



Multidrug-resistant Tuberculosis Treatment Outcomes: High Success Rates of The BPaL Regimen Across Diverse Resistance Profiles In Indonesia

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Abstract

Background: Multidrug-resistant tuberculosis (MDR-TB) remains a public health challenge in Indonesia, with 29,600 annual cases and conventional regimens achieving only 59% success. The Bedaquiline-Pretomanid-Linezolid (BPaL) regimen, which is a six-month all-oral treatment endorsed by the World Health Organization (WHO), offers a potential solution. Yet, real-world evidence in high-burden settings is limited. This study aims to assess the clinical efficacy and safety of the BPaL regimen across MDR-TB profiles in Indonesia.

Method: This retrospective cohort study conducted at Persahabatan Hospital, Jakarta (2021–2024), included 84 patients receiving the BPaL regimen and diagnosed via GeneXpert MTB/RIF or culture. Differences in treatment outcomes based on drug-resistance profiles were assessed using Fisher's exact test. Exploratory comparisons with historical-control success rates were performed using two-sided exact binomial tests.

Results: Treatment success was achieved in 77.4% of all patients. Among patients with drug-resistance profiles, success rates were 84.2% for RR-TB, 75.0% for MDR-TB, and 75.0% for pre-XDR-TB, with no significant between-profile difference ($P=0.596$). Overall success was higher than the 59% historical-control benchmark ($P<0.001$). Adverse events occurred in 28.6% of patients, primarily peripheral neuropathy (17.9%) and anemia (10.7%). Sputum conversion was observed in 85.7% of patients by the third month of treatment.

Conclusion: The BPaL regimen was associated with a high observed treatment-success rate and an acceptable safety profile in this real-world cohort. RR-TB showed the highest success rate, although treatment success did not differ significantly with drug-resistance profiles. These findings support continued programmatic use and evaluation of BPaL in Indonesia.

Keywords: BPaL, efficacy, Indonesia, MDR-TB, safety

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB), defined by resistance to at least isoniazid and rifampicin, poses a significant barrier to tuberculosis (TB) control globally, with Indonesia reporting 29,600 cases among 1.08 million total TB cases in 2023.¹ Local data indicate complex resistance profiles, compounded by prior treatment failure and diagnostic delays, which exacerbate the MDR-TB burden.²

Historical data from the same setting indicated a treatment-success rate of 59% with conventional regimens.³ Long treatment duration, treatment-related adverse effects, and adherence challenges can contribute to suboptimal outcomes. Limited diagnostic access and other social determinants may further compromise treatment outcomes and TB-control efforts.⁴

The six-month all-oral bedaquiline–pretomanid–linezolid (BPaL) regimen represents an important treatment option for eligible patients with multidrug-resistant/rifampicin-resistant TB (MDR/RR-TB) and pre-extensively drug-resistant TB (pre-XDR-TB).^{5,6} Clinical trials, including Nix-TB and ZeNix, have reported favorable treatment outcomes of approximately 84–93%.^{5,7} However, evidence from routine programmatic settings remains comparatively limited. Evaluating BPaL effectiveness and safety under routine care in Indonesia is therefore important to inform programmatic implementation.

Therefore, this study was conducted to provide a real-world assessment of the

clinical effectiveness and safety of the BPaL regimen for drug-resistant TB in Indonesia.

METHOD

The study was approved by Persahabatan Hospital's Institutional Ethical Review Board (No: 0278/KEPK-RSUPP/12/2024, 31 December 2024), in accordance with the Declaration of Helsinki. This retrospective cohort study was conducted at Persahabatan Hospital, Jakarta, from 2021 to 2024, adhering to with WHO guidelines.⁶ Data were anonymized, and informed consent was waived due to the retrospective design.

Patients with confirmed drug-resistant TB diagnosed by GeneXpert MTB/RIF or culture-based drug susceptibility testing were included if they initiated BPaL between 2021 and 2024 and had sufficient clinical records for analysis. Of 100 screened patients, 84 met the inclusion criteria, with 16 with MDR-TB, 38 with RR-TB, and 28 with pre-XDR-TB. For two patients, the resistance-profile category was not documented; these patients were retained as unclassified/not documented rather than imputed. To mitigate selection bias, all consecutive patients meeting the inclusion criteria were enrolled. Missing data were addressed through multiple imputation where applicable.

Patients received BPaL per WHO recommendations, were treated with bedaquiline (400 mg daily for 2 weeks, then 200 mg thrice weekly), pretomanid (200 mg daily), and linezolid (600 mg daily) for six months.⁶ Adverse events,

particularly linezolid-related toxicities, were monitored monthly and managed with dose adjustments (e.g., linezolid reduced from 600 mg to 300 mg) or temporary interruptions.^{6,8}

Data from electronic medical records were extracted, including demographics (age, gender), clinical characteristics (drug resistance profile, comorbidities), adverse events, sputum conversion, and treatment outcome. Outcomes were classified as successful if they were WHO-classified cure or treatment completion, and all other outcomes as unsuccessful. This binary classification was used because the source table did not provide a complete, internally consistent disaggregation of all unsuccessful outcome categories.

Categorical variables were summarized as frequencies and percentages, and age was summarized as median and interquartile range. The association between treatment success and the drug-resistance profiles was assessed using Fisher's exact test because of small expected cell counts. Overall and profile-specific treatment-success proportions were compared exploratorily with historical-control benchmarks using two-sided exact binomial tests. Multivariable logistic regression was not performed because the number of unsuccessful outcomes and subgroup sizes were insufficient for a stable multivariable model without risk of overfitting.

Statistical significance was defined as a two-sided $P < 0.05$. Analyses were conducted using IBM SPSS Statistics v25.0 and Stata v17.0.

RESULT

The cohort included 84 patients with a median age of 41 years (interquartile range [IQR]=32–50) and 61.9% male. Resistance profiles comprised 19.0% of MDR-TB, 45.2% of RR-TB, and 33.3% of pre-XDR-TB cases.

Table 1. Baseline characteristics and treatment outcomes (n=84)

Characteristics	n	%
Age, years [median (IQR)]	41 (32-50)	
Gender		
Female	31	36.9
Male	53	63.1
Drug Resistance Profile		
MDR-TB	16	19.0
Pre-XDR-TB	28	33.3
RR-TB	38	45.2
Unclassified/not documented	2	2.5
Comorbidities		
HIV-Positive	12	14.3
Diabetes	18	21.4
No comorbid	54	64.3
Adverse Events		
Peripheral Neuropathy	15	17.9
Anaemia	9	10.7
No adverse event	60	71.4
Treatment Outcomes		
Successful (cured/completed)	65	77.4
Unsuccessful	19	22.6

Comorbidities were noted in 14.3% of HIV-positive patients and 21.4% of patients with diabetes. Meanwhile, adverse events were reported in 24 patients (28.6%), predominantly peripheral neuropathy (17.9%) and anaemia (10.7%). The adverse events were managed with dose reduction or temporary interruption when clinically indicated, without documented permanent discontinuation of the BPAL regimen.

Table 3. BPAL treatment success compared with historical-control benchmarks by drug-resistance profile

Drug Resistance Profile	Successful	Unsuccessful	Historical-control Benchmark ³	P
MDR-TB	12 (75.0%)	4 (25.0%)	59.0%	0.216
Pre-XDR-TB	21 (75.0%)	7 (25.0%)	50.0%	0.013*
RR-TB	32 (84.2%)	6 (15.8%)	67.0%	0.024*
Total	65 (77.4%)	19 (22.6%)	59.0%	<0.001*

Based on sputum conversion, 72 patients (85.7%) achieved conversion by month 3, indicating rapid bacteriological clearance (Figure 1).

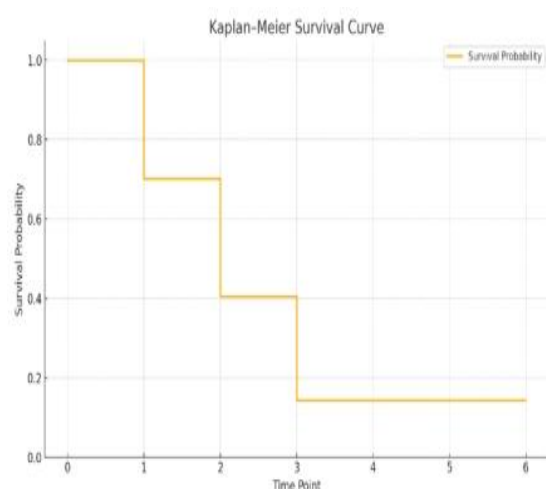


Figure 1. Kaplan-Meier curve illustrating time to sputum conversion among 84 patients treated with the BPAL regimen (85.7% achieved conversion by month 3).

Among the 82 patients with a drug-resistance profile, treatment success was 84.2% for RR-TB, 75.0% for MDR-TB and pre-XDR-TB, respectively, with not statistically significant ($P=0.596$), as shown in Table 2. Because of small subgroup sizes, no inferential claims were made for age, gender, HIV status, diabetes, or specific adverse events.

Table 2. Bivariate analysis of treatment success by documented drug-resistance profile

Drug Resistance	Successful	Unsuccessful	P
MDR-TB	12 (75.0%)	4 (25.0%)	0.596 ^a
Pre-XDR-TB	21 (75.0%)	7 (25.0%)	
RR-TB	32 (84.2%)	6 (15.8%)	

Note: ^aFisher's exact test

Overall, treatment success was achieved in 77.4% of all patients. Compared with historical-control success rates from the same setting, supplemented by WHO benchmarks, overall BPAL treatment success was higher (77.4% vs 59.0%; $P<0.001$). Profile-specific exploratory comparisons are shown in Table 3.³

DISCUSSION

The BPAL regimen achieved a 77.4% treatment-success rate in this cohort. In an exploratory comparison, this was higher than the 59% historical-control benchmark reported for conventional regimens in the companion analysis from the same setting ($P<0.001$).³ The observed success rate is directionally consistent with programmatic evidence from Thailand by Sangsayunh et al, with 82.1% favorable outcomes; the seven-country LIFT-TB initiative by Wares et al, with 90.9% interim treatment success; and Ukraine from a study by Dahl et al, with 86% treatment success.^{9–11} RR-TB had the highest success rate (84.2%), but the observed differences among RR-TB, MDR-TB, and pre-XDR-TB were not statistically significant ($P=0.596$).

The MDR-TB and pre-XDR-TB success rates in this cohort (both 75.0%) were lower than those reported in recent operational and programmatic cohorts,

including 98% treatment success in the Philippines by Flores et al and 95.3% for MDR/RR-TB and 90.4% for pre-XDR-TB in a prospective Belarus–Uzbekistan cohort by Sinha et al.^{12,13} Cross-study comparisons should be interpreted cautiously because of differences in eligibility criteria, regimen composition, patient characteristics, and programmatic conditions. The absence of a statistically significant between-profile difference in the present cohort indicates that resistance profile should not be interpreted as an independent determinant of treatment success from these data alone.

The lower observed success rate in this Indonesian cohort compared with Nix-TB and ZeNix may reflect differences in study design, patient heterogeneity, routine programmatic conditions, comorbidities, incomplete follow-up, and adverse-event-related dose modifications. Accordingly, the 77.4% rate should be interpreted as real-world programmatic effectiveness rather than a direct estimate of the intrinsic efficacy of the BPaL regimen.

The BPaL regimen demonstrated an acceptable safety profile, with 28.6% of patients experiencing adverse events, primarily peripheral neuropathy (17.9%) and anaemia (10.7%). These events were managed with dose adjustments or temporary interruptions, with no documented permanent discontinuation of the BPaL regimen in this cohort. This toxicity pattern is consistent with recognized linezolid-related adverse effects in drug-resistant TB treatment.^{5,8}

Of 14.3% HIV positivity and 21.4% diabetes was present in this cohort. However, the small subgroup sizes and limited number of unsuccessful outcomes did not support reliable inferential estimates of the association between these comorbidities and treatment success. Close clinical monitoring remains appropriate for patients with relevant comorbidities during BPaL treatment.⁶

The observed 77.4% treatment-success rate and 85.7% sputum conversion by month 3 support continued programmatic evaluation of BPaL in Indonesia.^{9,10} Although 85.7% of patients achieved sputum conversion by month 3, the remaining 14.3% were either censored or had no documented conversion during follow-up. These censored observations may include patients who were lost to follow-up, died, transferred to another facility, or had incomplete bacteriological documentation before conversion was confirmed. Thus, censored cases should not be interpreted solely as treatment failure.

Delayed or undocumented conversion nevertheless remains clinically relevant because it may reflect more severe disease, treatment interruption, comorbidities, or limitations in real-world follow-up. These findings underscore the importance of continued bacteriological monitoring and patient-retention measures during BPaL treatment. Because this study was not powered for subgroup analyses, it cannot establish whether HIV infection or diabetes modifies BPaL treatment success.

Global programmatic experience supports the feasibility of BPaL implementation across diverse settings.¹⁰ Integration should be accompanied by standardized adverse-event monitoring, patient-retention strategies, and access to rapid molecular diagnostics. Because BPaL-based regimens are incorporated into contemporary drug-resistant TB guidance, implementation efforts should focus on eligibility assessment, safe monitoring, and equitable access rather than interpreting the present single-center cohort as definitive comparative evidence.⁶

This study is limited by its single-center retrospective design, which may restrict generalizability. The tertiary-referral setting may not reflect district or rural services. The modest sample size (n=84), only 19 unsuccessful outcomes, and small subgroups limited the precision of comparative analyses and precluded a stable multivariable model. In addition, the submitted source table contained incomplete categorization for two resistance profiles and did not provide an internally consistent disaggregation of all unsuccessful outcomes; these were therefore reported conservatively without imputation.

CONCLUSION

The BPaL regimen was associated with a high observed treatment-success rate of 77.4% and an acceptable safety profile in this real-world cohort. RR-TB showed the highest numerical success rate (84.2%), although treatment success did

not differ significantly across documented resistance profiles. Sputum conversion by month 3 occurred in 85.7% of patients, and the principal adverse events were peripheral neuropathy and anaemia. The overall success rate was higher than the historical-control benchmark in an exploratory comparison, supporting continued programmatic use and evaluation of BPaL in Indonesia while emphasizing the need for larger multicenter studies and rigorous pharmacovigilance. Future multicenter studies with prospectively defined variables and complete outcome cross-tabulations are needed to validate these findings and permit robust multivariable modelling.

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