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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MEDECINS SANS FRONTIERES

MINISTRY OF LABOUR, HEALTH AND SOCIAL AFFAIRS OF GEORGIA

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

Improve treatment tolerance and adherence

Introduce new components of TB treatment

Lack of adequate evidence-based data
Limited data on efficiency and safety profiles

Introduce pharmacovigilance

Limited data on patients with co-morbidities

Lack of comprehensive information on drug interactions

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

Objectives

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

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)**

CEM for LZD and BDQ: main implementation stages

Preparatory phase

- Develop CEM programme
- Work out data collection forms
- Amendments to guidelines
- MoH RB order
- Evaluate and determine sentinel sites
- Negotiate with partners
- BDQ – national implementation plan

Basic CEM training for HCP

- CEM guidelines
- CEM protocol (LZD, BDQ)
- Ensure monitoring and safety (LZD, BDQ)
- M/XDR-TB management
- ADR verification and assessment methodology

Pilot phase (1 sentinel site)

CEM implementation in all sites (7 sites)

Monitoring visits (quarterly)

Interim results evaluation

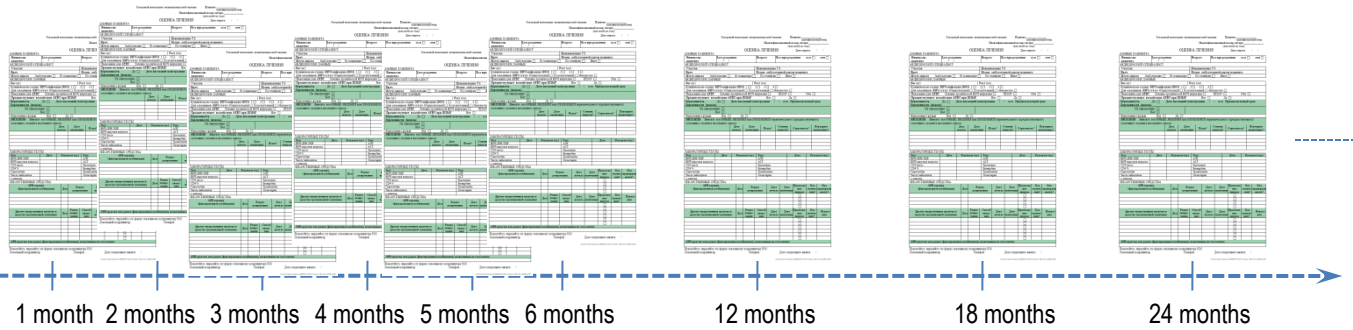
March 2016: LZD CEM – 205 patients, BDQ CEM – 182 patients

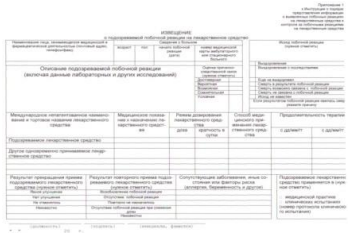
Monitoring to be completed in 2017–2018

Data analysis, final reports, recommendations and risk minimization measures

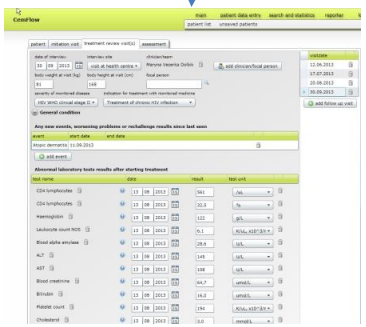
Cohort monitoring design

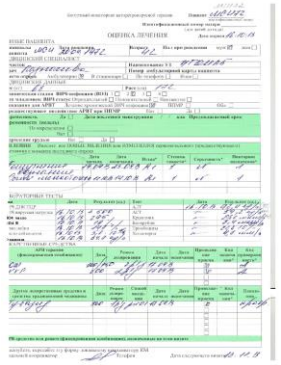
Cohort monitoring is a non-interventional, prospective, dynamic and descriptive epidemiological study





Data analysis and register





Vigibase
ADR national database

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^+, Mg^{2+}, 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 inductors*

Practical outcomes of VP implementation

Patient

- **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

BDQ / LZD

- **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**

TB therapist

- **Develop expertise** in monitoring and drug safety
- **Ensure implementation** of safety control and reporting and raise vigilance
- **Implement PV** in NTP

SWOT Analysis

STRENGTHS

- High level of medical assistance with TB drugs
- NPVS, GVP implementation
- Support from MoH
- Experience in CEM

WEAKNESSES

- Poor reporting culture
- Low motivation
- Limited professional and financial resources

OPPORTUNITIES

- Support from international and donor organizations
- Prospect for high-rate implementation of active VP methods and risk minimization measures
- Prospects for CEM implementation

THREATS

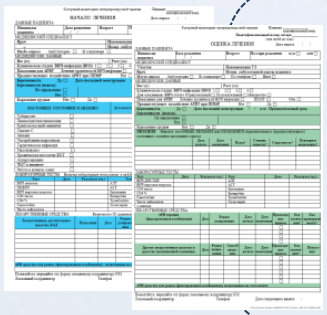
- Medical staff concerns about extra workload
- CEM long duration – adherence of patients and staff personnel

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

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

THANK YOU FOR YOUR ATTENTION!