# Belarus' experience in implementing and scaling up the use of BPaL(M)

**Dr Natalia Yatskevich, MD, PhD, Associate Professor**

**The 20th meeting of WHO BPaLM Accelerator Platform &**
**The 30th webinar of European Virtual Medical Consilium**

**31 October 2024**

# Prerequisites for the implementation of BPaL(M)

National TB policy, based on WHO guidelines


Regulatory framework

**Start of programme implementation BPaL: December 2022**

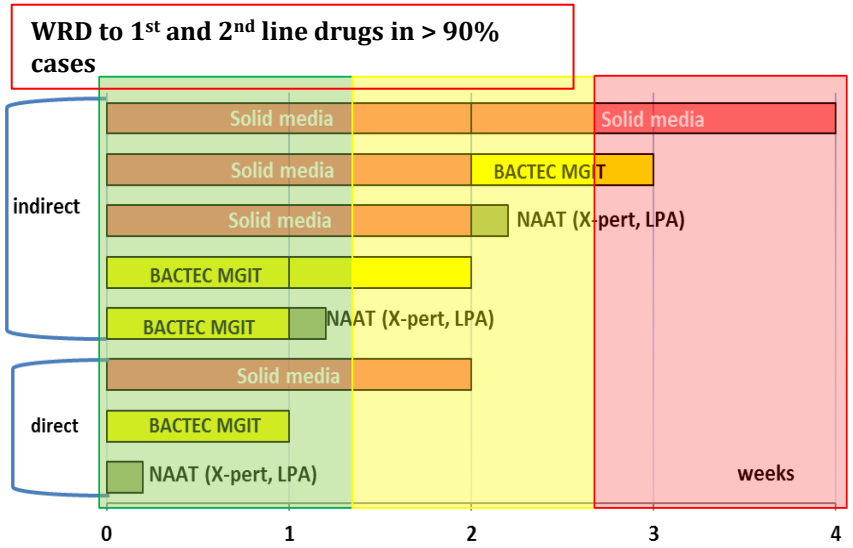
Lab. and diagnostic potential

**Acceptable time to treatment initiation**

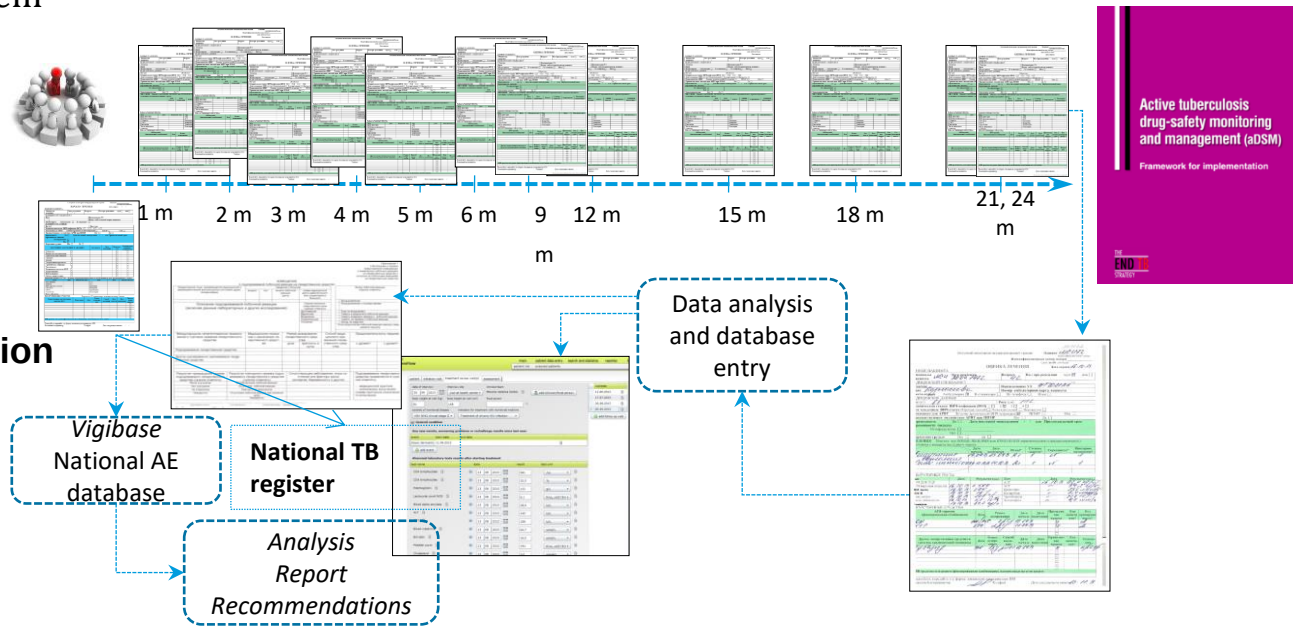
**1-st and 2-nd line DSTs, Bdq Pa Lzd Cfz Dlm**

**Sequencing equipment**

**MTB strains collection since 2015**




Active Drug Safety Monitoring (aDSM), Interaction with the Pharmacovigilance System




National PV system

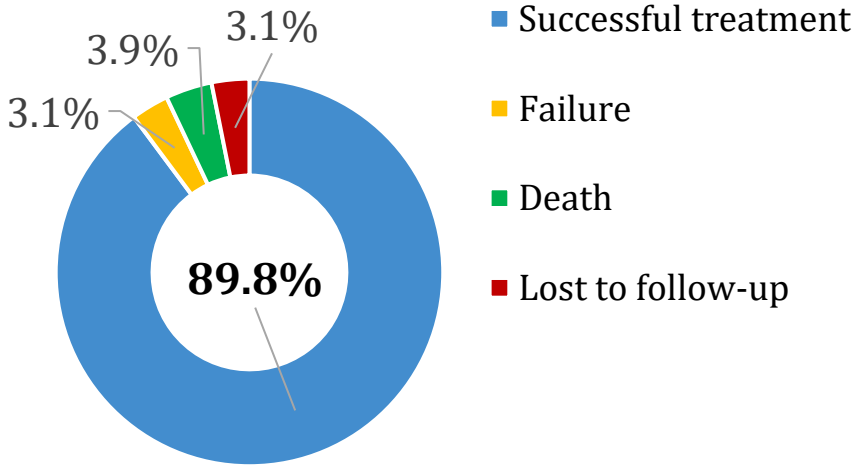
National PV policy, based on WHO guidelines
Spontaneous reporting: 5,4 per 100 000

CM - HIV, 2012
CM - HIV M/XDR-TB, 2013
CM - LZD, 2014
CM - BDQ, 2015
CM - DLM, 2016
CM - BDQ+DLM, 2016
aDSM - mSTR, 2018

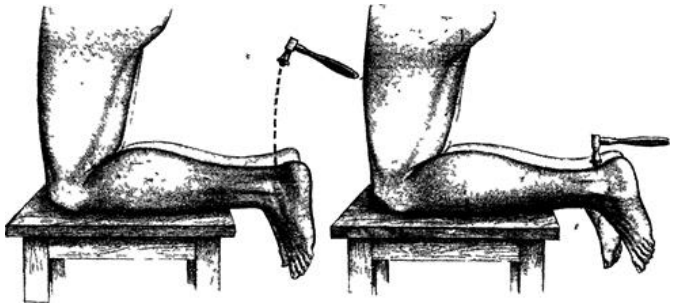
# RR-TB Consilium. Experience of the implementation of mSTR OR

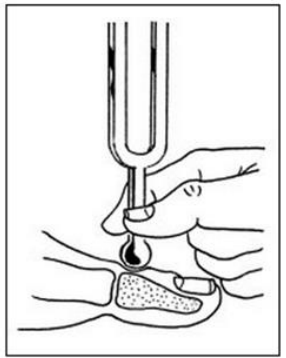
- RR-TB Concilium - since 2010, online – III 2020
- Regular monitoring visits

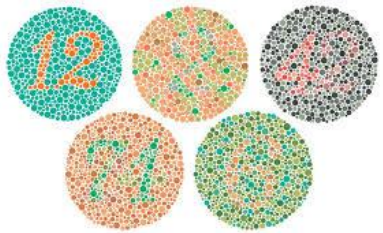
**Regional cohort**
n=540

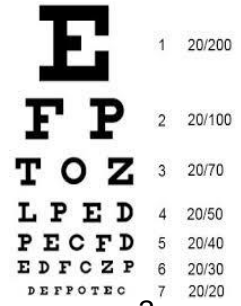



- aDSM skills, tools and assessment of neurological status, visual acuity and color perception
- quality check «Monitoring template»







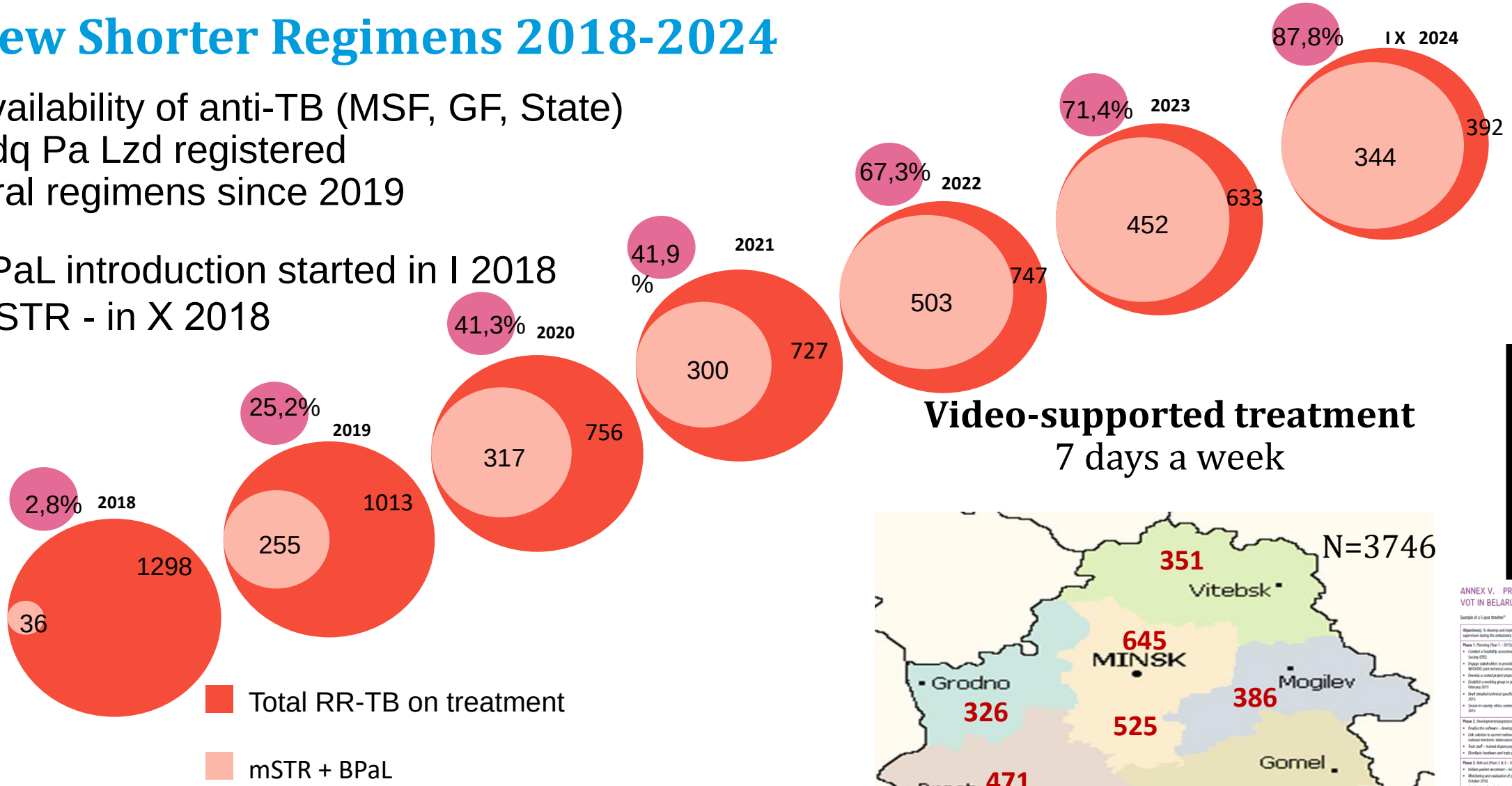



# Drug supply

## New Shorter Regimens 2018-2024

Availability of anti-TB (MSF, GF, State)
Bdq Pa Lzd registered
Oral regimens since 2019

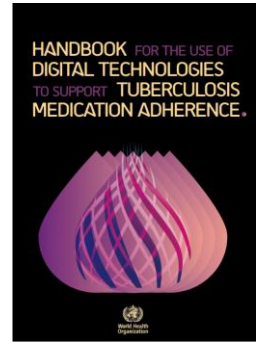
BPaL introduction started in I 2018
mSTR - in X 2018

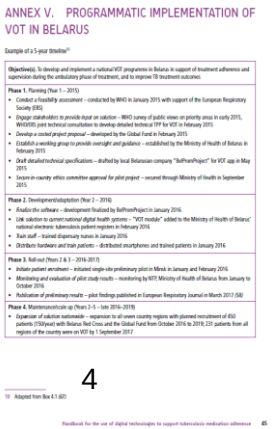



## Video-supported treatment

7 days a week





ANNEX V. PROGRAMMATIC IMPLEMENTATION OF VOT IN BELARUS

# BPaL(M/C) Experience : Clinical trial – TB-PRACTECAL

## Jan 2018 – Aug 2021 – 70 patients from Minsk and Minsk region

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis

Bern-Thomas Nyang'wa, M.B., B.S., Catherine Berry, B.Med., Emil Kazounis, M.Med.Sci., Ilaria Motta, Ph.D., Nargiza Parpieva, Sc.D., Zinaida Tigay, M.D., Varvara Solodovnikova, M.D., Irina Liverko, Sc.D., Ronelle Moodliar, M.B., B.S., Matthew Dodd, M.Sc., Nosipho Ngubane, M.B., B.Ch., Mohammed Rassool, M.B., B.Ch., Timothy D. McHugh, Ph.D., Melvin Spigelman, M.D., David A.J. Moore, M.D., Koert Ritmeijer, Ph.D., Philipp du Cros, M.B., B.S., and Katherine Fielding, Ph.D., for the TB-PRACTECAL Study Collaborators*

ABSTRACT

BACKGROUND

In patients with rifampin-resistant tuberculosis, all-oral treatment regimens that are more effective, shorter, and have a more acceptable side-effect profile than current regimens are needed.

From the Public Health Department, Operational Center Amsterdam (OCA), Médecins sans Frontières, Amsterdam (B.-T.N., K.R.); the Public Health Department,

The NEW ENGLAND JOURNAL of MEDICINE

**Table 1. Baseline Characteristics of the Patients.***

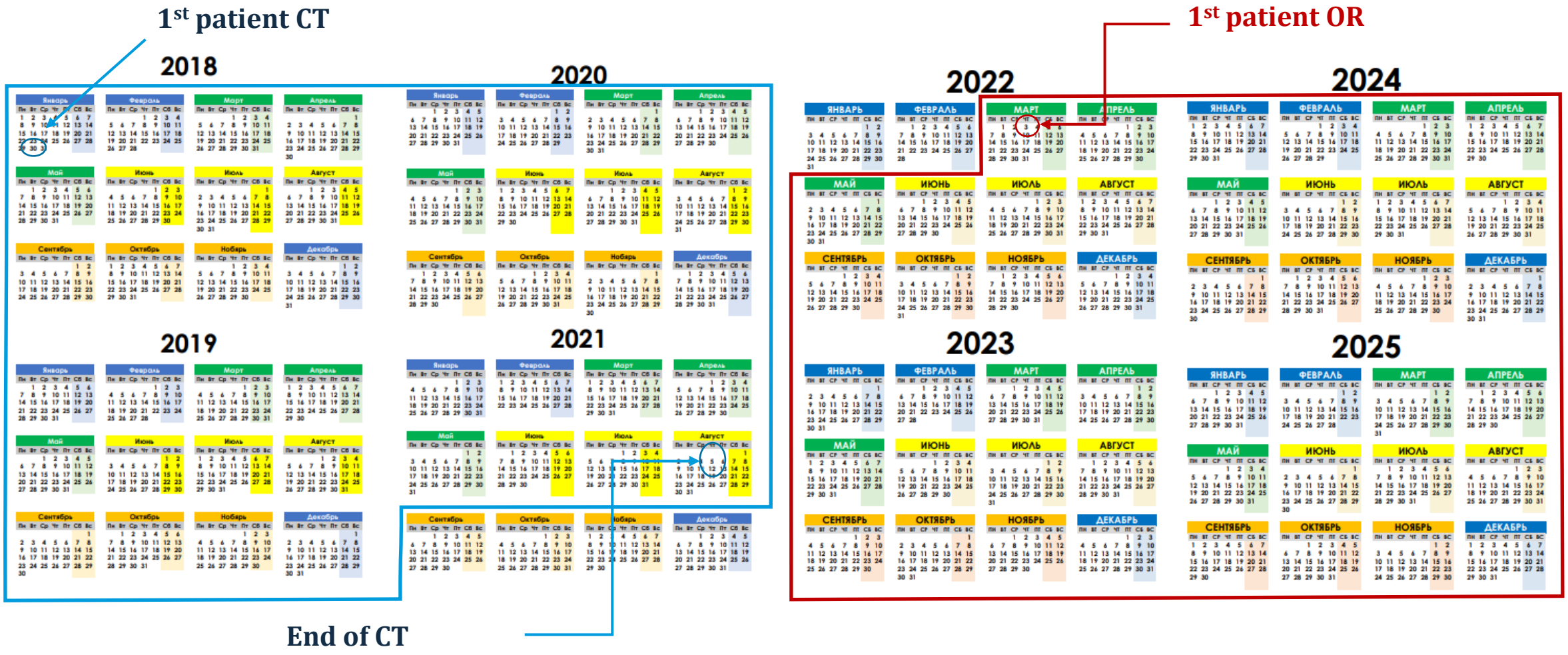
| Characteristic | Standard-Care Group | BPaLM Group | BPaLC Group | BPaL Group |
|---|---|---|---|---|
| **Intention-to-treat population** | | | | |
| No. of patients | 152 | 151 | 126 | 123 |
| Geographic distribution — no. (%) | | | | |
| Belarus | 29 (19.1) | 28 (18.5) | 21 (16.7) | 21 (17.1) |

| Outcome | n | % |
|---|---|---|
| Successful treatment | 60 | 85,7 |
| Excluded from the study | 10 | 14,3 |

## Nov 2021 – Jan 2022 - Ethics OR SMARRTT was approved by

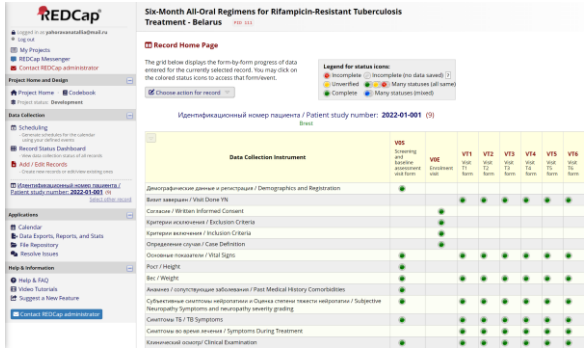
- the MSF Ethics Committee (EC)
- Independent EC of Belarus.

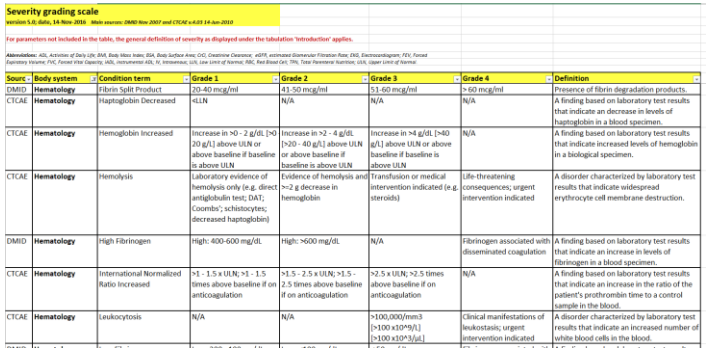
# BPaL(M) Experience: Clinical Trial (CT) and Operational Research (OR)

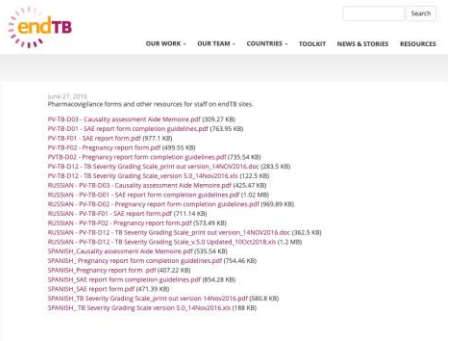


# BPaLM Treatment Monitoring

| | Investigation/Observation | Baseline assessment & Screening | Treatment Phase (W=Week) | | | | | | Follow-Up (M=Month) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | $W_T$ 4 | $W_T$ 8 | $W_T$ 12 | $W_T$ 16 | $W_T$ 20 | $W_T$ 24 | $M_F$ 6 | $M_F$ 12 |
| Clinical evaluation | Written informed consent | X | | | | | | | | |
| | Demographics, Medical History | X | | | | | | | | |
| | Clinical Examination[1] | X | X | X | X | X | X | X | X | X |
| | Treatment adherence | | X | X | X | X | X | X | | |
| | Concomitant treatment | | X | X | X | X | X | X | X | |
| | Adverse events | | X | X | X | X | X | X | X | X |
| Bacteriology | Sputum smear | X (2) | X | X | X | X (2) | X | X (2) | X | X |
| | Sputum culture | X | X | X | X | X | X | X | X | X |
| | mWRDT (GeneXpert)[2] | X | | | | | | | | |
| | Rapid test for FQ resistance[3] | X | | | | | | | | |
| | DST (R/FQ +/- Bdq +/- Lzd)[4] | X | | | | | | | (X) | (X) | (X) | (X) |
| Laboratory tests | Haemoglobin/platelets count / white blood count | X | X | X | X | X | X | X | X | X | | |
| | Serum creatinine (at baseline and if clinically indicated or ECG abnormalities) | X | | | | | | | | | | |
| | Serum potassium (at baseline and if clinically indicated or ECG abnormalities) | X | | | | | | | | | | |
| | Serum lipase (if clinically indicated) | X | | | | | | | | | | |
| | Serum liver enzymes | X | X | X | X | X | X | X | X | X | | |
| | Pregnancy test (female)[5] | X | | | | | | | | | | |
| | HIV and hepatitis test[6] | X | | | | | | | | | | |
| | Blood glucose/HbA1c[7] | X | X | X | X | X | X | X | X | X | X | X |
| Other | Chest X-ray[8] | X | | | | | | | X | | | |
| | ECG[9] | X | X | X | X | X | X | X | X | | | |
| | Visual acuity & BPNS[1] | X | (X) | (X) | (X) | (X) | (X) | (X) | | | | |



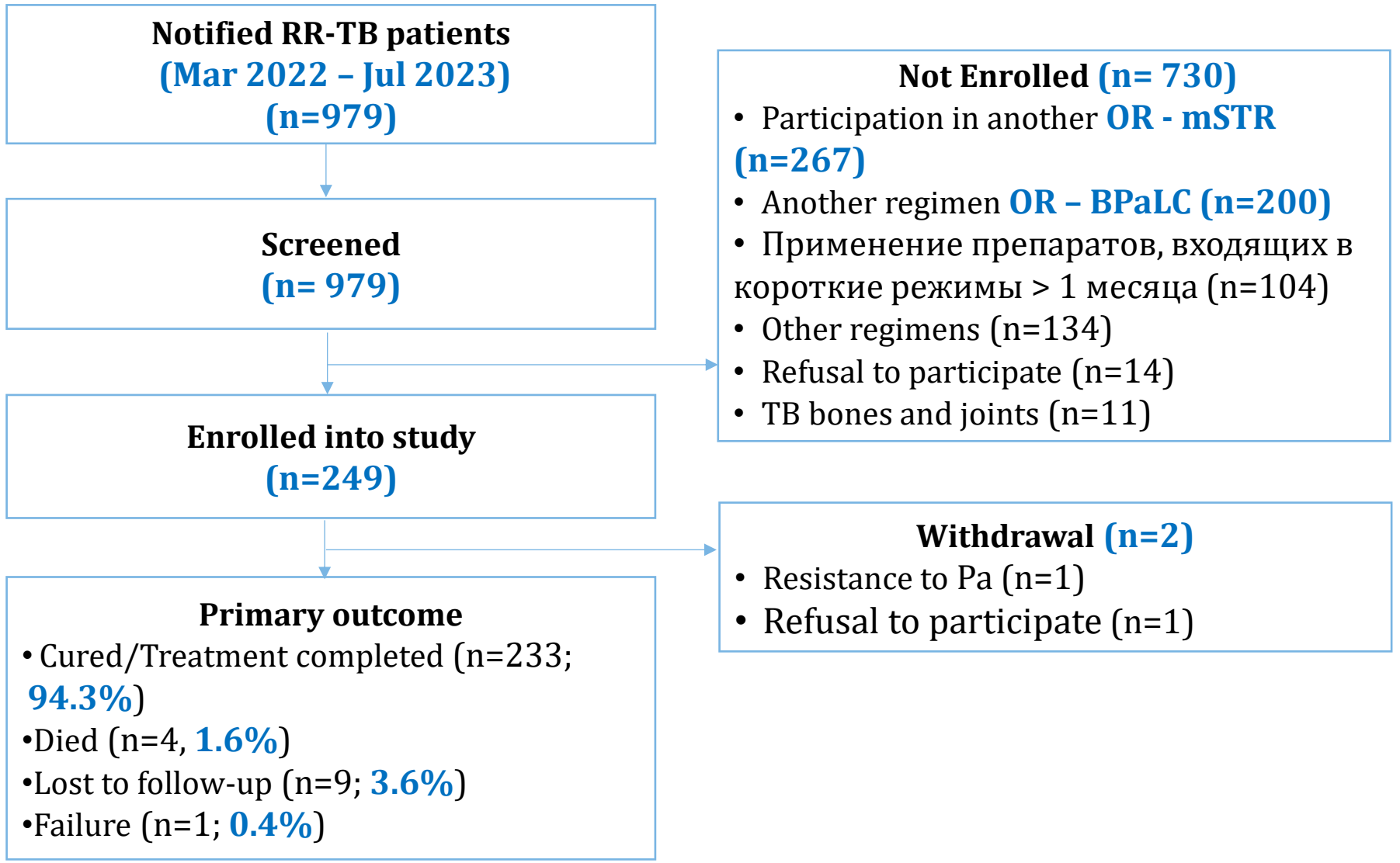



# Enrolment flow diagram

**247 patients completed the treatment (treatment start date Март 2022 – Июль 2023)**

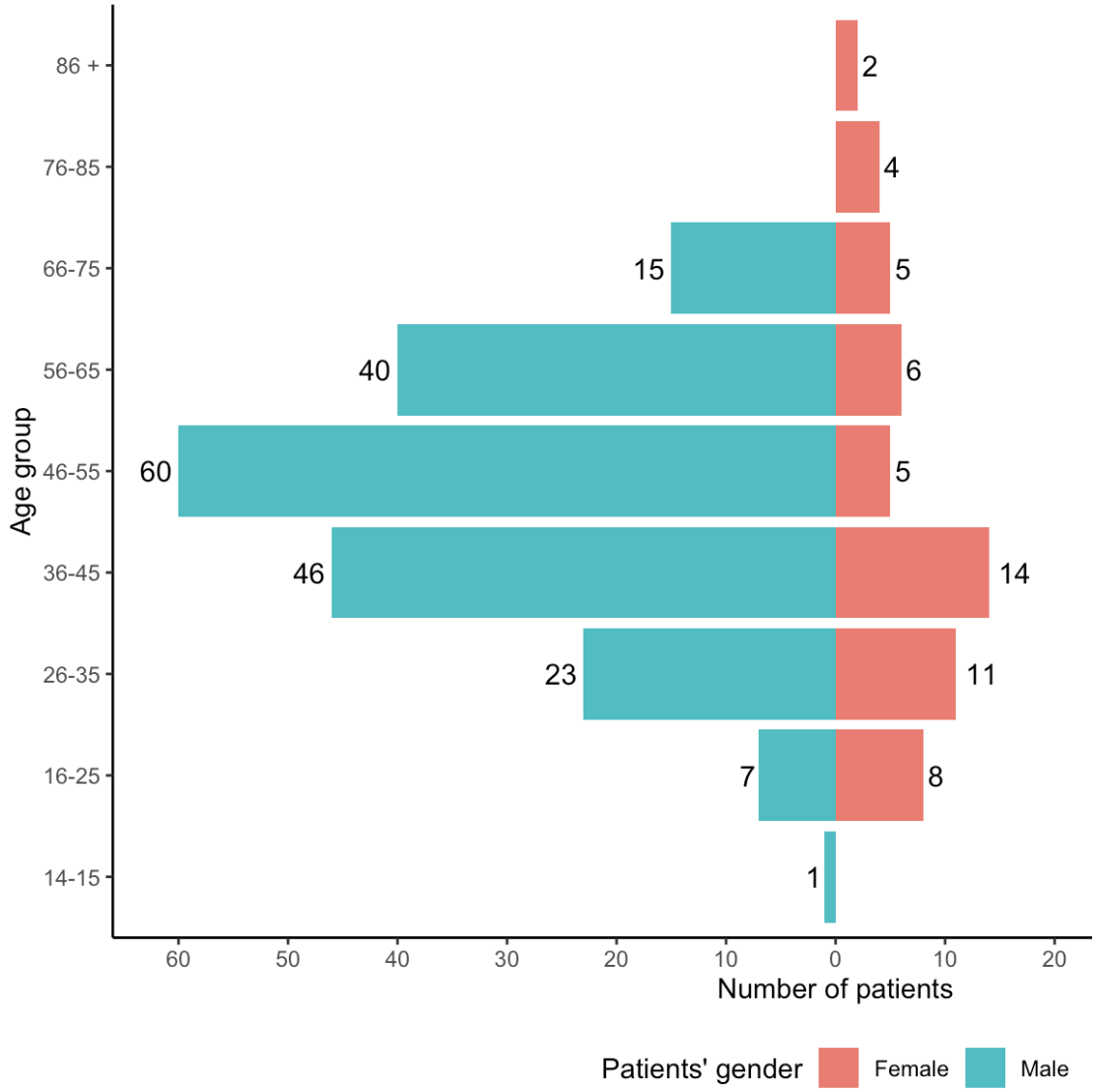
**Total number of enrolled patients: Feb 2022 – Aug 2024 - 722 patients**



# Experience with use of BPaLM

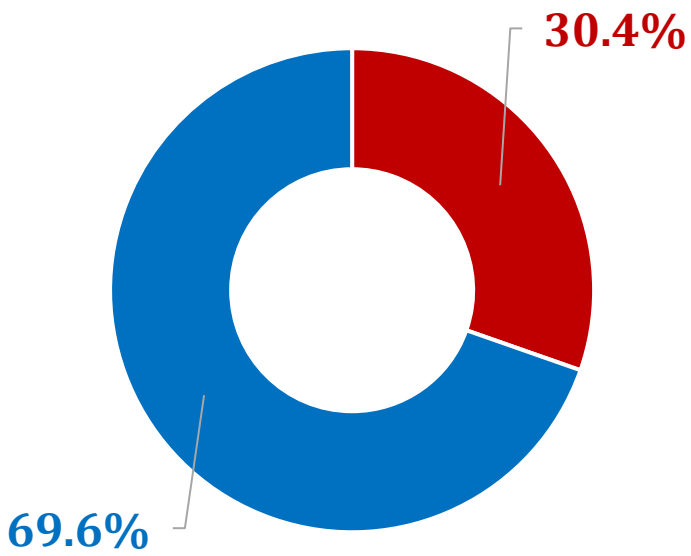
**02.03.2022 -** first patient enrolled,
**247 patients**
completed the treatment
**(treatment start date**
**Mar 2022 – Jul 2023)**

| | |
|---|---|
| **History of TB** | - 52 (**21,1%**) |
| **BMI<18.5 kg/m2** | - 47 (**19,0%**) |
| **Homeless** | - 4 (**1,6%**) |
| **In the penitentiary system.** | - 14 (**5,7%**) |
| **Psychoactive substances** | - 5 (**2,0%**) |

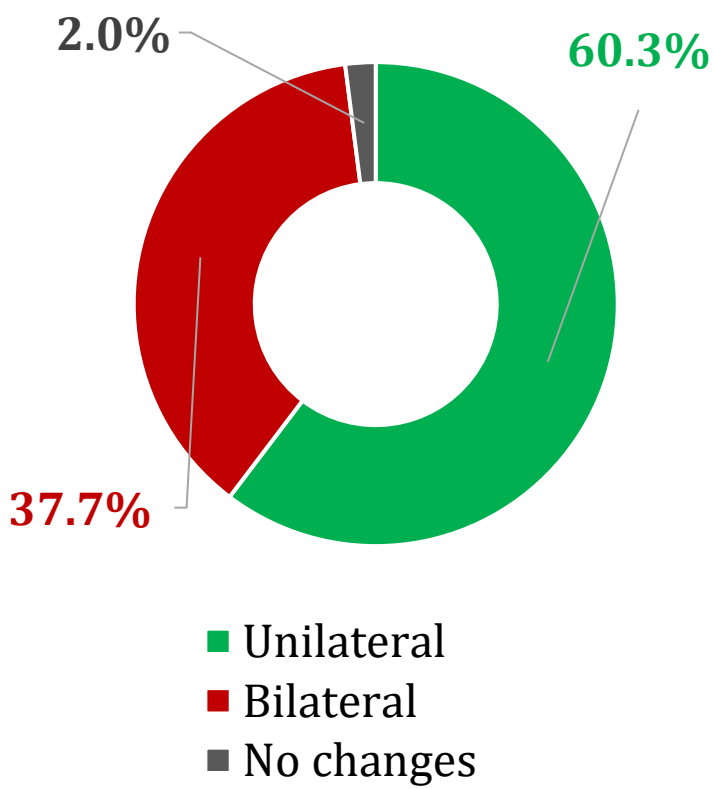


# BPaLM, характеристика ТБ процесса, n=247

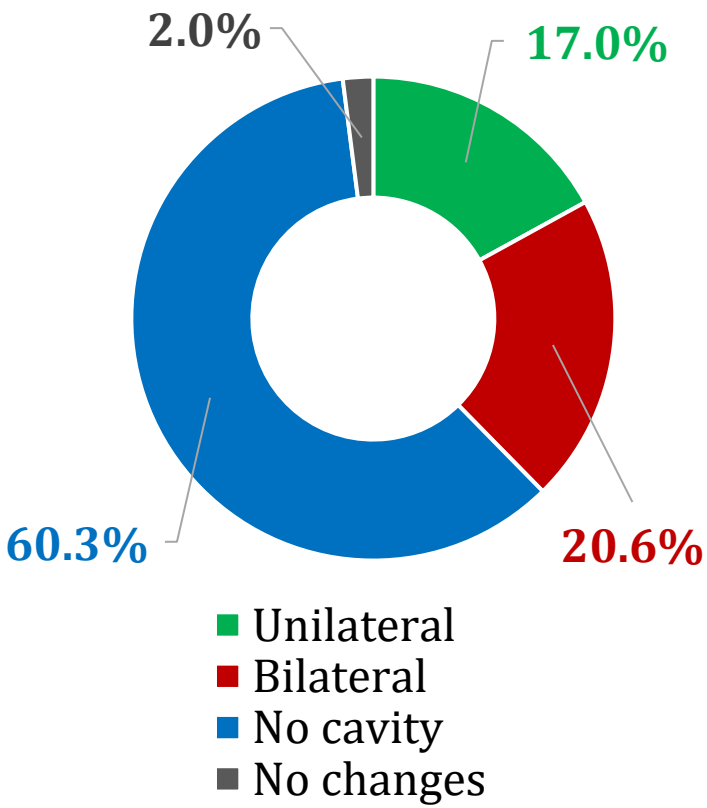
## Sputum smear



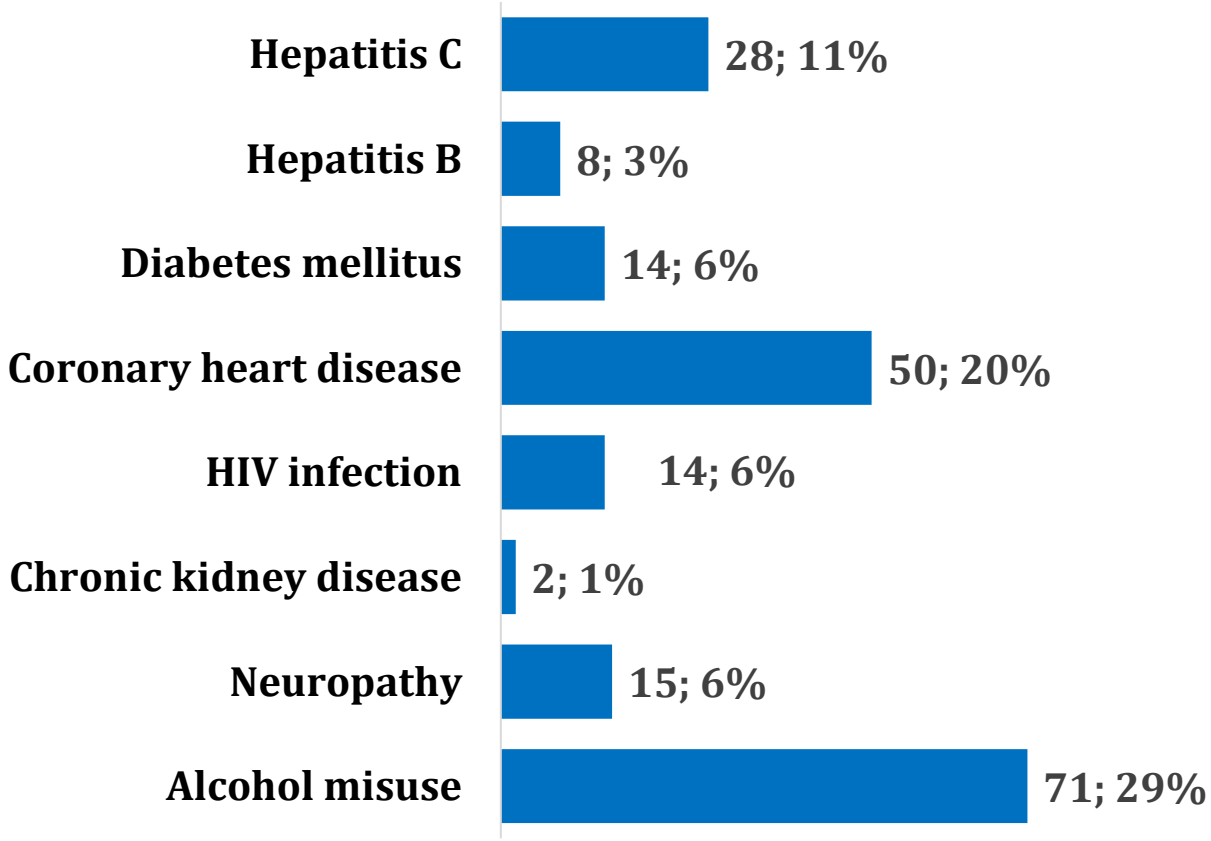

## Changes in chest X-ray



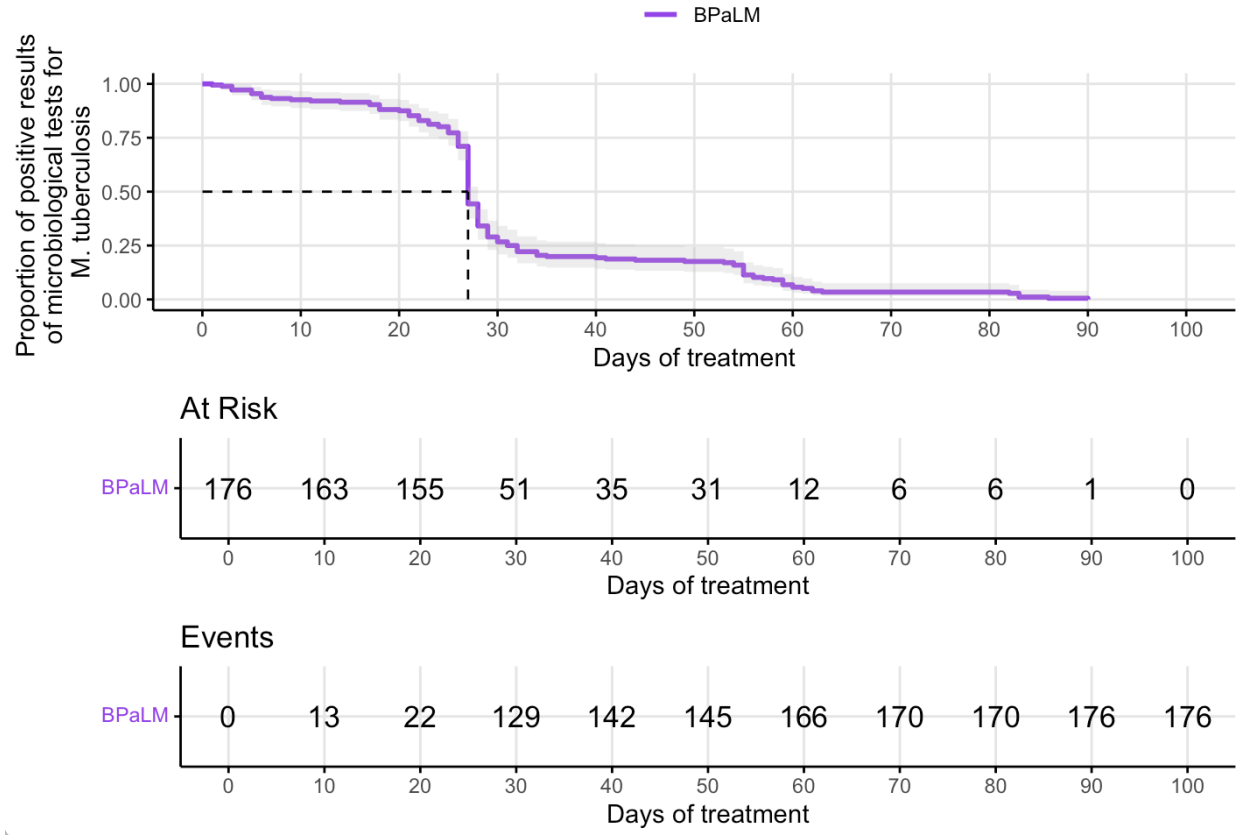

## Presence of a cavity



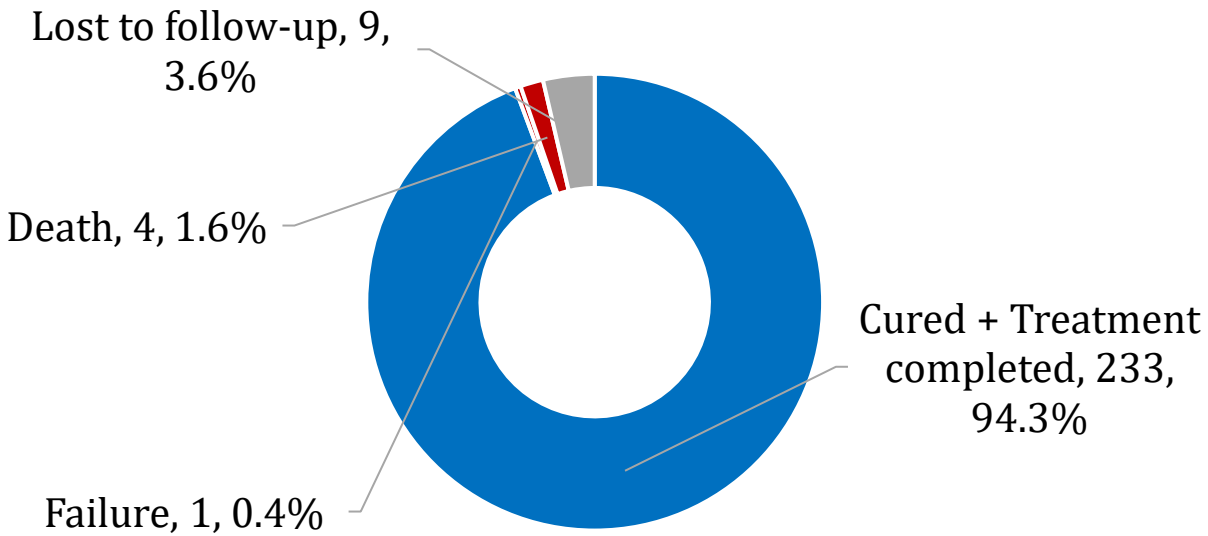
# BPaLM, Patient' characteristics, n=247



# Results

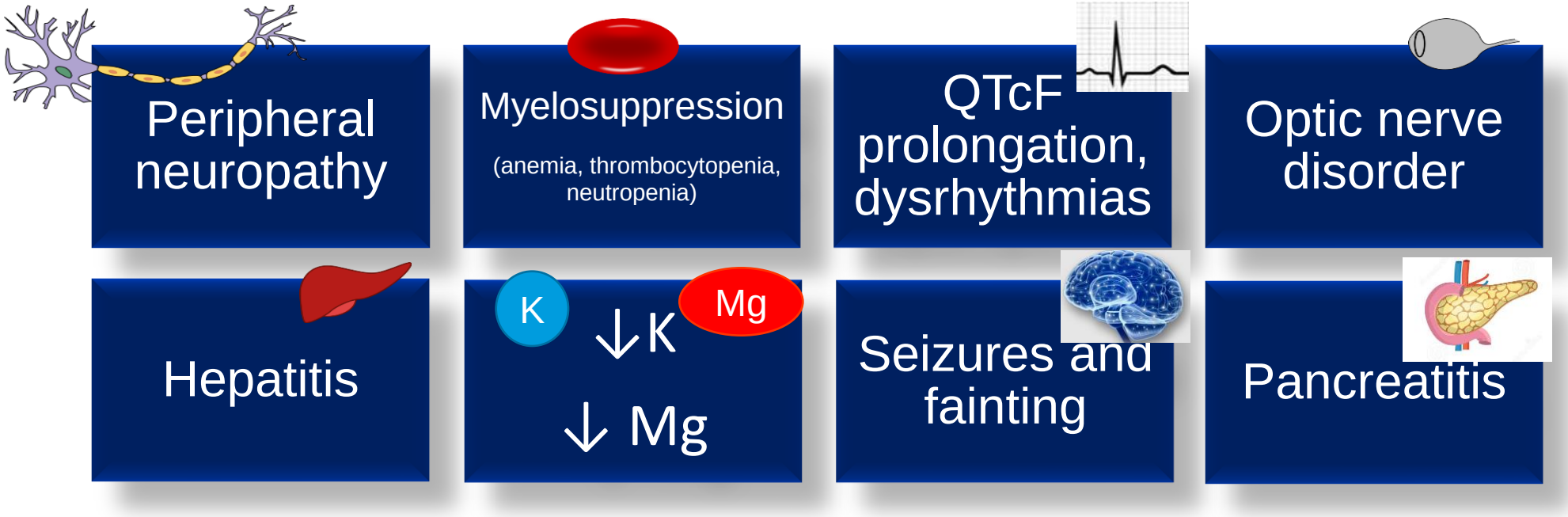


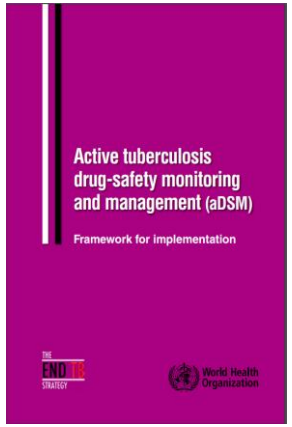

**Treatment success – 94.3%**




Median (IQR) time to culture conversion was 27 (26-31) days

# Active Drug Safety Monitoring and Management (aDSM), BPaLM n=249



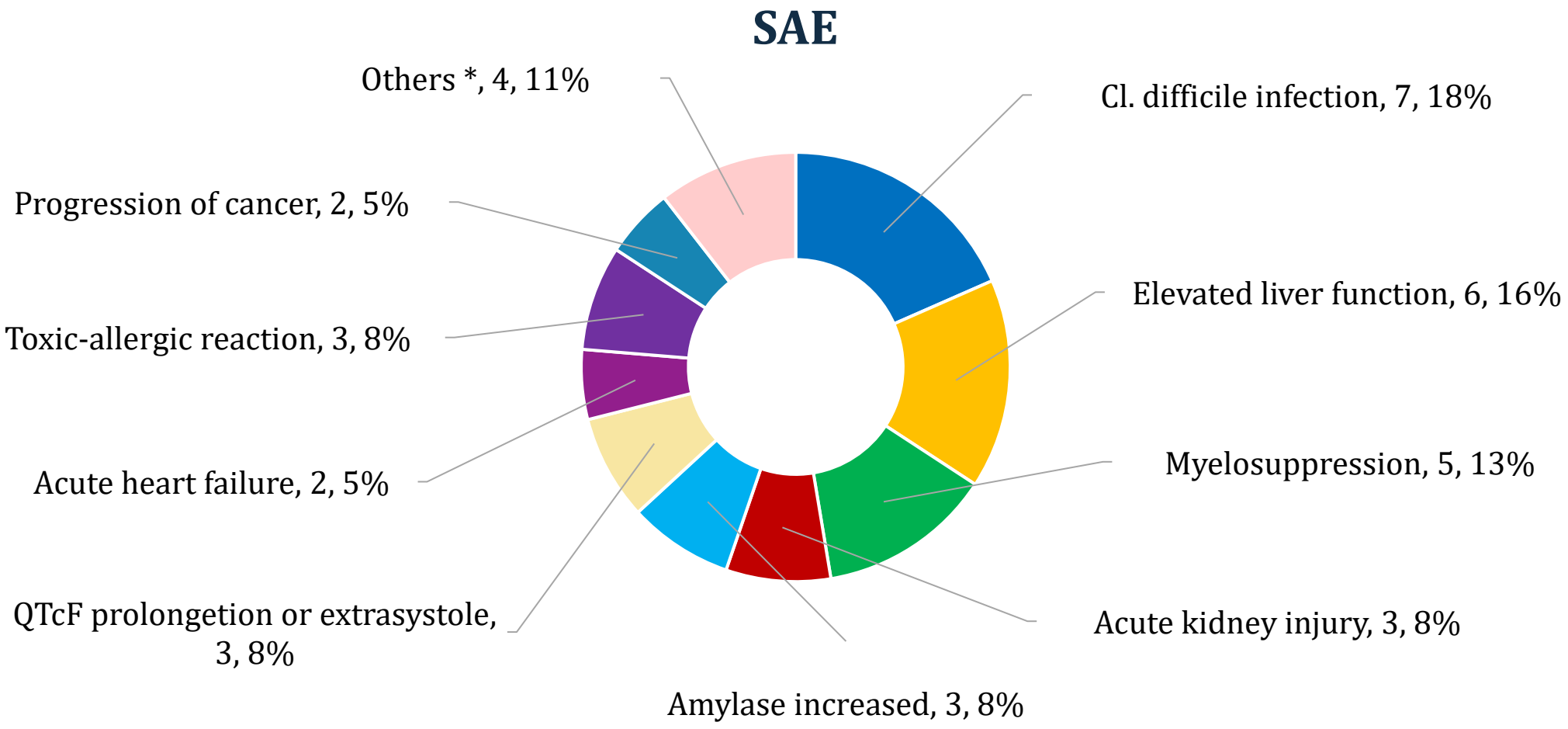




**«Intermediate package»:**

**Serious adverse events - 38 у 29 пациентов**

**Adverse events of special interest – 3 у 3 пациентов**

# BPaLM safety profile, n=249

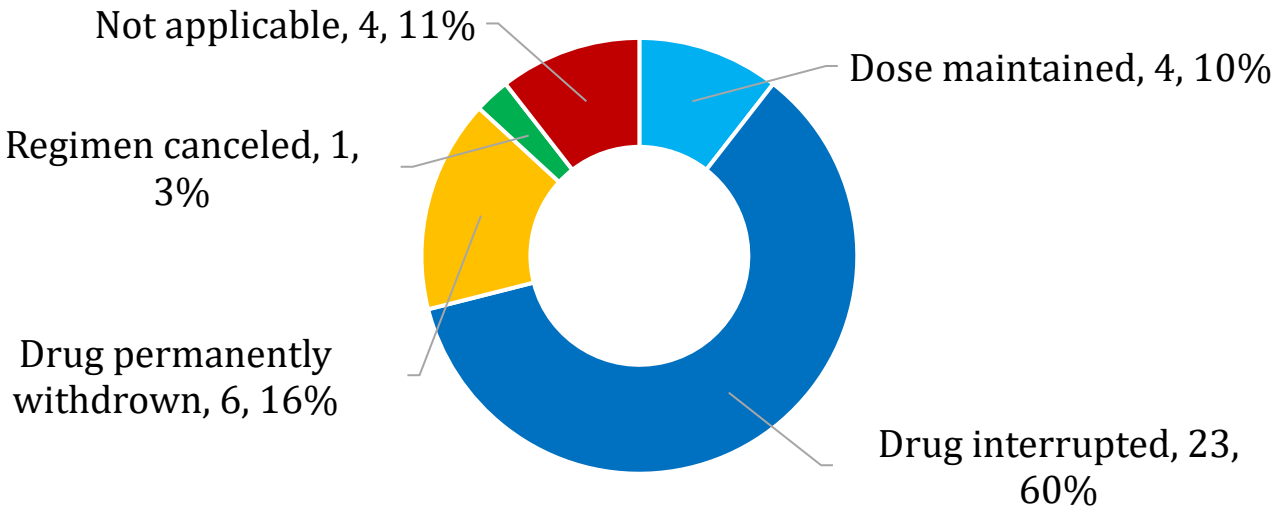



**11.6 %** of patients had SAEs

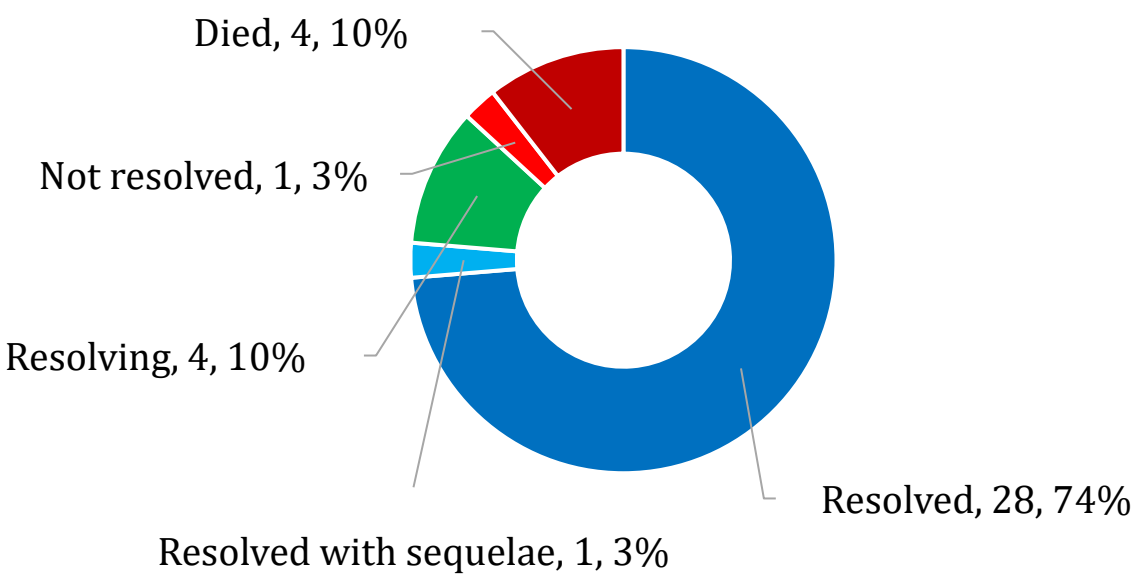
* Others: fracture - 1, intestinal bleeding - 1, intestinal ischemia - 1, intestinal motility disorder - 1

# BPaLM safety profile, n=249

## Actions to manage SAE

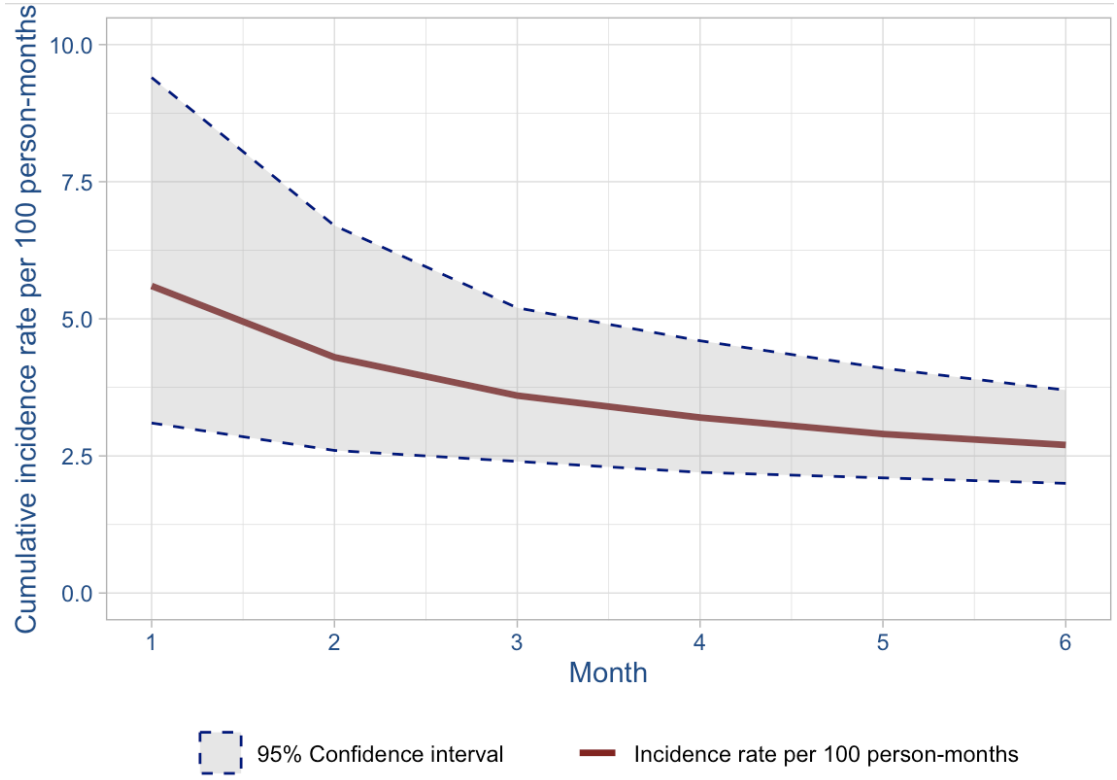



## SAE outcomes

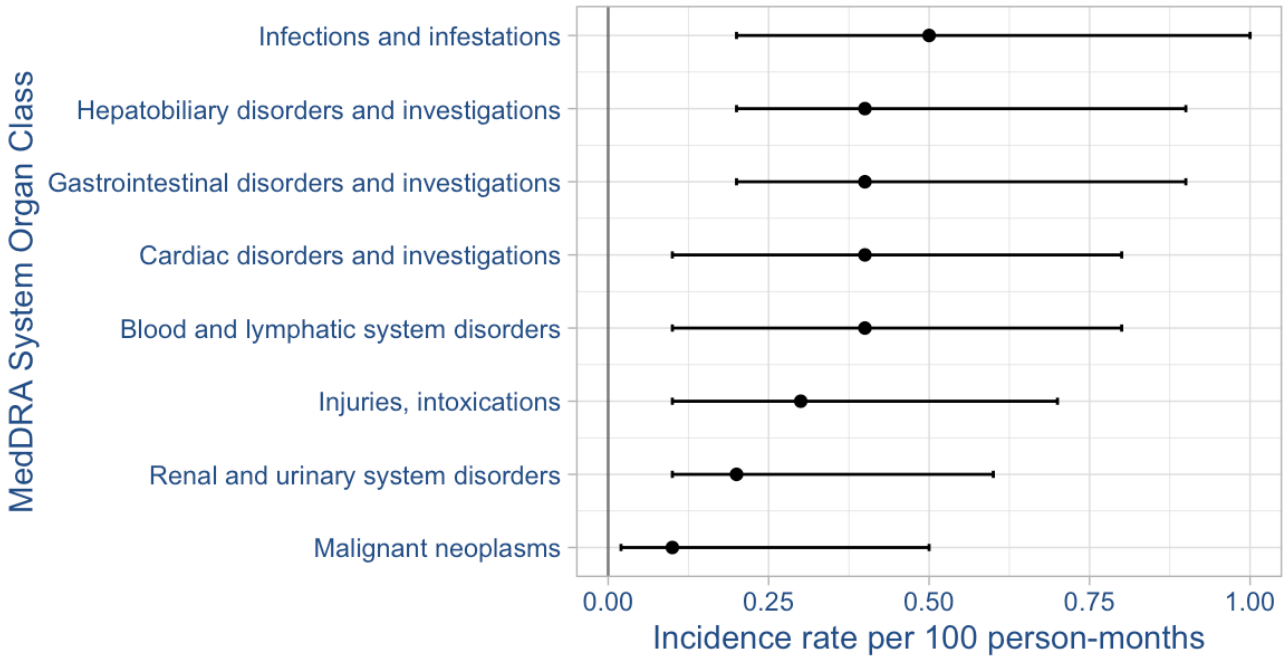


# BPaLM safety profile, n=249

## Cumulative incidence rate of SAE




## Incidence rate of SAE

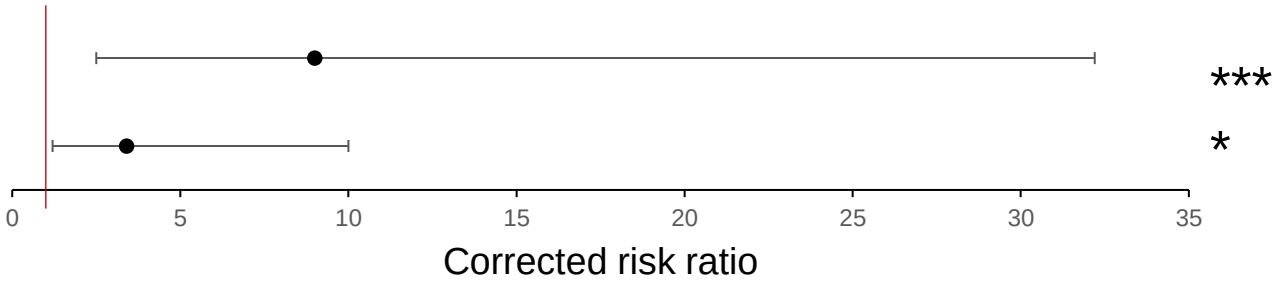


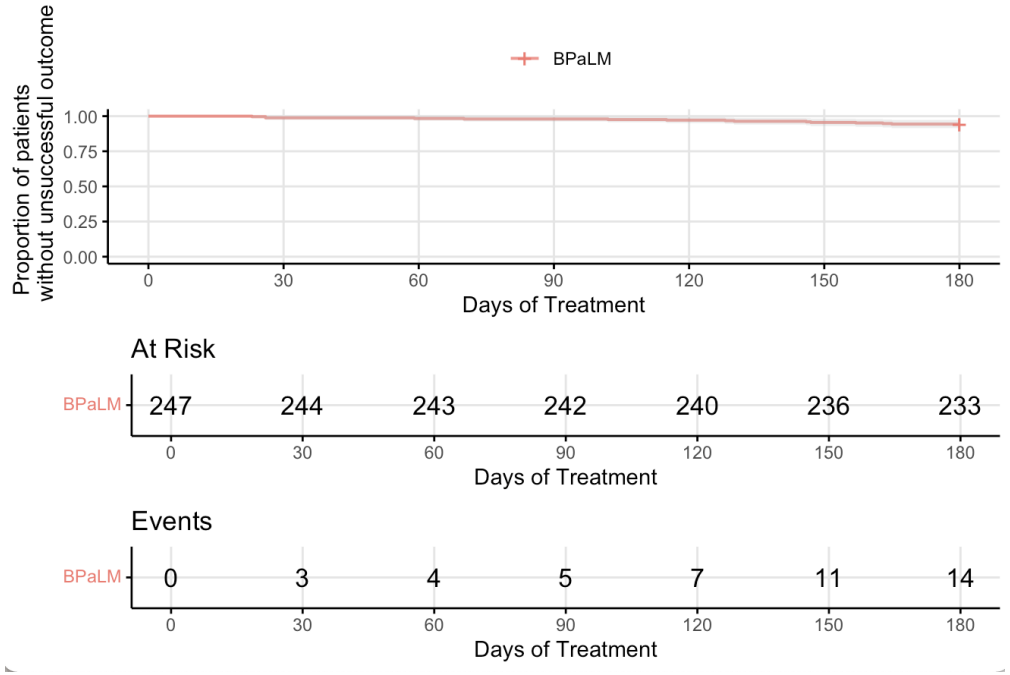

**Median time to AE occurrence was 75 (26-119) days**

# Predictors of unfavourable treatment outcomes, BPaLM, n=247

Sputum smear positive result at treatment start

Alcohol misuse



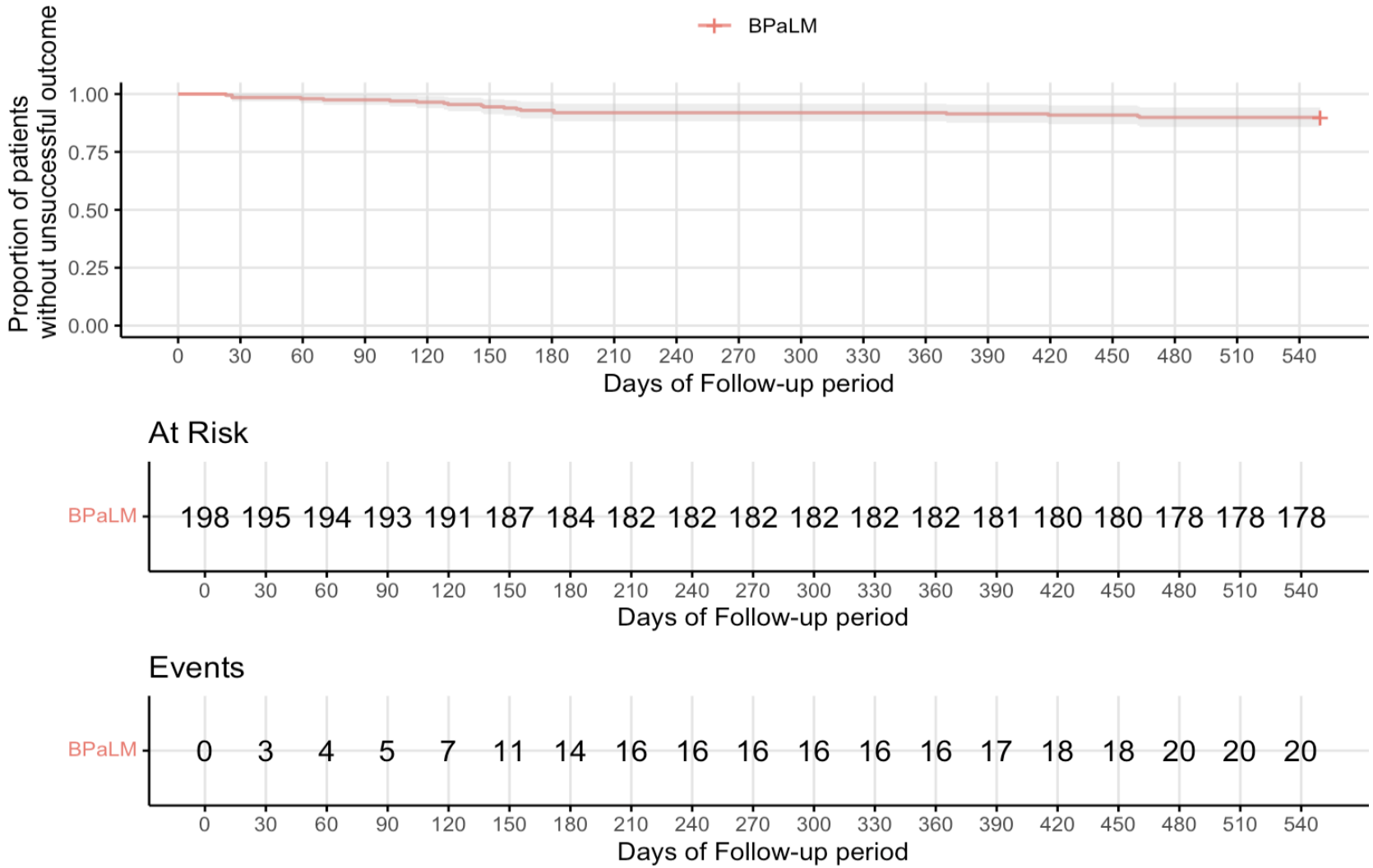




*** - p = 0,00076

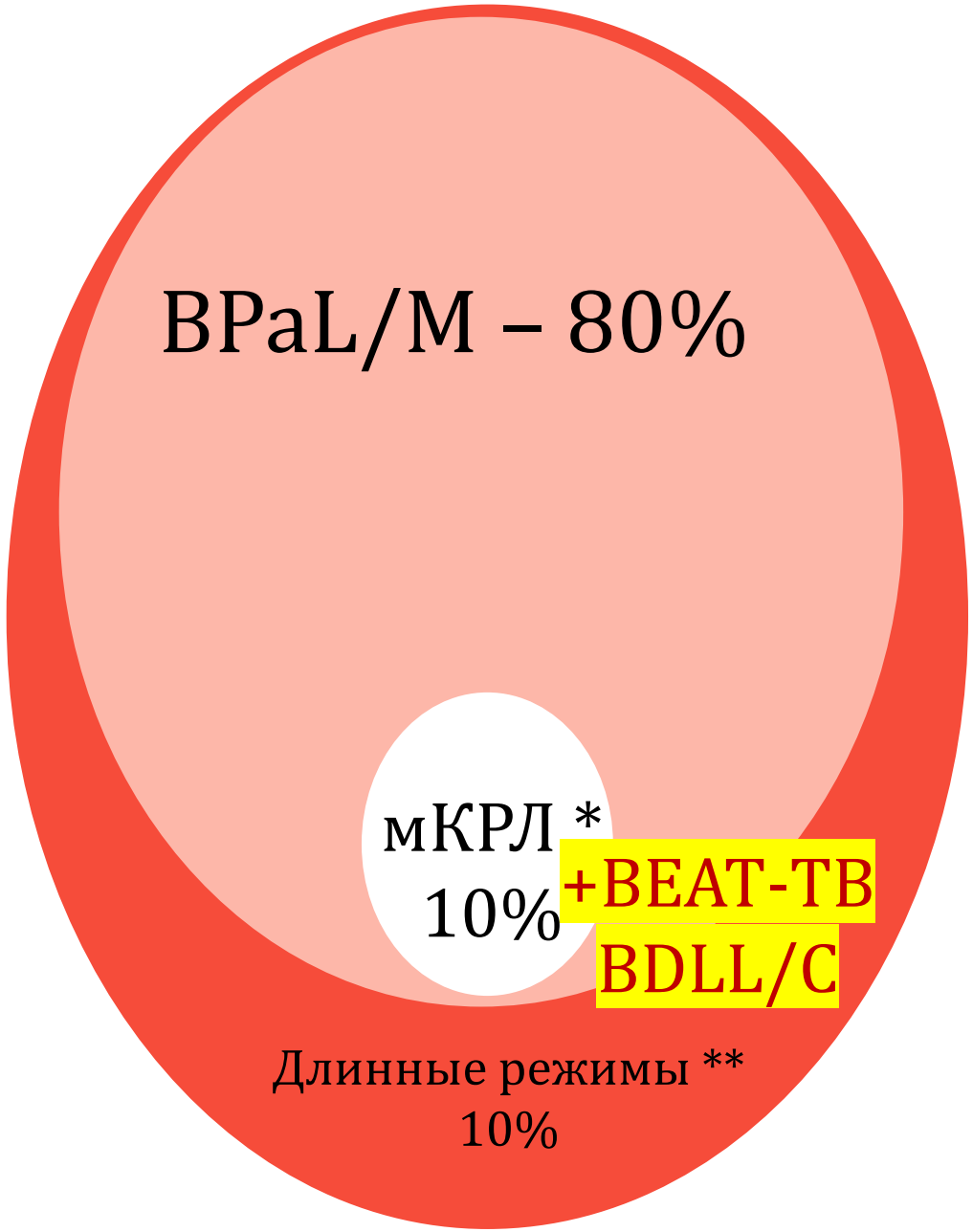
* - p = 0,022

Multivariate regression analysis by Cox proportional Hazards method

# Follow-up, BPaLM, n=198




89.9%




# Внедрение BPaL/M в Беларуси - 2025

* mSTR – 10%: children < 14 years of age, pregnant, lactating women

** Longer regimens - 10%:

- severe extrapulmonary TB (CNS, miliary, bone and joint)
- resistance to Bdq, Lzd, Pa, Lfx, Cfz, Dlm
- treatment failure due to lack of conversion, clinical response, additional resistance
- loss to follow-up
- intolerance to BPaL or mSTR drugs
- conditions that require a personalized approach

# Acknowledgements


- **Thanks to all operational research participants,**
- **Doctors Without Borders (Médecins Sans Frontières (MSF),**
- **WHO regional office for Europe,**
- **Global Fund to Fight AIDS, Tuberculosis and Malaria,**
- **NTP, regional monitors,**
- **Staff of the Republican Scientific and Practical Center for Pulmonology and Tuberculosis, Minsk,**
- **Staff of all TB facilities in Belarus.**