Safety and Effectiveness of the BPaL Regimen: Preliminary Analysis of the First Multi-country Operational Research Cohort

V. Mirtskhulava,[1] S. Foraida,[2] E. Burhan,[3] J. Sugiharto,[4] B. Myrzaliev,[5] A. Toktogonova,[6] I. Flores,[7] D.R. Omanito,[8] N. Parpieva,[9] K. Safaev,[9] D. Van Luong,[10] N.B. Hoa,[10] The LIFT-TB Project Study Group

[1]KNCV TB Plus (former KNCV Tuberculosis Foundation), Division TB Elimination and Health System Innovations, The Hague, Netherlands, [2]TB Alliance, TB Alliance, New York, United States of America, [3]Persahabatan Central General Hospital, Persahabatan Central General Hospital, Jakarta, Indonesia, [4]Yayasan KNCV Indonesia, Yayasan KNCV Indonesia, Jakarta, Indonesia, [5]KNCV TB Plus (former KNCV Tuberculosis Foundation), Operations Devision, The Hague, Netherlands, [6]National Tuberculosis Center, Research, Bishkek, Kyrgyzstan, [7]Jose B. Lingad Medical Center, Jose B. Lingad Medical Center, San Fernando, Philippines, [8]Department of Health, Disease Prevention and Control Bureau, Manila, Philippines, [9]Republican Specialized Scientific-Practice Medical Centre of Phthisiology and Pulmonology, Republican Specialized Scientific-Practice Medical Centre of Phthisiology and Pulmonology, Tashkent, Uzbekistan, [10]Central Lung Hospital, Central Lung Hospital, Hanoi, Viet Nam

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Title

Scientific Research Abstract Text

Background: Individuals suffering from drug-resistant tuberculosis (DR-TB) have been subjected to ineffective, toxic treatment regimens for years. However, the TB Alliance's BPaL regimen, which comprises Bedaquiline, Pretomanid, and Linezolid, provides a highly effective, all-oral, six-month alternative. In June 2020, the World Health Organization (WHO) recommended using the BPaL1200 regimen under operational research (OR) conditions. Subsequently, in the updated guideline released in December 2022, the WHO recommends the programmatic scale-up of the BPaL600 regimen.

Design/Methods: Indonesia, Kyrgyzstan, the Philippines, Uzbekistan, and Viet Nam introduced the BPaL regimen under OR conditions. Between May 2021 and March 2023, 319 individuals with multidrug- or rifampicin-resistant (MDR/RR-) TB with treatment intolerance, non-response, or additional fluoroquinolones resistance (pre-XDR-TB) were enrolled in the OR. The findings of this multi-country OR will serve as essential supplementary evidence in establishing the safety and effectiveness of BPaL usage under programmatic conditions.

Results: The OR cohort had a median age of 40 years (IQR: 29-52), with 187 males (58.6%) out of the total. At baseline, 176 individuals (55.2%) were culture positive, and 158 individuals (89.8%) reported no growth in MGIT culture after one month of BPaL treatment. End-of-treatment outcomes were available for 146 individuals (45.8%) as of February 2023, and 138 individuals (94.5%) completed BPaL treatment successfully. Of these, 88 individuals (60.3%) reported adverse events of special interest that led to discontinuation or interruption of the full BPaL regimen or Linezolid only or permanent dose reduction of Linezolid in BPaL. Two individuals (1.4%) were classified as treatment failures due to BPaL discontinuation. Table 1 summarizes the effectiveness and safety of the BPaL regimen.

Table 1. The BPaL Regimen Effectiveness and Safety in the multi-country OR Cohort with End-of-treatment outcomes, N=146

End-of-treatment outcomes	**Number (%)**
Cured	95 (65.1%)
Treatment completed	43 (29.4%)
Treatment failed	3 (2.1%)
Lost to follow-up	1 (0.7%)
Died	4 (2.7%)
Treatment Success (Cured and Treatment completed)	138 (94.5%)
AESI leading to discontinuation or interruption of the full BPaL or Lzd only or permanent dose reduction of Lzd in BPaL	
Individuals with at least one AESI	88 (60.3%)
Individuals with more than one AESI	24 (16.4%)
Individuals with Peripheral neuropathy	45 (30.8%)
Individuals with Myelosuppression	35 (24.0%)
Individuals with Optic neuritis	7 (4.8%)
Individuals with QT prolongation	2 (1.4%)
Individuals with Hepatotoxicity	1 (0.7%)

AESI, Adverse Event of Special Interest; Lzd, Linezolid

Conclusions: The treatment success rate in this multi-country OR cohort is comparable to the Nix-TB, ZeNix, and TB PRACTECAL studies' treatment success rates. The BPaL regimen will be programmatically scaled-up to manage eligible individuals with pre-XDR-TB in these countries and beyond.

Summary

Summary: WHO recommends programmatic scaling-up of BPaL for pre-XDR-TB treatment. Operational Research in Indonesia, Kyrgyzstan, the Philippines, Uzbekistan, and Viet Nam will provide essential supplementary evidence in establishing the safety and effectiveness of BPaL usage under programmatic conditions.

Other Fields

Country of research: Indonesia, Kyrgyzstan, Philippines, Uzbekistan, Viet Nam

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