

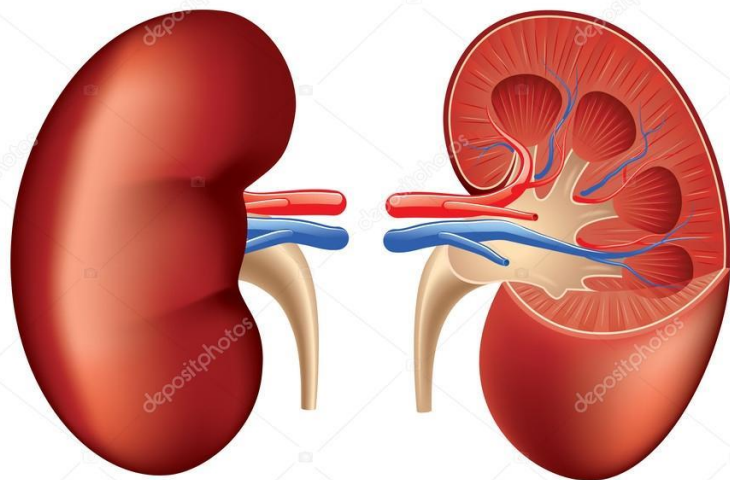
BELARUS EXPERIENCE IN MANAGEMENT OF MDR / RR-TB PATIENTS WITH RENAL FAILURE IN THE FRAMEWORK OF THE MSTR OPERATIONAL STUDY

12th Webinar of
the Virtual Medical Concilium (VMC)
as part of the Regional Operations Study of
All-Oral Modified Shorter
MDR / RR-TB Treatment Regimens

Yatskevich Natalia
MD, PhD, Assoc. Prof.

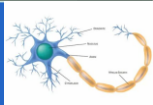
Republican Research Center of Pulmonology and Phthisiology,
Belarus

December 17, 2021



Adverse Events of Special Interest (AESI)

Peripheral neuropathy



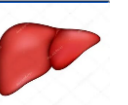
Myelosuppression



QTcF interval Prolongation the



Hepatitis



Optic neuritis



Hypokalemia

Acute renal failure



Dosages of mSTR drugs in patients with renal insufficiency (GFR < 30 ml / min)

Bdq	In patients with mild to kidney injury no adjustment is required (dosage is not determined for severe renal insufficiency, use with caution)
Lfx	750-1000 mg / kg / dose 3 times a week
Lzd	No adjustment required
Cfz	No adjustment required
Cs	250 mg once a day, or 500 mg / dose 3 times a week
Dlm	No adjustment is required in patients with mild to moderate renal injury (dosage is not determined for severe renal impairment, use with caution)

Adverse Reactions to Levofloxacin

Adverse Reactions to Levofloxacin	Effects on the central nervous system
	Peripheral neuropathy
	Tendon rupture
	QT interval prolongation
	Acute renal failure
	Diarrhea associated with <i>Clostridium difficile</i>
	Risk of aortic aneurysm and dissection
	Photosensitization
	Hypersensitivity reactions

Adverse reactions to cycloserine

Adverse reactions to cycloserine	Effects on the central nervous system
	Peripheral neuropathy
	Acute renal failure
	Elevated transaminase levels
	Hypersensitivity reactions

Clinical case

Date of birth (DD / MM / YYYY)		13/10/1951	
Sex		Male	
History of TB treatment		Drug resistance	
New / previously treated with first- or second -line drugs	New	DS/PDR/RR/ MDR/pre-XDR/XDR	RR-TB
TB site		Co-infections	
Pulmonary TB/ Extrapulmonary TB	Pulmonary TB	HIV test VHC and VHB tests	24.09.2020 - NEGATIVE
<i>Detection of M.tuberculosis</i>		History of contact with a TB patient	Not reported
Smear microscopy result	AFB negative		
Culture result	MTC		
Molecular Test Result (s)	Xpert MTB/RIF Ultra – MTB+Rif resistance LPA-FQ – MTB+FQ susceptible		

Pre-treatment test results

Parameter	Result (23.09.2020)	Unit	Severity
Hemoglobin	134	g / l	
Leukocytes	7,94	x10 ⁹ /l	
Platelets	262	x10 ⁹ /l	
Erythrocytes	4,34	x10 ¹² /l	
Creatinine	118.2	Mcmol / L	
eGFR	53.8	ml / min	2
K	4,9	Mmol / l	
Mg	0,84	Mmol / l	
Ca	2,3	Mmol / l	
Bilirubin	10,2	Mcmol / L	
ALT	48	U / L	
AST	38	U / L	
Albumen	37,4	g / l	
Glucose	4,8	Mmol / l	

Clinical case

Microscopy and culture results:

Month of treatment	Specimen collection date	Microscopy result	Specimen collection date	Culture result
0	23.09.2020	Negative	23.09.2020	MTC
1	12.11.2021	Negative	12.11.2021	Negative
2	14.12.2021	Negative	14.12.2021	Negative
3	12.01.2021	Negative	12.01.2021	Negative
4	11.02.2021	Negative	11.02.2021	Negative
5	11.03.2021	Negative	11.03.2021	Negative
6	12.04.2021	Negative	12.04.2021	Negative
7	12.05.2021	Negative	12.05.2021	Negative
8	14.06.2021	Negative	14.06.2021	Negative
9	12.07.2021	Negative	12.07.2021	Negative

DST results:

Month of treatment	Specimen collection date	Test method	H	R	E	Z	Am	Lfx	Fq	Bdq	Lzd	Cfz	Dlm
0	23.09.2020	LPA	R	R			S		S				
0	23.09.2020	GeneXpert		R									
0	23.09.2020	Bactec	R	R	S	S	S	S		S	S	S	S

Clinical case

Diagnosis: Infiltrative pulmonary tuberculosis, MBT "+", **RR**, FG 0.

Comorbidities:

Ischemic heart disease. Atherosclerotic cardiosclerosis. Sinus bradycardia. Atherosclerosis of the aorta and coronary arteries. Insufficiency of the aortic valve with grade 1 regurgitation . HI NYHA FCII. Stage 2 Arterial hypertension , risk 4.

Pos-pulmonary embolism condition (09.2020).

Varicose of the lower extremities, C4 by CEAP.

Test results

Creatinine before treatment initiation: 118.2 Mmol / L, eGFR - 53.8 ml / min (Grade 2)

Treatment initiation date : 01.10.2020

Creatinine 10/06/2020: 192 Mmol / L, **eGFR - 29.9 ml / min** (Grade 3)

Month of treatment	0	1	2	3	4	5	6	7	8	9
Parameter										
Creatinine, Mmol / L	118.2	128	135,7	133,3	134,5	151,6	149	161	162,8	175
eGFR, ml / min	53.8	48,9	45,5	46,5	46	39,8	40,7	37	36,5	33,5
K, Mmol / l	4,9	4,4	4,8	4,2	5	4,6	4,9	4,6	4,6	4,85
Mg, Mmol / l	0,84	0,79	0,81	0,82	0,75	0,77	0,74	0,67	0,81	0,77
Bilirubin, Mmol / L	10,2	19	9,9	14,6	13,9	14,7	4,9	4,5	10	17,3
ALT, U / L	48	20	20	12	27,5	14	23	24	25,7	29,5
AST, U / L	38	28	38	24	25,1	34	28	29	36,5	35,7

Test results

Treatment: Bdq, Lfx, Lzd, Cfz, Cs, Pyridoxine, Folic acid, rivaroxaban, antihypertensive therapy

Month of treatment	0	1	2	3	4	5	6	7	8	9
Parameter										
Hemoglobin, g/l	134	155	114	112	126	140	145	129	143	142
Erythrocytes, x10 ¹² /l	4,34	5	3,62	3,45	4,37	4,25	4,3	3,97	4,36	4,4
Platelets, x10 ⁹ /l	262	123	207	153	125	148	169	131	135	155
Leucocytes , x10 ⁹ /l	7,94	6,77	8,5	6,33	6,7	9,14	6,0	6,7	6,9	6,4

Month of treatment	0	1	2	3	4	5	6	7	8	9
Parameter										
QTcF, m/s	386	401	411	432	440	420	440	415	410	437
Heart rate, beats per minute	54	72	52	64	68	82	81	80	74	56

Pre-treatment test results

Ultrasound examination of kidneys:

24.09.2020	Right	Left
Location	In the lying position - normal	In the lying position - normal
Contours	smooth	smooth
Size	106x44 mm	110x48 mm
Parench.layer	14 mm uniform	14 mm uniform
Echogenicity	normal	normal
calix	N	N
Pelvis	N	N
Details	parenchymal cyst 12x10 mm	-

Conclusion: right kidney cyst

Clinical case

Treatment: Bdq, Lfx, Lzd, Cfz, Cs, Pyridoxine, Folic acid, rivaroxaban, antihypertensive therapy

Creatinine before treatment initiation: 118.2 $\mu\text{mol} / \text{L}$, eGFR - 53.8 ml / min (Grade 2)

Treatment initiation date : 01.10.2020

Creatinine **06.10.2020**: 192 $\mu\text{mol} / \text{L}$, eGFR – 29,9 мл/мин (Grade 3)

Creatinine **03.12.2020**: 119,8 $\mu\text{mol} / \text{L}$, eGFR – 52,9 мл/мин

Creatinine **19.01.2021**: 147,0 $\mu\text{mol} / \text{L}$, eGFR – 41,3 мл/мин

Start date	Lfx	Bdq	Lzd	Cfz	Cs	Comments on adherence to therapy
01.10.2020	1 g	400 mg	600 mg	100 mg	750 mg	Adherent
07.10.2020	1 g 3 t/w	400 mg	600 mg	100 mg	750 mg 3 t/w	Adherent
15.10.2020	1 g 3 t/w	-	600 mg	100 mg	750 mg 3 t/w	Adherent
16.10.2020	1g 3 t/w	200mg 3 t/w	600 mg	100 mg	750 mg 3 t/w	Adherent
04.12.2021	1 g	200mg 3 t/w	600 mg	100 mg	750 mg	Adherent
20.01.2021	1 g 3 t/w	200mg 3 t/w	600 mg	100 mg	750 mg	Adherent

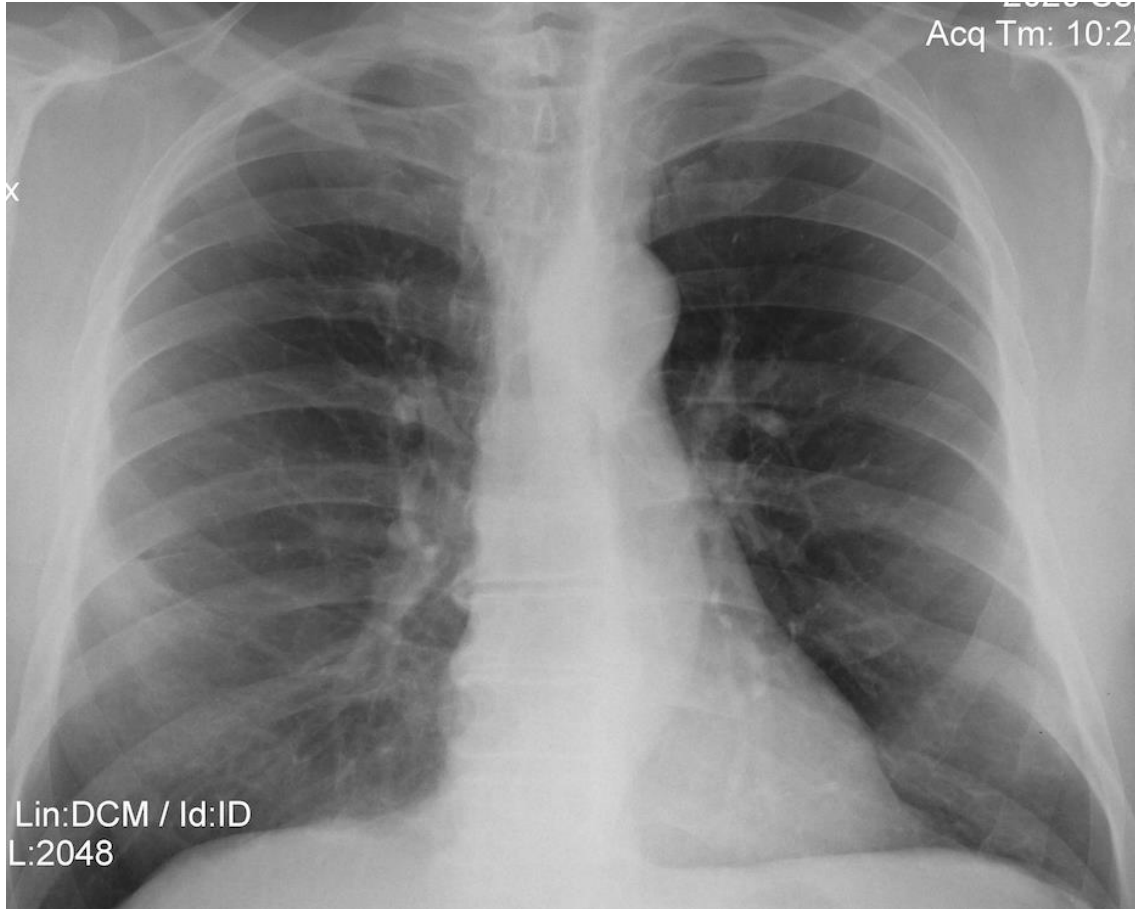
Test results

Month of treatment	0	1	2	3	4	5	6	7	8	9
Parameter										
Creatinine, Mmol / L	118.2	128	135,7	133,3	134,5	151,6	149	161	162,8	175
eGFR, ml / min	53.8	48,9	45,5	46,5	46	39,8	40,7	37	36,5	33,5
K, Mmol / l	4,9	4,4	4,8	4,2	5	4,6	4,9	4,6	4,6	4,85
Mg, Mmol / l	0,84	0,79	0,81	0,82	0,75	0,77	0,74	0,67	0,81	0,77
Bilirubin, Mmol / L	10,2	19	9,9	14,6	13,9	14,7	4,9	4,5	10	17,3
ALT U / L	48	20	20	12	27,5	14	23	24	25,7	29,5
AST, U / L	38	28	38	24	25,1	34	28	29	36,5	35,7

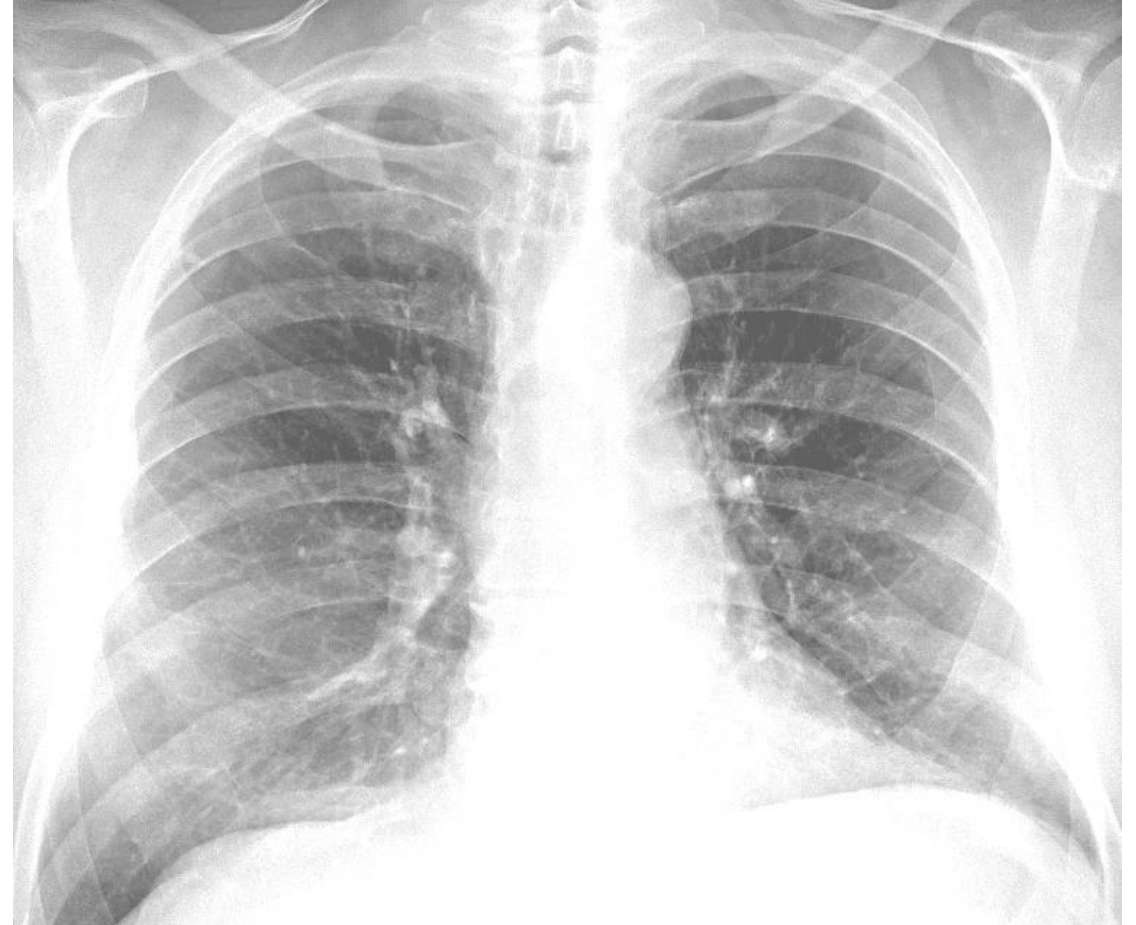
Definition of causation categories

	Certain	Probable	Plausible	Doubtful
Temporal association	yes	yes	yes	yes
Explained by comorbidities / drugs	no	no	possible	no
Pharmacological / toxicological mechanism	yes	yes	possible	no
Positive results of discontinuation	yes	yes	Data not available / doubtful	No data / NO
Positive results of re-prescribing	yes	Was not indicated / Not known	Was not indicated / Not known	No data / NO

Clinical case



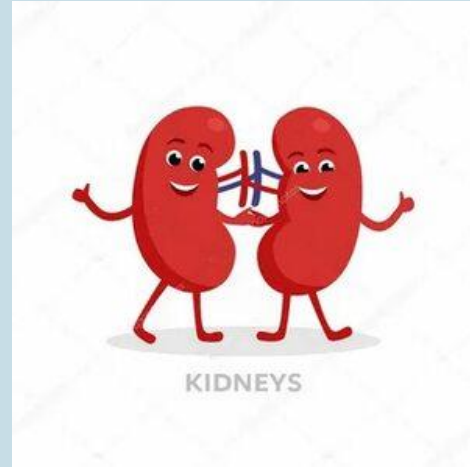
Plain chest radiography on 17.09.2020 –
Increased lung marking and mid-zone lung tissue infiltrates on the right.



Plain chest radiography on 24.06.21 - an intensive focus on the right in the 2nd intercostal space; lung marking the mid-zone is increased and deformed, regression of infiltrative changes on the right

Test results 3 months after the end of treatment

Parameter	Result (28.10.2020)	Units	Severity
Creatinine	130,5	Mcmol / L	
e GFR	47,7	ml/ min	2
Direct bilirubin	5,4	Mcmol / L	
ALT	31,7	U / L	
AST	24,3	U / L	
Albumin	38,2	g/L	
Glucose	6,1	Mmol/ L	



THANK YOU FOR YOUR ATTENTION