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

5th TB Symposium – Eastern Europe and Central Asia
Ministry of Labour, Health and Social Affairs of Georgia
and Médecins Sans Frontières

22- 23 March, 2016, TBILISI, GEORGIA

Steps Taken in the Implementation of aDSM in GEORGIA

Nino Lomtadze, M.D., MSc
Head of Surveillance and Strategic Planning Department, National Center for Tuberculosis and Lung Diseases
Country Context (I)

- Georgia was a high MDR/XDR-TB prevalence country pre 2016:

  - 2014:

    | New MDR TB cases | Previously treated MDR TB cases | XDR-TB cases |
    |------------------|---------------------------------|--------------|
    | 11.6%            | 39.2%                           | 15% XDR TB   |
    | (range 2005-14: 6.8%-11.6%) | (range 2005-14: 26.4%-40.3%) | (range XDR 2009-14: 9%-20%) |
    |                  |                                 | (range FQR 2009-14: 12%-30%) |

- In 2012 cohort:
  - RR-TB treatment success rate 49% (range 2008-12: 56%-49%)
  - XDR-TB treatment success 27% (range 2008-12: 39%-22%)

Overall, ~30% of RR-TB patients annually (~150 patients) eligible for introduction of new group 5 TB drugs in Georgia.
Country Context (II)
Chronology of access to New TB Drugs

2013
• **Start** BDQ Compassionate Use (CU) Program

From 2014
• MSF supported **scale up** of CU & programmatic use of BDQ and CU of DLM

Aug 2015
• Programmatic use of BDQ through **USAID Donation Program**

Nov 2015
• **Universal access** to diagnosis/treatment for TB including ‘pre-XDR’/XDR-TB
• **National TB guidelines**: up to date, endorsed by MoH, include M/XDR treatment regimens and new drug safety monitoring schedule (WHO guidance)

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New TB Drug Exposure and Preliminary Results

Patients enrolled on new treatments (as of **March 2016**):

- **Bdq:** 162 patients
  - 20 through CU
  - 142 through programmatic use (drug source MSF and USAID)
- **Dlm:** 12 patients (CU)

Preliminary outcomes (N=174)

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<thead>
<tr>
<th>Outcome</th>
<th>Bedaquiline</th>
<th>Delamanid</th>
<th>TOTAL</th>
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<tbody>
<tr>
<td>Cured/Completed</td>
<td>6</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Loss to FU</td>
<td>10</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Un-evaluated (Emigrated)</td>
<td>4</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Died</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Still on Treatment</td>
<td>136</td>
<td>10</td>
<td>146</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>162</strong></td>
<td><strong>12</strong></td>
<td><strong>174</strong></td>
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So far, 6 months Bdq course completed by 48 patients, and 6 months Dlm course completed by 4 patients

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Country Context (IV)
Pharmacovigilance (PV)

Pre 2014
• PV “naïve” country in any disease context.

May-Jul 2014
• MSF supported training on treatment of XDR-TB
  • Focus on monitoring & management of AEs and reporting of SAEs
  • MSF managed SAE reporting and collection of non-serious AEs into MSF clinical database

Déc 2014
• National BDQ Implementation Plan developed with the USAID TPP TA
  • Approved by National TB Council chaired by the Minister of Health himself

Jan 2015
• Technical Working Group created to coordinate new drug implementation, including PV, led by NCTLD
  • MoH-approved new voucher funding for safety monitoring linked with new drug use, incl. ECG investigations, liver function tests, etc.

Apr 2015
• Primary Candidate to receive BDQ through USAID & Janssen Therapeutics’ donation program in parallel with the TA in PV

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The following took place BEFORE the aDSM decisions and recommendations from the July Geneva meeting became at least audibly available...
Pharmacovigilance (PV)

- Technical assistance to establish PV system:
  - USAID, in collaboration with USAID/SIAPS

- Preparation of PV system:
  - Decision to report any AE of clinical importance (per “Companion Handbook” recommendations of CEM)
  - Development of comprehensive baseline and monthly AE reporting developed by USAID/SIAPS experts in collaboration with the NCTLD and MoH
  
  - Not implemented

- Training of trainers on clinical management of adverse events in line with the severity grading was conducted (USAID/SIAPS TA)
What happened AFTER the “Vigilant” Georgian TB society heard about aDSM decisions and recommendations from the July Geneva meeting ...
Meeting of partners to **reassess TB PV needs** (NTP, USAID/SIAPS MSF, USAID/URC)

- **Goal**: establish new framework for introduction of active TB drug safety management and monitoring (aDSM) for new anti-TB drugs - latest recommendations.

**DECISIONS:**

1. **Core package:**
   - Requiring monitoring for and reporting of all **SAEs among all drug-resistant TB patients** being on treatment as part of routine programmatic practice,

2. **Sentinel site:**
   - Through MSF endTB project for the collection of **intermediate & advanced packages** that includes **SAEs** as well as **AEs of clinical significance**.
aDSM Practical Steps of Implementation (I)

- Translation and adaption of SAE form, completion guidelines and severity grading scale from endTB for use at National Level

SAE Form:

<table>
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<tr>
<th>SAE Form</th>
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Completion Guidelines:

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Ministerial decree on a mandatory reporting rules and practices of SAEs for patients during DR-TB treatment

- Submitted for Ministerial endorsement – to be endorsed by end of March 2016

- **Practical training** on PV recording and reporting of NCTLD staff by MSF endTB PV unit Officer

- **Flow of safety data:**
  - **SAEs** collected by doctors should be reported to “PV committee/Georgia PV officer” at NCTLD
    - Then reported to endTB PV unit and MoH Pharmaceutical Department
  - **Non SAE** data collected by endTB project entered into clinical database on site
  - endTB PV unit will provide **feedback** and **support** to Georgia PV officer on a regular basis: *Quarterly reports & Individual CIOMS reports*

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USAID/SIAPS granted NCTLD PV committee an access to the Pharmacovigilance Monitoring System (PViMS)

3 WebEx PViMS tutorials hosted by the SIAPS Senior Technical Officer Conducted

The system compatibility with the in-country PV unit requirements have been evaluated and set

Q1 2016

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Challenges

Human resources

• No creation of PV dedicated positions with relevant contracts at National and/or Ministerial level
  • increased workload for persons deemed responsible
• Lack of experience in PV amongst those designated to follow at central level

Underreporting

• Due to the pending normative act from the Ministry SAEs from regions might be underreported
• Lack of clear understanding of the aDSM concepts at regional and district level
  • Cascade training to be supported by MSF and USAID/SIAPS

Language constraints due to legal documents

• The term “Adverse Event” does not exist in any legal documents, such as in Pharmaceutical Products Law or existing ministerial decrees and normative acts, while “Side Effects” is used
• Thus to abide the newly developed SAE reporting sub normative act to an existing law and decree we had to restrict terminology to legal language
• Led to confusion among doctors

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The way forward

- SAE basic information entered into a **simple Excel spreadsheet** before **central PV database** before PViMS database is fully operational
  - USAID/SIAPS will provide a central PV database developed based on “PViMS” system
  - MSF PV unit will follow-up SAE and provide a standard CIOMS report for each SAE to the NTP.

- Stepwise takeover by Government of **all AE reporting**:
  - Meanwhile quarterly reports on SAE and non SAE will be done by MSF PV unit.

- **Continue intensive collaboration** with all partners working for safe administration of new TB drugs (cascade trainings in aDSM concepts / WHO, USAID/SIAPS, MSF / endTB).

- Integration of drug management and AE issues in the **new HMIS TB module**.

- Further **building NTP capacities for AE management and PV** which will be also required for introduction of shorter MDR treatment regimens in the near future that Georgia is hoping for.

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Acknowledgements:

- National Center for Tuberculosis and Lung Diseases;
- Partners:
  - WHO
  - Global Fund TB Program in Georgia (GEO-T-NCDC)
  - MSF-France
  - USAID/SIAPS
  - Ministry of Labor, Health and Social Affairs in Georgia
- TB Doctors and TB patients in Georgia

Thank you!

Contact Email: nlomtadze@gmail.com