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## Preliminary data on safety and effectiveness of six-month all-oral regimens in patients with rifampicin-resistant tuberculosis in Belarus

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### Introduction

The total duration of treatment for rifampicin-resistant tuberculosis (RR-TB) in Belarus prior to December 2022 was 18-20 months. The efficacy of treatment with such regimens is low, with the WHO's Global TB Report suggesting that efficacy was around 73% in Belarus in 2018. The development of effective short regimens for RR-TB treatment is urgent. In Belarus, six-month long treatment with all-oral regimens is used in patients with RR-TB, under operational research conditions, following WHO recommendations.

### Methods

A preliminary assessment of the effectiveness of six-month all-oral regimens containing bedaquiline, pretomanid, linezolid, and moxifloxacin or clofazimine (BPaLM/BPaLC), was performed in a cohort of RR-TB patients. Treatment outcomes, time to culture conversion, and time to adverse event (AE) occurrence, AE types, frequency, and outcomes are described.

### Ethics

This study was approved by the MSF Ethics Review Board (ERB) and by the Belarus Ministry of Health ERB.

### Results

Of 177 patients who were enrolled from February 2022 to July 2022, one patient was excluded due to linezolid resistance; this patient continued treatment under an individualised regimen. Of the rest of the cohort (133 (76%) male, 43 female (24%); median age, 44 years (interquartile range, IQR, 25-29 years), 93.2% (164/176) had a favourable treatment outcome, 11 patients were lost to follow-up, and one died. 52 (30%) patients had a sputum smear positive result at treatment start, 59 (34%) a cavitory lesion on chest X-ray, and 42 (24%) patients had been previously treated. 12 patients (7%) were HIV-positive; 23 (13%) had had hepatitis C infection; 45 (26%) abused alcohol, and 6 (3%) of patients had diabetes mellitus. Median time to culture conversion was 27 days (IQR, 25-29). In 96.0% of patients, culture conversion was achieved within 2 months of treatment. 9% of patients had serious AE's (SAE). Out of total 19 SAE's, 12 resolved, two resolved with sequelae, three were resolving at the time of assessment, one did not resolve, and one was fatal. Median time from treatment start to the first SAE was 92.5 days (IQR, 12.5-143). The most frequent SAE's were elevated liver function (6 (32%) cases), acute kidney injury (4 (21%) cases), and amylase increased/pancreatitis (3 (16%) cases). Two cases also revealed cancer or progression of cancer; one showed QTcF prolongation; one, anemia, one, thrombotic cerebral infarction, and one, *Clostridium difficile* infection. Two cases of cancer and thrombotic cerebral infarction (a patient with a long-standing history of multiple strokes) were assessed as unrelated to study drugs. The one death from cancer was assessed as not related to treatment. Permanent withdrawal of one study drug (linezolid or clofazimine) was done only in three instances (15.8%).

### Conclusion

The effectiveness of six-month all-oral regimens in this cohort was very high (93.2%). BPaLM/BPaLC regimens were observed to be characterised by a good safety profile. Further data are necessary to evaluate longer-term treatment outcomes.

### Conflicts of interest

None declared.