

Introducing two new drugs for resistant tuberculosis

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Background

Multidrug-resistant tuberculosis (MDR-TB) remains a serious public health problem. Scarcity of safe, effective drugs contributes to the unfavorable outcomes, reported as 50% globally. The endTB project, funded by UNITAID, aims to expand access to two new anti-TB drugs: bedaquiline and delamanid, and other drugs repurposed for TB, as well as generating evidence about the effectiveness and safety of MDR-TB regimens containing these drugs.

Methods

This multi-centre prospective observational cohort study is conducted in 17 countries and includes patients treated with a bedaquiline - and/or delamanid-containing MDR-TB regimen in an endTB site who consent to participate. The study captures routine programmatic patient data in a standardised electronic medical record. Serious Adverse Events (SAE) are reported to a Pharmacovigilance Unit.

Results

From April 2015 to December 2017, 1,708 patients were included. Median age was 37 years (range: 13-87), 65% were male, 41% had a body mass index below 18.5 Kg/m², 67% had extensively drug-resistant (XDR) or pre-XDR TB.

Of the patients with at least 6 months of follow-up period, 15.9% had at least one SAE in the first 6 months of treatment. Most common SAEs were increased liver enzymes and prolonged QTcF interval, reported in 3.3% and 1.7% of the patients respectively. In total, 5.2% patients had a SAE with fatal outcome.

Of the patients with positive culture at treatment initiation and at least 6 months of follow-up period, 84.8% (95%CI: 81.5-87.6) converted by 6 months. Of those who converted and had at least 12 months of follow-up period, 7.7% (95%CI: 7.2-8.2) reverted by 12 months.

Conclusion

Preliminary analyses show promising results in a large cohort of patients with highly resistant and extensive TB disease treated with bedaquiline or delamanid under programmatic conditions. Safety reporting was adequate with no unexpected safety issues attributed to the new drugs. Culture conversion rates were high although subsequent culture reversion in some patients requires further analyses.

The endTB observational study shows promising safety and treatment results using bedaquiline and delamanid to treat patients with highly resistant and severe forms of TB.