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

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Belarus experience in CEM for bedaquiline and linezolid

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National cohort monitoring projects: *goals*

**M/XDR-TB:** 32.7% among new cases

76.6% among previously treated patients

34.5% – LTFU and treatment failures

**Role of TB ADR:** increase in incidence/mortality, LTFU, treatment failures, increase in drug resistance

- Lack of adequate evidence-based data
- Limited data on efficiency and safety profiles
- Limited data on patients with co-morbidities
- Lack of comprehensive information on drug interactions

**Introduce pharmacovigilance**

**Improve treatment tolerance and adherence**

**Introduce new components of TB treatment**

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Goals and objectives of active drug safety monitoring

**Goals:**
- reduce risks for MDR-TB patients associated with second-line drugs
- develop structured and standardized data to formulate policies for new TB drugs use

I. Exposure to treatment when **benefits outweigh risks:**
   - provide control at drug administration stage (inclusion/exclusion criteria)
   - ensure systemic clinical and laboratory evaluation on safety parameters
   - take immediate measures if adverse effects found

II. Develop structured and standardized data on safety and efficiency profiles of new TB drugs:
   - collect, record and evaluate data on safety and efficiency parameters
   - data on profile modifying risk factors
   - data on efficiency of measures aimed at ADR monitoring/prevention/management

**Objectives**
Review of main system components

NTP

- Hierarchy in management and subordination
- Republican consilium
- National TB register
- Adequate clinical and laboratory basis
- National TB policy based on WHO recommendations
- National guidelines on TB and M/XRD-TB treatment

NPVS

- National PV centre and PV policies
- Regulatory frameworks based on GVP
- Member of the WHO Programme for International Drug Monitoring
- Persistent efforts in VP implementation, experience in active drug safety monitoring (CEM)

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CEM for LZD and BDQ: main implementation stages

Preparatory phase
- Develop CEM programme
- Work out data collection forms
- Evaluate and determine sentinel sites
- Negotiate with partners

Basic CEM training for HCP

Pilot phase (1 sentinel site)

CEM implementation in all sites (7 sites)

Monitoring visits (quarterly)

Interim results evaluation

March 2016: LZD CEM – 205 patients, BDQ CEM – 182 patients

Monitoring to be completed in 2017–2018

Data analysis, final reports, recommendations and risk minimization measures

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Cohort monitoring design

Cohort monitoring is a non-interventional, prospective, dynamic, and descriptive epidemiological study

Vigibase
ADR national database

Data analysis and register

Analysis
Report
Recommendations

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Inclusion, monitoring and risk minimization

**Throughout treatment:**
- Regular ECQ monitoring and QTcF assessment
- Regular laboratory monitoring of AST, ALT, bilirubin, GGT, ALP, lipase, creatinine, GRF, TSH, K+, Mg2+, blood count, glucose
- Regular clinical monitoring, audiogram, ophthalmologist’s and neurologist’s examination

**At inclusion stage:**
- QT interval ≤ 400 ms
- AST, ALT exceed UNL < 3 times, bilirubin exceed UNL < 1.5 times
- No medical history of heart rhythms disorders (torsade de pointes, ventricular arrhythmia) or coronary artery diseases

**Therapy withdrawal if:**
- QT interval > 500 ms
- AST, ALT exceed UNL > 5 times, or AST, ALT, bilirubin exceed UNL > 2 times

**Control of interaction with:**
- QT-prolonging drugs (fluoroquinolones, clofazimine)
- Hepatotoxic drugs
- Inhibitors (ART, ketoconazole) and CYP3A4 inducers

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Practical outcomes of VP implementation

- **Drug administration control**: include patients with a favourable benefit-risk ratio
- **Condition control**: thorough monitoring of drug efficiency and safety parameters throughout therapy to determine deviations and take response measures
- **Provide personal approach** in evaluation of risk factors
- **Improve safety, adherence** and therapy results

- **Control drug administration**, avoid inadequate administration and monitoring; and decrease drug resistance risks
- **Collect structured and standardized data** on efficiency and safety profiles of new TB drugs, including their use as part of various ATT regimes and co-morbidities management — **amend currently available data**
- **Collect qualitative data on risk parameters** (severity, risk factors, profile modifying factors, probability, prevention possibility, and monitoring and correction efficiency) — **amend currently available data**

- **Develop expertise** in monitoring and drug safety
- **Ensure implementation** of safety control and reporting and raise vigilance
- **Implement PV** in NTP
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Experience in optimization at CEM implementation stage

Build a basis for implementation
- Adapt national M/XDR-TB guidelines
- Guidelines approval in MoH RB (order)
- National implementation programme (BDQ)
- Elaborate and align CEM programme based on current recommendations

Develop data collection forms
- Determine optimal parameters for safety and efficiency monitoring (BDQ – WHO guidelines)
  - Adapt to local standards/protocols
  - Prevent redundancy/duplication
- Optimize data entry (code panels, pre-filled forms)
  - Approval (internal and external experts)

Select sentinel sites
- Relevant clinical and laboratory basis available for programme implementation
- Staff personnel with required professional training

Determine key staff personnel
- Relevant professional level and experience in clinical management of M/XDR-TB patients
- Commitment to patient-oriented approach
- Desire to take part in CEM

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Experience in optimization at CEM implementation stage (2)

**Organize staff trainings**
- Provide CEM and protocol specifics training, and conduct interim meetings to evaluate results

**Structure processes at CEM implementation stage**
- Establish the coordination board and expert advisory board on data evaluation (NTP and NVP)
  - Outline functions and responsibilities
- Work out short guidelines on CEM and form filling
  - Introduce standard operational procedures
- Determine procedures for data collection and reporting
  - Optimize workload
- Convene monitoring visits within the multisite project
  - Develop a tool for e-data transfer

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THANK YOU FOR YOUR ATTENTION!