Lessons Learnt from the roll-out of BPaL-based Regimens as Operational Research In Uzbekistan

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BACKGROUND

- TB incidence in Uzbekistan in 2023 (WHO, 2024)
  - Total TB incidence: 20, 000 (57 per 100 000)
  - MDR/RR-TB incidence: 3, 900 (11 per 100 000)
- Total TB cases notified: 15, 449
  - MDR/RR-TB: 1, 959

IMPLEMENTATION OF BPaLM/C REGIMENS

2016 - 2022

- TB-PRACTECAL Clinical Trial
- 208 patients recruited

Jan – June 2022

- Operational Research
- Study protocol approved by MSF and Uzbekistan ERBs

June - Nov 2022

- Training of healthcare workers
  - 63 TB MDs
  - 341 GPs
  - 469 Nurses

June 2022

- Patient recruitment started and ongoing

10th April 2025

- Data cutoff point for the interim analysis

2024

- Data analysis and report writing

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INCLUSION CRITERIA

- 18 years or older
- Has bacteriologically or molecularly confirmed TB with evidence of resistance to at least rifampicin (or clinically diagnosed with strong contact history with MDR/RR-TB)
- Signed ICF

EXCLUSION CRITERIA

- Unable to take oral medication
- Known resistance to BPaL or prior use of BPaL >1 months.
- Has a known allergy to any of the drugs in the MDR/RR-TB regimen.
- Has a QTcF interval of ≥ 500 msec at baseline
- TB meningo-encephalitis, osteo-arthritis, osteomyelitis, septic arthritis or brain abscess
- Patients who are currently on an MDR-TB treatment for more than 4 weeks and not failing.
- Pregnant women

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TREATMENT REGIMENS AND FOLLOW-UP TIMELINE

- Bdq-Pa-Lzd-Mfx for 24 weeks
- Bdq-Pa-Lzd-Cfz for 24 weeks
- Clinical and bacteriological monitoring:
  - once every 4 weeks during the treatment phase
  - once every 6 months after the end of treatment

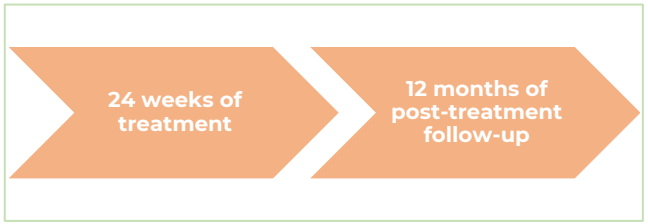

Table 3: Study timelines

	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								

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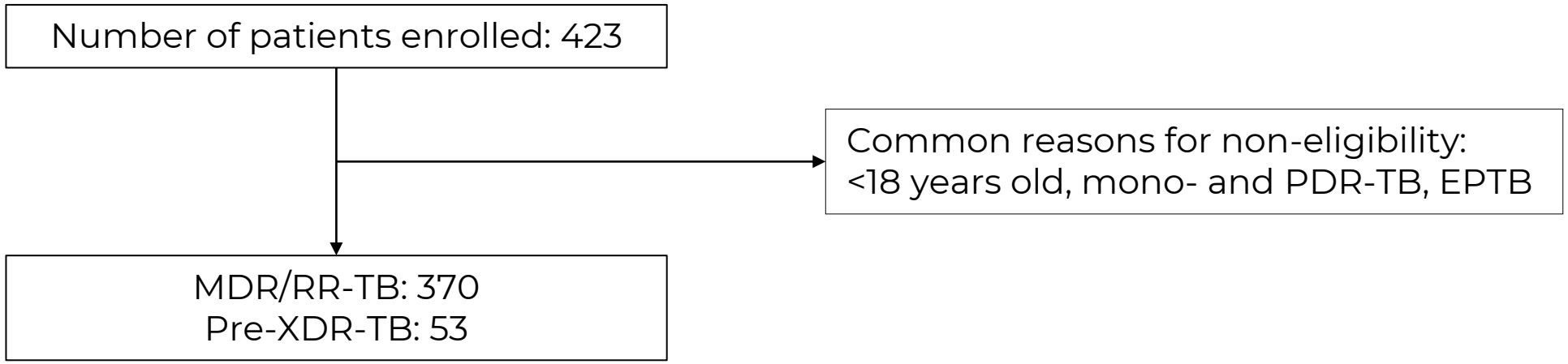
ENROLMENT PERIOD

- 01 June 2022 to 31 Dec 2024



MDR/RR-TB: multidrug-resistant/rifampicin resistant tuberculosis,
Pre-XDR-TB: pre-extensively drug-resistant tuberculosis
PDR: poly-drug resistant tuberculosis,
EPTB: extrapulmonary tuberculosis

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BASELINE CHARACTERISTICS OF STUDY POPULATION

Characteristics		Total = 423, (100%)	MDR/RR, N = 370	Pre-XDR, N = 53
Gender:	Female	189 (45%)	168 (45%)	21 (40%)
Age in year (median, IQR)		40 [29 – 57]	43 [29– 58]	33 [26 – 50]
Body mass index <18.5 kg/m2		125 (30%)	107 (29%)	18 (34%)
Site of the disease:	Pulmonary TB	419 (99%)	366 (99%)	53 (100%)
Previous treated TB		128 (30%)	111 (30%)	17 (32%)
Chest X-ray changes:	Cavity lesion	242 (58%)	203 (55%)	39 (74%)
Sputum smear:	Positive	230 (54%)	198 (54%)	32 (60%)
Present of Diabetes mellitus:	Yes	59 (14%)	53 (14%)	6 (11%)
HIV status:	Positive	6 (1%)	5 (1%)	1 (2%)
Hep B status:	Positive	10 (2%)	7 (2%)	3 (6%)
Hep C status:	Positive	20 (5%)	16 (4%)	4 (8%)

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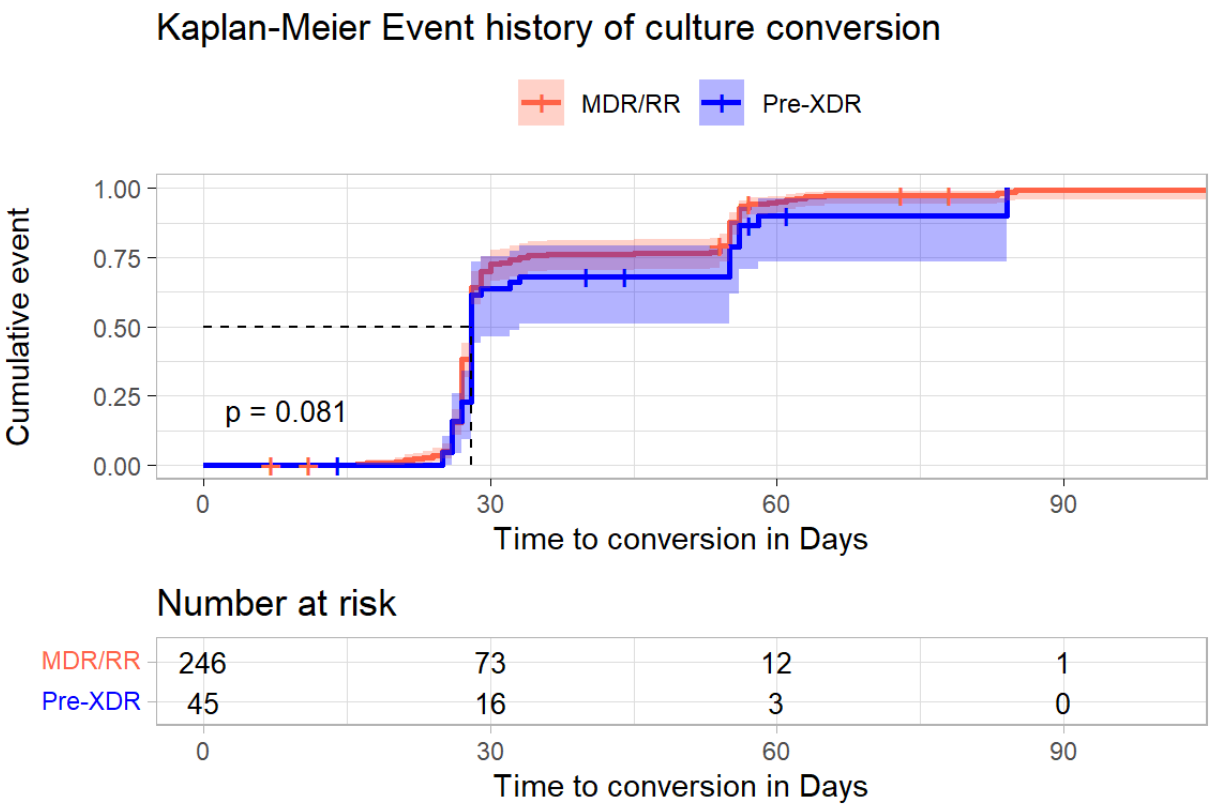
RESULTS: CULTURE CONVERSION

	Total	MDR/RR-TB	Pre-XDR-TB
Baseline culture			
Positive	291	246	45
Negative	84	80	4
Unknown	48	44	4
Time to culture conversion in days Median [IQR]	28 [27 – 32]	28 [27 – 32]	28 [28 – 39]



RESULTS – PRIMARY OUTCOMES

- Overall treatment success was achieved in 95% of the cases
  - MDR/RR: 96%
  - Pre-XDR: 83%

	Overall, N = 389	MDR/RR, N =337	Pre-XDR, N = 52
Cured at the end of treatment	350 (90%)	308 (91%)	42 (81%)
Treatment was completed	19 (5%)	18 (5%)	1 (2%)
Patient died during treatment	9 (2%)	7 (2%)	2 (4%)
Lost to follow-up	1 (1%)	0	1 (2%)
Treatment failed	2 (1%)	1 (1%)	1 (2%)
Patient withdrew his/her consent	2 (1%)	1 (1%)	1 (2%)
Not evaluated	6 (2%)	2 (1%)	4 (8%)

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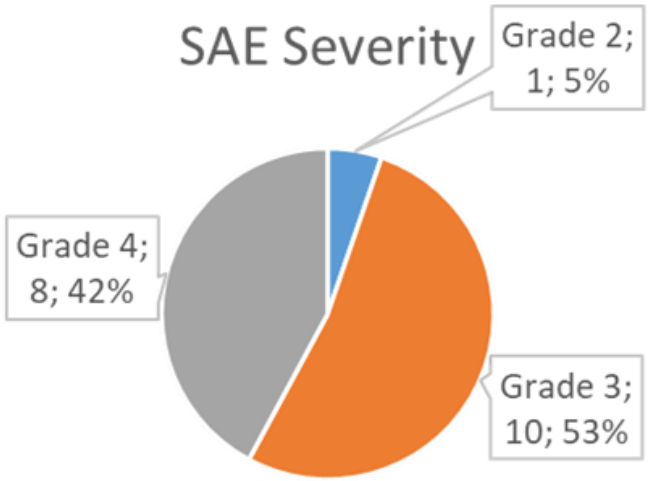
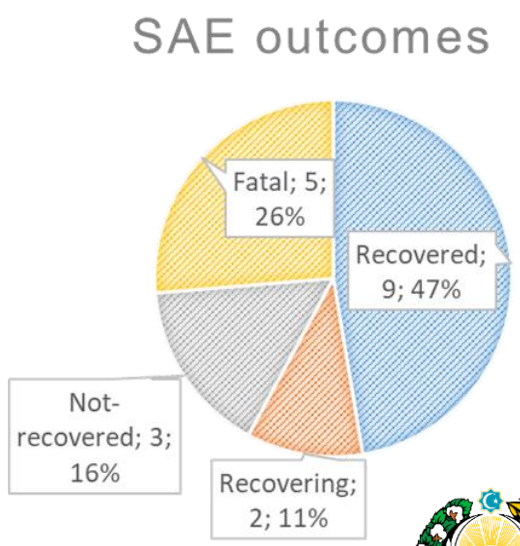
SAFETY PROFILE

Types of serious adverse event	N = 19	Percentage
Gastrointestinal disorders	1	5%
General disorders and administration site conditions	2	11%
Hepatobiliary disorders	2	11%
Investigations	5	26%
Metabolism and nutrition disorders	1	5%
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	11%
Nervous system disorders	1	5%
Psychiatric disorders	1	5%
Respiratory, thoracic and mediastinal disorders	1	5%
Skin and subcutaneous tissue disorders	3	16%

- Serious Adverse Events (SAEs): 4.5%, 19/423
  - BPaLM: 3.8%, 14/370
  - BPaLC: 9.4%, 5/53





CONCLUSIONS

- The BPaLM/C treatment regimens is effective with an overall **95%** treatment success rate for RR/MDR-TB treatment
- The BPaLM/C treatment regimens is safe, only **4.5%** of the patients developed grade 3 or higher adverse events

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