverage

Longer regimens

Problem:

Pto – excessive existing stock

Achievements:

Bdq – registered in Belarus, Dec 2018

Cfz for 450 patients - first time will be procured via GDF for the cost of the national budget, Feb 2019

“Belarus - Early Implementer new RR-TB regimens”
- Additional GF funding (1 150 000 USD)
Transition plan 2019-2021 (1)

- Analysis of the epidemiological situation, forecasting of RR-TB patients number in 2020-2021 (with a monthly patient enrollment plan)

- Data collection for RR-TB regimens currently used and drugs stock

- Determine the priority treatment regimens for RR-TB patients in accordance with the new WHO guidelines

- Planning for the gradual inclusion of all RR-TB patients on new regimens

- Data analysis, assessment and calculation of TB drugs need for 2020-2021
Transition plan 2019-2021 (2)

- Plan for government TB drugs procurement for 2020-2021 new updated treatment guidelines
- Development and introduction a tool for tracking and comparing planned and actual data on the patients’ recruitment
- Preparation and approval of new national guidelines for RR-TB treatment with updated WHO recommendations (1 Mar 2019)
- Training of national specialists to manage RR-TB patients with new national guidelines
- Assessment and strengthen laboratory system
Expectations from partners

rGLC/WHO/ StopTB

Technical assistance in
• Review and evaluation of the transition plan
• Assessment of the drug management system
• Prediction of drug needs
• Development of routine monitoring of drug stocks (early warning system)
• Redistribution of $Pto$ existing stock (all partners)

Joint Stop TB / GLC mission 4-8 Mar 2019

WHO

• Review of the NTP surveillance system
  WHO mission, August 2019
• Advocacy of new drugs inclusion in the public procurement plan
• Assistance in international procurement mechanism implementation:
  - training for Belfarmacija and Belmedtekhnika
  - change in procurement legislation

WHO, MSF, other partners

• Funding and assistance for expanding of AUD MSF project
Thank You!