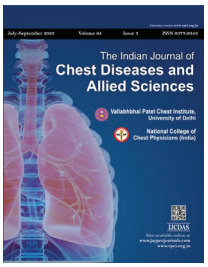
LETTER TO THE EDITOR

Evaluating Improved Success Rate of Newer 6–9-month Treatment Regimen under Conditional Access Program in Patients with Drug-resistant Tuberculosis



This article is available on www.vpci.org.in

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Received on: *27 September 2022;* Accepted on: *10 October 2022;* Published on: *05 December 2022*

Keywords: Multidrug-resistant tuberculosis, Research, Tuberculosis.
The Indian Journal of Chest Diseases and Allied Sciences (2022): 10.5005/jp-journals-11007-0053

Abbreviations used in this Article

TB = Tuberculosis; DR-TB = Drug-resistant tuberculosis; BPaL = Bedaquiline, pretomanid, and linezolid; CAP = Conditional access program; BDQ-CAP = Bedaquiline under conditional access program; aDSM = Active drug safety monitoring and management; BPaLM = BPaL in combination with moxifloxacin; MDR-TB = Multidrug resistant tuberculosis; RR/MDR-TB = Rifampicin resistant/Multidrug resistant tuberculosis.

We read with interest the editorial by Dr. D Behera entitled "To End Tuberculosis, India must Embrace Innovation: Lessons from the ZeNix Trial Results" in Volume 64, Issue 2 (April–June 2022) of *Indian Journal of Chest diseases and Allied Sciences*.[1]

Dr. D Behera has very aptly quoted that the COVID-19 pandemic has shown us how innovations, research adoption, and implementation of research have helped various countries including India to tackle this global COVID-19 pandemic effectively and very fast. However, in this process, control of tuberculosis (TB), globally as well as in India, suffered and there was a significant reduction in the notification rate and probably an increase in the mortality of TB in India.

As per the Global TB Report – 2021, globally 10.7 million people developed TB disease and about a quarter of the world's TB cases were reported from India in 2020. In India, almost 30% of the global drug-resistant tuberculosis (DR-TB) patients were reported in the same year.[2] To accomplish global goals, it is essential to address TB in India. As diagnostic networks expand and new TB medications become available, India had a chance to enhance the detection and successful results of DR-TB treatment. Hence it is very essential that we adopt the newer anti-TB drugs or new regimens which are being researched and tested globally. One of them as mentioned by Dr. Behera also is the bedaquiline, pretomanid, and linezolid (BPaL) regimen which has shown good results in different dosages and durations of linezolid in many trials including the ZeNix trial.[1]

Currently, to achieve TB elimination by 2025 in India, it is very essential that we use the current year 2022, and the coming year 2023 very effectively otherwise we are definitely going to miss the target. In India, modified BPaL is being tried for pre extensively drug-resistant TB (pre-XDR TB) patients under a multicentric study coordinated by NIRT, Chennai, across various sites spread all over the country. In case we wait for the study to be completed and the results to be published it will take at least 1–2 years or more and we might miss the bus by waiting for that period. So, it is suggested that we should do the mid-term analysis of this study, and compare the results with the results of other studies in this regard already done globally. In case they are matching, we should implement this regimen in a conditional access program (CAP) across the country in selected sites as was done with bedaquiline under a conditional access program (BDQ-CAP). The BDQ-CAP was launched at six sites across the country after providing extensive training and strengthening laboratory testing, pretreatment evaluation, active drug safety monitoring and management (aDSM), and follow-up systems. The interim analysis of a cohort of multi drug resistant tuberculosis (MDR-TB) cases of the 620 patients with MDR-TB from one of these sites showed that 513 (83%) patients had sputum culture conversion within 6 months, with the median time to culture conversion of 60 days with minimal and manageable adverse events.[3] The coordinated efforts led to a quick countrywide scale-up of BDQ and the shorter treatment regimen, despite concerns about the use of a new medicine with potentially major adverse drug responses. These encouraging outcomes assisted the national program in expanding the usage of bedaquiline and other new

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How to cite this article: Gupta A, Singla R. Evaluating Improved Success Rate of Newer 6–9-month Treatment Regimen under Conditional Access Program in Patients with Drug-resistant Tuberculosis. Indian J Chest Dis Allied Sci 2022;64(3):133–134.
Source of support: Nil
Conflict of interest: None

drugs such as delamanid across the country with good results. As also mentioned by Dr. Behera, it is reemphasized here that a regimen such as modified BPaL if found effective, could improve India's drug-resistant TB success rate, which at present is much lower than the average for the world and its contemporaries, varying between 36 and 46%.[1] The existing DR-TB therapies, which take 18–24 months and require follow-up throughout, are stretching the already overburdened healthcare system, especially in this era of the ongoing pandemic. A 6-month regimen might help streamline the delivery of DR-TB treatment drugs.

World Health Organization rapid communication in early May 2022 mentioned other shorter oral regimens for MDR-TB which have shown good results globally.[4] These include a new 6-month regimen based on BPaL in combination with moxifloxacin (BPaLM) based on to be written as such as they are trial names (TB-PRACTECAL) randomized clinical trial and the modified all-oral shorter regimens (6–9 months or 9–12 months) containing all three group A medicines based on NeXT trial. Even BPaLM may be considered for rifampicin resistant/multidrug resistant tuberculosis (RR/MDR-TB) patients by our national program to be tried in selected sites in India under the CAP in MDR-TB so that we can adopt it earlier and improve the results of MDR-TB treatment across the country.

To conclude, it is high time that we accelerate our efforts so that the menace of TB, especially DR-TB, can be tackled at a rate that our country needs. Information exchange about preliminary findings significantly improves the experience regarding newer treatment between and among countries. The gradual introduction of modified, shorter DR-TB regimens will allow for learning lessons and the resolution of problems. This modified model's application for national expansion may help to combat the threat of DR-TB.

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