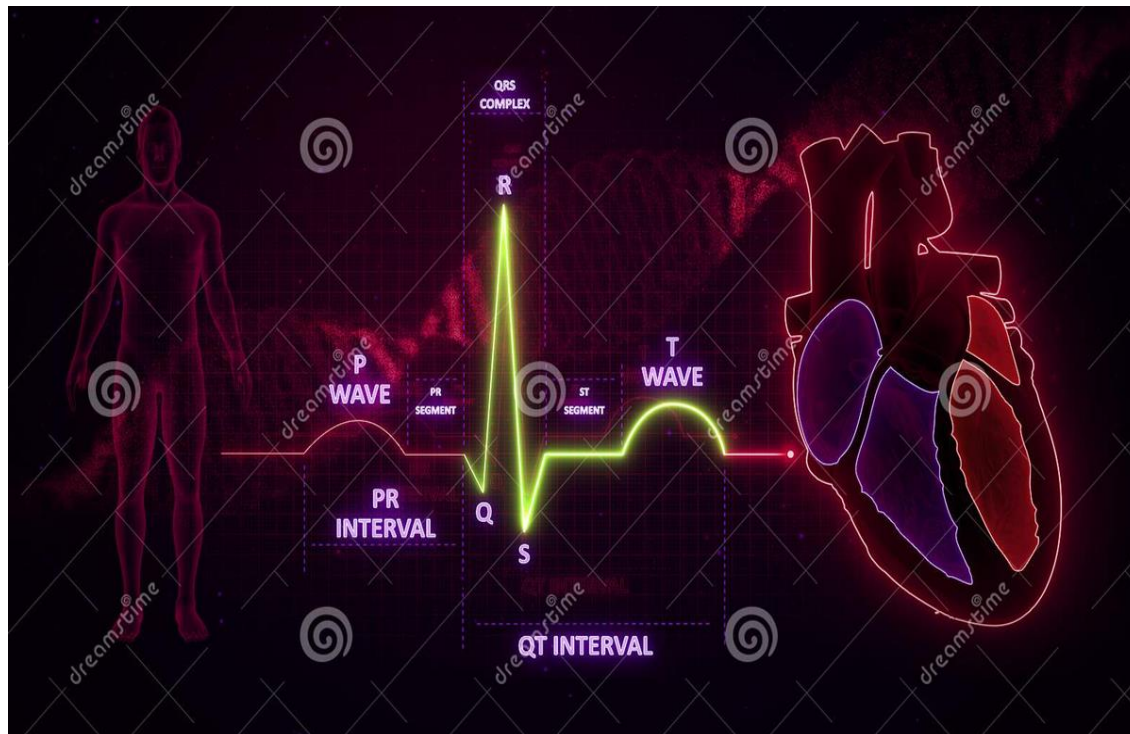


Cardiotoxicity of TB drugs.

Clinical cases

September 3, 2021
Moldova

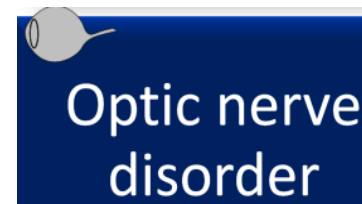


Adverse events (AE) of clinical interest

1. Периферическая
нейропатия



5. Неврит
зрительного
нерва



2. Миелосупрессия



6. Гипокалиемия



3. Удлинение
интервала QTcF



7. Острая
почечная
недостаточность
(ОПН)

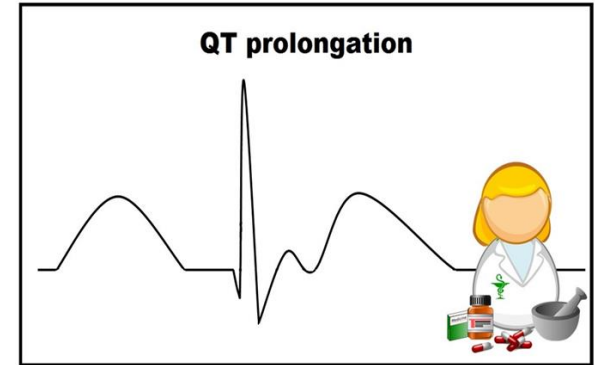


4. Гепатит



QT interval prolongation

- **Drug: Bdq**



- Other potential TB drugs: Dlm, Cfz, Mfx, Lfx
- Other potential drugs: erythromycin, clarithromycin, quinidine, ketoconazole, fluconazole, and antipsychotics all carry risks, including haloperidol, chlorpromazine, and risperidone.
- Many antiemetics (ondansetron / granisetron, domperidone), methadone and some antiretrovirals, as well as genetic factors, including long QT syndrome and hypothyroidism, can also cause QT interval prolongation

Clinical case 1

- A 29-year-old patient was first diagnosed with pulmonary TB when she was self-referred to the family doctor in December 2020.
- Evaluation results at the primary health care level:
 - ✓ X-ray of 01/25/2021 - multiple polymorphic foci on the right S₁₊₂, S₆,S₉.
Regional lymphangitis
 - ✓ 02/09/2021 AFB sputum smear microscopy - negative
 - ✓ 02/09/2021 Xpert MTB / RIF Ultra - MTB + RIF resistant

Clinical case 1

Past medical history

- No history of TB
- No contacts with TB patients recalled
- Does not smoke, does not abuse alcohol, denies intravenous drug use
- Concomitant diseases: congenital heart disease; atrial septal aneurysm with a small defect.
- The patient was diagnosed with infiltrative tuberculosis S1+2, S6, S9 of the right lung; a new MDR-TB case; congenital heart defect; atrial septal aneurysm with a small defect; moderate pulmonary hypertension; grade 1 heart failure NIHA; bilateral mixed hypoacusis.

Evaluation results (prior to treatment initiation)

- Sputum smear microscopy result of 02/09/2021: AFB - negative.
- Xpert MTB / RIF Ultra result of 02/09/2021 - MTB + RIF-resistant
- LPA-FQ - MTB + FQ susceptible
- **CBC** (04.02.2021): HB-116 g/l, RBC - 4.1×10^{12} /l, PLT- 262×10^9 /L, WBC- 4.2×10^9 /L, ESR - 22 mm / h
- **Biochemical blood test results** (04.02.2021): ALT - 49 U/L, AST-25 U/L, bilirubin - 6.9 μ mol /L, Creatinine - 93 μ mol/L, K - 4.19 mmol/L, Mg - 0.79 mmol / L, Na - 140.0 mmol /L, Ca - 2.12 mmol/L, fasting blood glucose - 5.97 mmol / l
- **VHC and VHB tests** of 04.02.2021 – negative
- **ECG** of 02/04/2021: sinus rhythm, QRS axis - normogram, QTcF interval - 468, heart rate - 65

Treatment tactics

16.02.2021 - enrolled for mSTR with : Lfx Bdq Lzd Cfz Cs (+ pyridoxine).

Microscopy and culture results:

Month of treatment	Specimen collection date	Microscopy result	Specimen collection date	Culture result
0	09.02.2021	Neg.	09.02.2021	Complex MTB
1	16.03.2021	Neg.	16.03.2021	Neg.
2	15.04.2021	Neg.	15.04.2021	Neg.
3	18.05.2021	Neg.	18.05.2021	Neg.
4	16.06.2021	Neg.	16.06.2021	Neg.
5	16.07.2021	Neg.	16.07.2021	Pending
6	16.08.2021	Neg.	16.08.2021	Pending

DST results

Month of treatment	Specimen collection date	Method used	H	R	E	Z	S	Am	Lfx	Mfx	Eto/Pto	Cs	PAS	Bdq	Lzd	Cfz	Dlm
0	09.02.2021	LI	R	R	S	S	-	S	S	S	R	-	-	S	S	S	S

Treatment – drugs and dosages

Initiation date	Lfx mg/day	Bdq mg/day	Lzd mg/day	Cfz mg/day	Cs mg/day	Dlm	Comments on treatment adherence
16.02.2021	1000	400	600	100	750		Vitamin B₆ indicated
03.03.2021		200					
27.05.2021	discontinued	discontinued		discontinued			Potassium supplements indicted
03.06.2021			discontinued		discontinued		
07.06.2021	1000		600	100	750		Daily intake
05.07.2021			300				

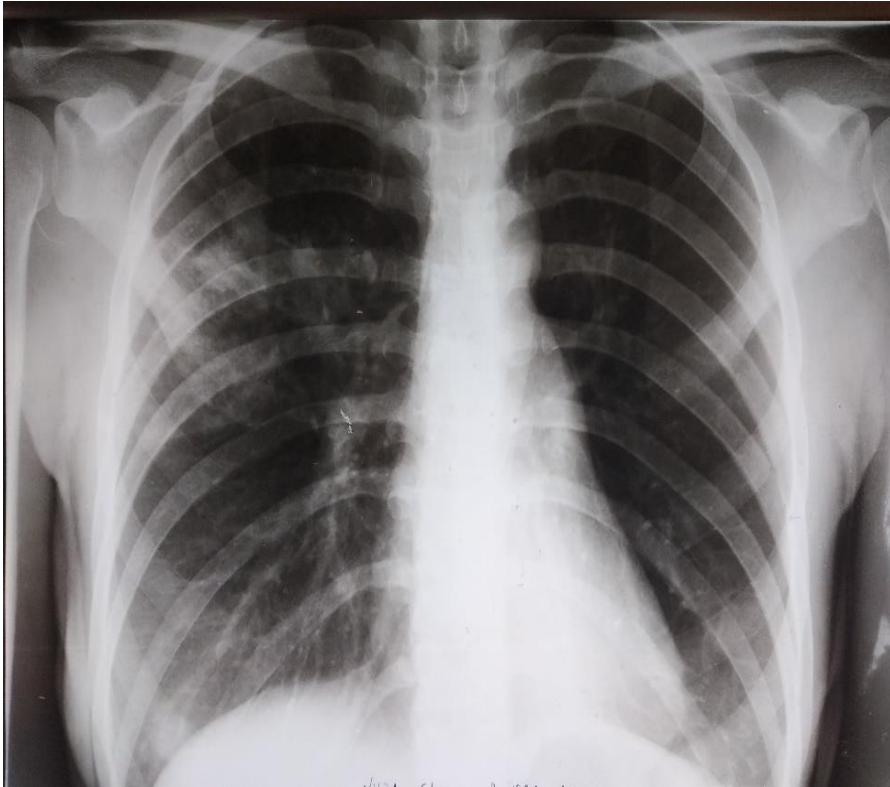
ECG over time (dates and description, including QTcF):

Evaluation date	Heart rate (per minute)	QTcF Interval (ms)
15.02.2021	65	370
01.03.2021	68-70	360
15.03.2021	73	380
15.04.2021	50	489
16.04.2021	54	437
18.05.2021	62	460
26.05.2021	56	512
27.05.2021 (Lfx Bdq Cfz discontinued)	59	480
28.05.2021	60	465
29.05.2021	111	548
01.06.2021	66	499
03.06.2021 (Lzd Cs discontinued)	65	468
04.06.2021	69	473
05.06.2021	63	473
07.06.2021 (The following regimen was indicated: Lfx Lzd Cfz Cs)	78	489
16.06.2021	62	490
29.06.2021	61	499
12.07.2021	60	474
10.08.2021	59	474
16.08.2021	64	466

Chest x-ray

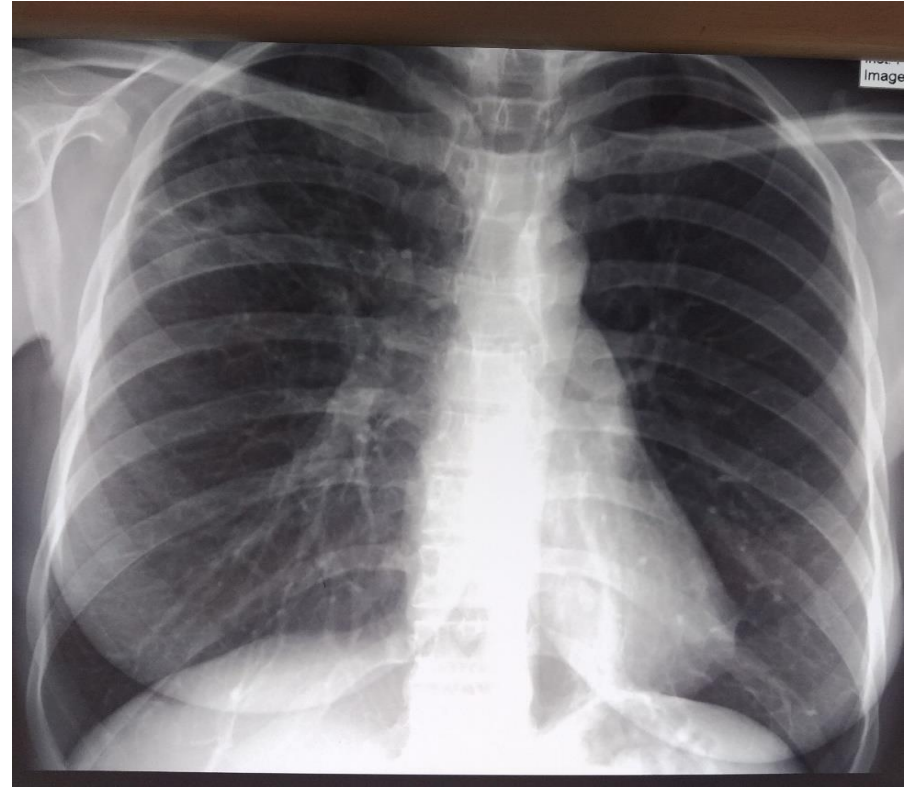
15.01.21 (at month 0)

**Multiple polymorphic foci on the right
S₁₊₂, S₆, S₉. Regional lymphangitis.**



16.08.2021 (at month 6)

**Regression of infiltrative changes on
the right.**



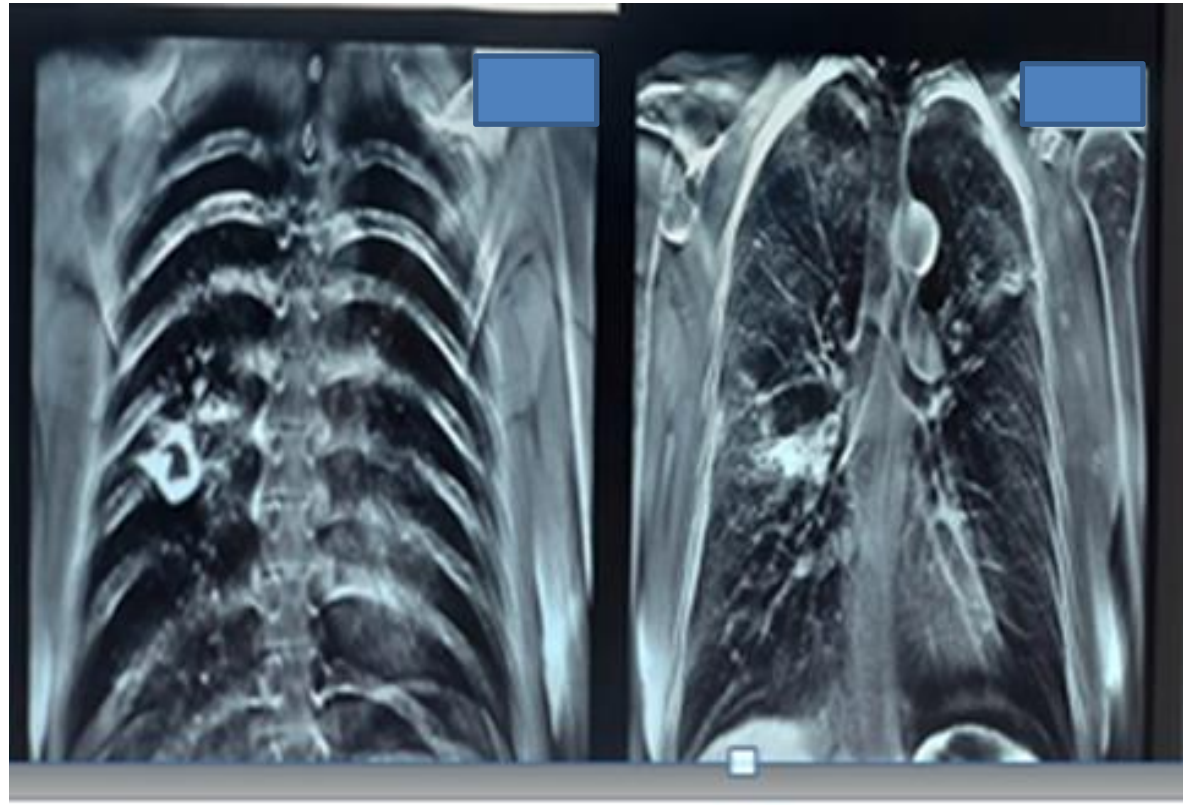
Clinical case 2

- A 57-year-old patient, first diagnosed with pulmonary TB in 2009, relapse in 2014.
- In both cases, she was successfully treated with the first-line drugs.
- In August 2020, she turned to her family doctor with complaints of productive cough for more than one month, shortness of breath on exertion, fever up to 38.5 ° C over the past week, general weakness, decreased appetite, weight loss by 5 kg over the past two months.

Clinical case 2

Chest X-ray of 10/18/2020 - Bilateral infiltrative pulmonary TB S6 / S1S2.

Tomosynthesis 10/30/2021: Polymorphic TB foci in S6 on the right and in S2 on the left, cavities with the thickened walls, segmental cirrhosis.



Clinical case 2

- On 26.10.2020 – AFB sputum smear microscopy- negative,
- On 26.10.2020 Xpert MTB/RIF Ultra – MTB+RIF- resistant
- No concomitant pathologies.
- Patient's history - 15 years of smoking (at the time of admission, she did not smoke for 3 years), recurrent alcohol abuse (at the time of admission, no alcohol abuse), denies any intravenous drug use.
- The patient was diagnosed with infiltrative pulmonary TB S6/S1S2 in the destruction phase, AFB positive, Xpert MTB/RIF Ultra – MTB+RIF resistant (26.10.2020). Relapse.

Clinical case 2

- On 10/28/2020 - hospitalized at the Research Institute of Phthisiopulmonology with a subsequent presentation to the Central Committee on DR-TB Management (10/29/2021) where a decision was made on the enrollment for mSTR in the framework of the operational study after screening and signing of the patient's informed consent.
- On 30.10.2020 – enrolled for mSTR with Lfx Bdq Lzd Cfz Cs.

ECG over time (dates and description, including QTcF):

Evaluation date	Heart rate (per minute)	QTcF Interval (ms)
30.10.2020	75	366
11.11.2020	65	401
01.12.2020	70	421
29.12.2020	85	393
28.01.2021	80	407

Clinical case 2

- At the next monitoring visit on 02/25/2021 QTcF - 462 mc, heart rate - 62 / min, single supraventricular extrasystoles.
- No complaints related to CVS.
- Electrolytes within normal limits (K^a + - 3.65 mmol / l, Mg + - 0.80 mmol / l, Na + - 14.8 mmol / l, ionized Ca + - 1.14 mmol /l)
- The patient was admitted to the hospital on 27.02.21 - 25.03.21, with due consideration of AE - lengthening of the QTcF interval.
- In the inpatient clinic, the following was prescribed: Potassium, Magnesium, group V vitamins

ECG over time (dates and description, including QTcF):

Evaluation date	Heart rate (per minute)	QTcF Interval (ms)
27.02.2021	72	440
01.03.2021	70	442
17.03.2021	70	390

Clinical case 2

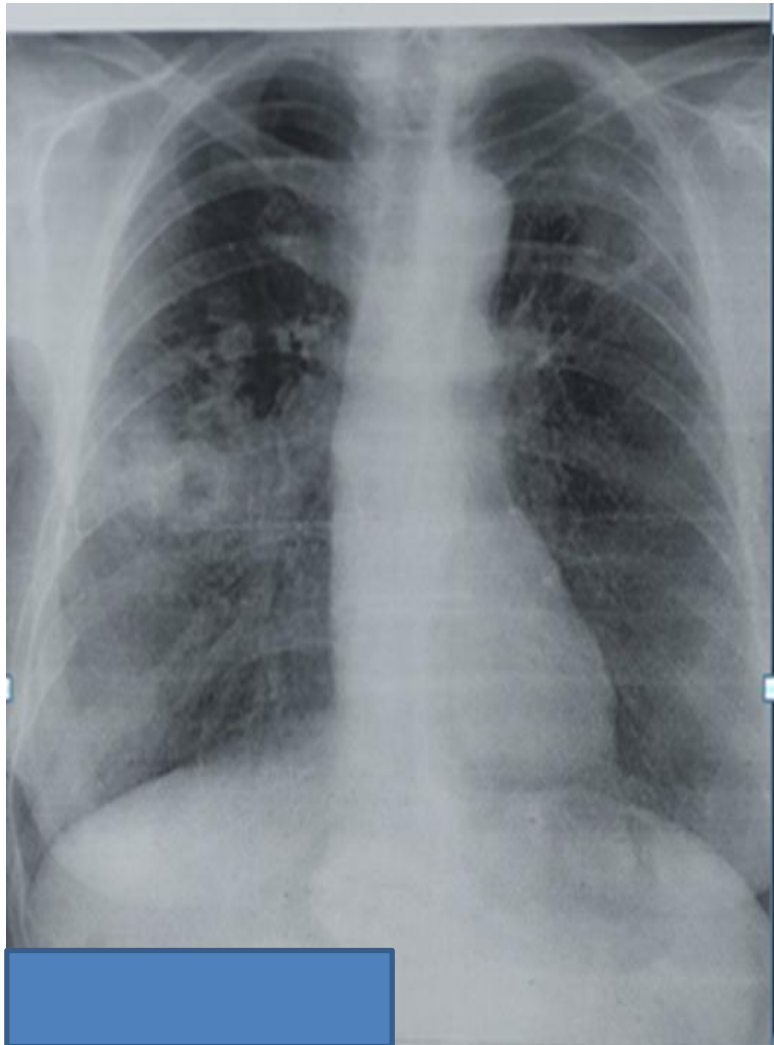
- The patient was discharged from the inpatient clinic without any electrolyte deficiency (K^a + - 4.88 mmol /l, Mg + - 0.70 mmol /l, Na + - 139.6 mmol /l, ionized Ca + - 1.26 mmol /l, with improved hemoglobin up to 11.4 g / dL and erythrocytes up to 3.8×10^6 / uL.
- During the subsequent monitoring visits:

Month of treatment	Heart rate	QTcF interval (ms)
6	70	421
7	72	420
8	70	380
9	74	417

- 9 negative smear microscopy results and 6 negative cultures were obtained, 3 are pending
- The patient successfully completed treatment on 07/29/2021.

18.10.2020

27.07.2021



Thank you for your attention!

