



Catching up with WHO guidelines of DRTB; shorter, easier, better”

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The treatment scope of drug resistant tuberculosis (DRTB) has been evolving quickly. Ever since the Bangladesh regimen brought in a fresh impetus to treatment of DRTB (WHO rapid communication 2018),¹ the subsequent recommendations by WHO has been up to date and has quickly incorporated the findings of evidence generated. The recent guidelines incorporate the evidence generated from trials including ZeNix and TB-PRACTECAL. The evolution of treatment guidelines has ensured a paradigm shift in the way the treatment landscape of DRTB is viewed and has brought in a much welcome shift towards relatively shorter duration of treatment.

The ZeNix trial used bedaquiline–pretomanid–linezolid. Linezolid was used in two different doses (1200mg and 600mg) for durations of 9 weeks and 24 weeks. Patients included had extensively drug-resistant (XDR) tuberculosis, pre-XDR tuberculosis (as per the older definition) and MDR-TB which was non-responsive or treatment intolerant. With the dose of 600mg of linezolid given for 26 weeks, favorable outcomes were achieved in 84% of the cases. This dosage and duration had the most favorable overall risk-benefit ratio.²

TB PRACTECAL trial used all oral 24-week regimen of bedaquiline, pretomanid, linezolid, and moxifloxacin (BPALM) which was compared with a 9-to-20-month standard-care regimen. BPALM resulted in superior cure rates compared to the longer WHO standard of care regimen (89% vs 52%) with far less toxicity (20% vs 59%).³

STREAM Stage 2 had one arm with a 9 month all oral Bedaquiline based regimen (4 INH and Prothionamide) with (9 Bedaquiline, Levofloxacin, Clofazimine, Ethambutol and Pyrazinamide). STREAM stage 2 has shown that 9 month bedaquiline-containing regimen is not only non-inferior but superior to a 9-month injectable-containing regimen. The STREAM stage 2 fully oral regimen avoided the toxicity of aminoglycosides.⁴

In this background, WHO recent guidelines advocate the use of 6-month regimens based on ZeNix and TB PRACTECAL data, a 9-month regimen based on STREAM STAGE 2 data, and longer individually designed 18 month regimens where shorter regimens cannot be applied.⁵ The latter regimen being consistent with the regimens advocated in the National guidelines on DRTB management 2019.⁶

While both ZeNix and TB-PRACTECAL used Pretomanid, which is unavailable in the country, the results of the endTB and endTB.Q trials are awaited which use Bedaquiline, Linezolid and Delamanid in both Fluoroquinolones (FQ) susceptible and FQ

resistant respectively. The results of these two trials will further the evidence for regimens which include Delamanid.^{7,8}

While the WHO recommendations are rapidly evolving, national guidelines usually tend to lag behind creating a know-do gap specially in the context of management being done in the lines of NTP guidelines. The national guidelines in drug resistant tuberculosis management has not been updated since the end of 2019. The glaring need for change in guidelines is seen in the context of continued use of injectable Aminoglycosides in the 9-month regimen. In the context of the change in recommended regimens, it is imperative that new changes are incorporated in to the national guidelines at the earliest.

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