Management of Patients Withdrawn from the mSTR Operational Research in Kazakhstan

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Operational Research

Evaluation of Safety and Efficacy of Modified Shorter All-Oral Treatment Regimens (mSTR) for RR/MDR-TB in Kazakhstan

Ethics Approval

- This operational research is conducted according to two protocols: PIH and WHO.
- The PIH Protocol was approved by the Local Ethics Committee (LEC) under the NSCP of the Ministry of Health of the Republic of Kazakhstan (No. 51 of 14.05.2020).
- The WHO Protocol was approved by the Local Ethics Committee (LEC) under the NSCF of the Ministry of Health of the Republic of Kazakhstan (No. 58 of 11.09.2020) and by the WHO Research Ethics Review Committee on 09.10.2020 (no. ERC. 0003467)

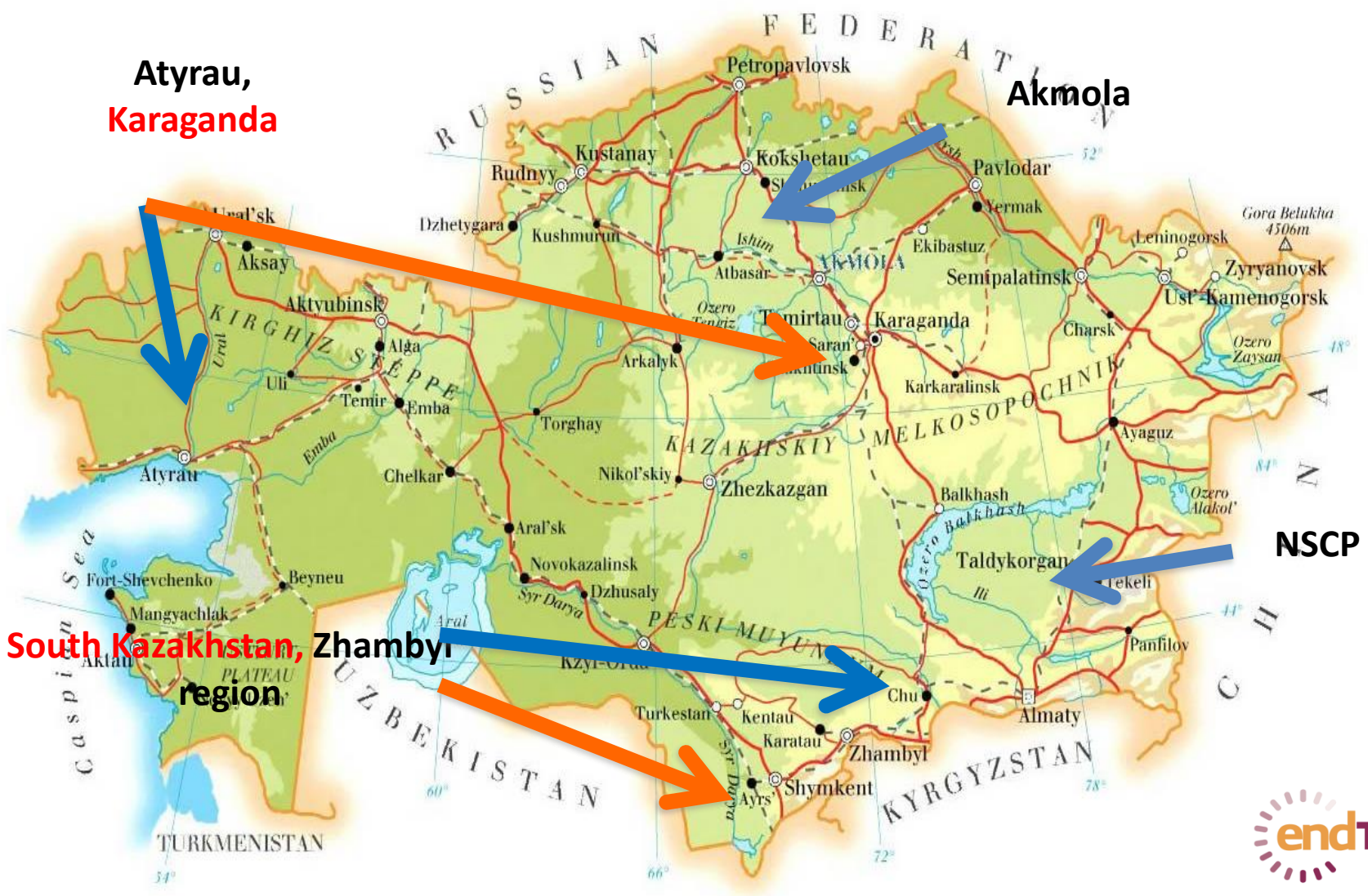
Primary Objective:

Evaluate efficacy and safety of shorter 39-week treatment regimens for RR-TB within the framework of the NTP of the Republic of Kazakhstan.

Study sites:

Five regions of the Republic of Kazakhstan (Turkestan, Karaganda, Akmola, Atyrau, Zhambyl regions) with the possibility of expanding to other regions.

Treatment Sites



All-Oral RR-TB Treatment Regimens Used in the Study

For adult patients:

- Bdq-Dlm-Lzd-Lfx-Z (39 weeks) PIH
- Bdq-Dlm-Lzd-Lfx-Cfz (39 weeks) PIH, WHO
- Bdq-Lzd-Lfx-Cfz-Cs (39 weeks) WHO

39 weeks – 273 doses

Patient Enrollment and Treatment Regimens

Patient enrollment started on September 22, 2020. As of May 01, 2021, 214 patients have been enrolled.

Akmola region – 32 patients (-1)

Atyrau region – 49 patients (-2)

Zhambyl region – 24 patients (-1)

Karaganda region – 32 patients (-2)

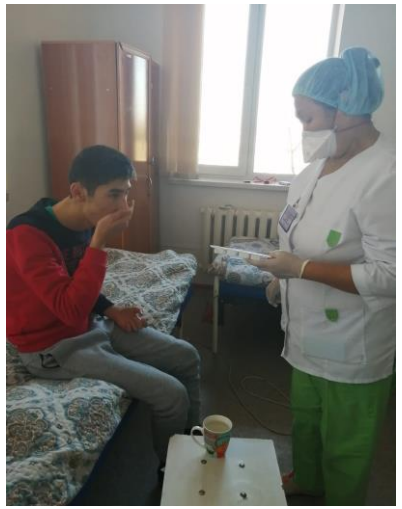
Turkestan region, Shymkent –73 patients (-8)

Treatment regimens:

Bdq-Dlm-Lzd-Lfx-Z – 55 patients

Bdq-Dlm-Lzd-Lfx-Cfz – 12 patients

Bdq-Lzd-Lfx-Cfz-Cs – 147 patients



Patient Enrollment and Treatment Regimens (contined)

Patient enrollment started on September 22, 2020. As of May 01, 2021, 214 patients have been enrolled.

15 patients have been withdrawn from the study

and continued treatment on ITR due to detected d

resistance to one or several anti-TB drugs

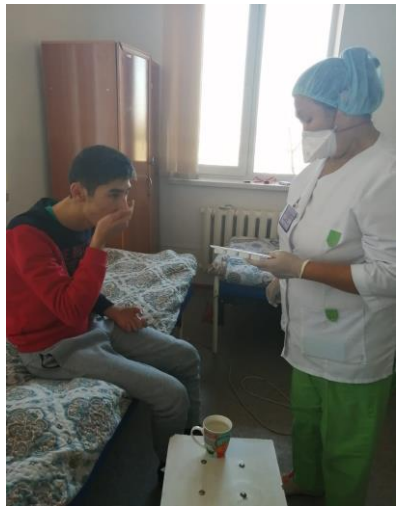
used in the mSTR

Discontinued treatment regimens:

Bdq-Dlm-Lzd-Lfx-Z – 4 patients

Bdq-Dlm-Lzd-Lfx-Cfz –2 patients

Bdq-Lzd-Lfx-Cfz-Cs – 9 patients



Groupings of Drugs Recommended for ITR

GROUP	DRUG	ABBREVIATION
Group A: Include all three drugs in the chemotherapy regimen (except in cases when they cannot be used)	Levofloxacin OR Moxifloxacin	Lfx Mfx
	Bedaquiline	Bdq
	Linezolid	Lzd
Group B: Add both drugs to the chemotherapy regimen (except when they cannot be used)	Clofazimine	Cfz
	Cycloserine OR Terizidon	Cs Trd
Group C: Add to have a complete chemotherapy regimen and when drugs from groups A and B cannot be used	Ethambutol	E
	Delamanid	Dlm
	Pyrazinamide	Z
	Imipenem-cilastatin OR Meropenem	Ipm-Cln Mpm
	Amikacin (OR Sreptomycin)	Am/(S)
	Ethionamide OR Prothionamide	Eto Pto
	Para-aminosalicylic acid	PAS

Principles of Drug Selection for ITR

- If only one or two Group A drugs can be used, both group B drugs should be included in the regimen. If the regimen cannot be made up exclusively of group A and B drugs, the regimen must be supplemented with group C drugs.
- It may be advisable to start patients with a high probability of discontinuation of two group A drugs before the end of treatment (for example, if health risks due to pre-existing comorbidities require early discontinuation of both bedaquiline and linezolid) on treatment with five effective drugs instead of four. The above mentioned principles apply to most MDR-TB patients, including those with additional resistance to fluoroquinolones or other drugs.

Case Study 1

- Patient T. age 37, male
- Diagnosis: Infiltrative TB of the right lung in the decay phase, MTB (+), 1B registration group. New case
- Date of mSTR treatment start 14.12.2020. Treatment regimen: Bdq Lfx Lzd Cfz Cs
- Baseline smear microscopy 1+, DST XpertMTB Rif-positive, Rif-resustant. Hain test of 15.12.2020: susceptibility to fluoroquinolones.
- Bactec DST results of 15.02.2021: resistance to HRLfx; susceptibility to EZCmAmLzdCfzMfx
- Switched to ITR 15.02.2021. Treatment regimen: Bdq Lzd Cfz EZ Cs
- Continues treatment for up to 18-20 months

Case Study 2

- Patient T. Age 40, female.
- Diagnosis: Infiltrative tuberculosis of the upper lobe of the right lung, MTB (+), 1B RG. Relapse after 2 episodes of TB treatment (1 and 2 categories)
- Date of mSTR treatment start 18.02.2021. Treatment regimen: Bdq Lfx Lzd Cfz Cs
- Baseline smear microscopy 6AFB, DST XpertMTB Rif-positive, Rif-resistent, Hain test (from Bactec) of 11.03.2021: Resistance to fluoroquinilones.
- Switched to ITR on 11.03.2021. Treatment regimen: Bdq Lzd Cfz Dlm Cs
- Bactec DST results of 25.03.2021: resistance to HRZMfxLfx; susceptibility to ECmAmLzdCfzEto
- Continues treatment for up to 18-20 months

Case Study 3

- Patient M. Age 32, female
- Diagnosis: Infiltrative tuberculosis of the left lung, MTB(+),1B RG. New case
- Date of mSTR treatment start 21.04.2021. Treatment regimen: Bdq Lfx Lzd Cfz Cs
- Baseline smear microscopy results 2+, DST XpertMTB Rif-positive, Rif-resistent. Hain test of 13.04.2021 resistance to HR, susceptibility to fluoroquinolones and aminoglycosides
- Bactec DST results of 14.05.2021: resistance to HREKmLfxMfx; susceptibility to CmAmLzdCfzEtoMfx1.0
- Switched to ITR on 14.05.2021. Treatment regimen: Bdq Lzd Cfz Dlm Cs
- Continues treatment of up to 18-20 months

Thank you for your attention!