Review Article

Recent advancements in tuberculosis (TB) treatment regimens

Shyamala Ravikoti[1], Vikas Bhatia[2], Saykkulandai Kuppuswamy Mohanasundari[3]

[1]Department of Microbiology, AIIMS Bibinagar, Telangana, India, [2]Executive Director, Department of Community and Family Medicine, AIIMS, Bibinagar, Telangana, India, [3]College of Nursing, AIIMS, Bibinagar, Telangana, India

Abstract

Tuberculosis (TB) remains a global health challenge, with an estimated 10.6 million new cases and 1.3 million deaths in 2022. Recent years have seen a 3.9% increase in TB incidence, reversing prior declines. Drug-resistant TB poses significant hurdles, with multidrug-resistant (MDR) and rifampicin-resistant (RR) TB affecting 410,000 individuals, yet only 175,650 were diagnosed and treated. Advances in TB treatment include the World Health Organization's recommended 6-month BPaLM regimen (Bedaquiline, Pretomanid, Linezolid, Moxifloxacin), demonstrating 89% treatment success for MDR/RR-TB cases. Innovative diagnostics like molecular tests, IGRA, CAD for chest radiography, and new skin tests enhance detection accuracy. Vaccine development is promising, with 16 candidates in clinical trials. Emerging drugs and regimens aim to shorten treatment duration and improve outcomes. This article reviews recent advancements in TB treatment regimens, diagnostics, and vaccines, emphasizing the importance of these innovations in addressing drug-resistant TB and improving global TB control efforts.

Keywords: Antitubercular agent, bedaquiline, linezolid and moxifloxacin, multidrug-resistant, pretomanid, tuberculosis

Introduction

The global incidence rate of tuberculosis (TB) in 2022 was approximately 134 cases per 100,000 population, with an estimated 10.6 million new TB cases, including 5.8 million men, 3.5 million women, and 1.3 million children. People living with HIV accounted for 6.3% of the total. This represented a 3.9% increase in TB incidence between 2020 and 2022, reversing previous declines. TB caused an estimated 1.3 million deaths in 2022, including 167,000 among people with HIV.[1]

Address for correspondence: Dr. Saykkulandai Kuppuswamy Mohanasundari,
College of Nursing, AIIMS, Bibinagar, Telangana, India.
E-mail: roshinikrishitha@gmail.com

Received: 18-07-2024 **Revised:** 30-08-2024
Accepted: 16-09-2024 **Published:** 21-02-2025

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1237_24

Eight countries-India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, and the Democratic Republic of the Congo—accounted for over two-thirds of global TB cases. Despite substantial global efforts to save 75 million lives since 2000, a significant gap persists between estimated TB cases and those diagnosed, with around 3.1 million cases undiagnosed or unreported in 2022.[2]

Drug-resistant TB remains a significant challenge, with an estimated 410,000 people developing multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) in 2022. However, only about 175,650 were diagnosed and started on treatment. The treatment success rate for drug-resistant TB was 63% globally. Conventional regimens for MDR/RR-TB and XDR-TB involve prolonged treatment durations, high pill burdens, and the use of painful injectable medications, leading to poor adherence and treatment outcomes.[1]

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Ravikoti S, Bhatia V, Mohanasundari SK. Recent advancements in tuberculosis (TB) treatment regimens. J Family Med Prim Care 2025;14:521-5.

Recent advances in TB treatment regimens have focused on shorter, more effective, less toxic, and less burdensome options. Trials combining new drugs (bedaquiline, delamanid, and pretomanid) with repurposed ones (linezolid and moxifloxacin) have produced shorter, all-oral treatments. For example, the Nix-TB trial in South Africa demonstrated that a 6-month regimen of bedaquiline, pretomanid, and linezolid (BPaL) had a 90% success rate for MDR-TB and extensively drug-resistant TB (XDR-TB). However, high doses of linezolid in the trial caused significant side effects. The follow-up ZeNix trial found that a lower dose of linezolid was equally effective with fewer side effects.[2]

Médecins Sans Frontières sponsored several trials, including TB PRACTECAL, which showed that adding moxifloxacin (BPaLM) resulted in better cure rates (89%) and fewer side effects than the longer standard regimen (52%).[2] Other trials, like endTB, endTB-Q, and BEAT India, have also reported encouraging results, highlighting shorter and more effective treatments for MDR-TB and XDR-TB.[3] Additionally, 92 countries have adopted 9-month oral regimens for MDR/RR-TB. New WHO guidelines now include these shorter regimens based on recent trial data and recommended the new 6-month treatment regimen for individuals with MDR/RR-TB, this includes bedaquiline (B), pretomanid (Pa), linezolid (L), and moxifloxacin (M), collectively referred to as BPaLM [Table 1] and for those with pre-XDR-TB, the regimen can be used without moxifloxacin (BPaL).[2]

This article examines the latest advancements in TB management, highlighting innovative drug regimens that promise to enhance patient outcomes, reduce the burden of treatment, and address the growing threat of drug-resistant TB. This article briefly touches on the area of diagnostics, and vaccines for TB. By understanding these emerging drugs, healthcare professionals can better manage TB cases, particularly those involving drug-resistant strains, thus contributing to the global effort to control and eventually eradicate TB.

New Treatment Regimen for Drug-Resistant TB

Bedaquiline (B)

Bedaquiline (trade name B) is a medication primarily used in the treatment of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). Chemically known as (R)-6-bromo-2-methoxy-2,3-dihydroimidazo[2,1-b][1,3]thiazole-5-carboxylic acid methylamide, it belongs to the diarylquinoline class of compounds.[4] Bedaquiline works by inhibiting mycobacterial ATP synthase, crucial for energy production in Mycobacterium tuberculosis (M.TB), thereby exerting a bactericidal effect against resistant TB strains. After oral administration, Bedaquiline is slowly absorbed, reaching peak plasma concentrations within 5 hours. It undergoes hepatic metabolism primarily via CYP3A4 enzymes and is mainly excreted through feces. The drug has a long elimination half-life of approximately 5.5 months, allowing for less frequent dosing after an initial loading phase.[5] Resistance to Bedaquiline can develop through mutations in the atpE gene, which codes for the drug's target ATP synthase. Cross-resistance with similar drugs like TMC207 is possible.[6] Therefore, monitoring for resistance during treatment and using combination therapy with other anti-TB medications are recommended to minimize resistance development.[3]

Clinical trials have demonstrated Bedaquiline's efficacy in reducing time to sputum culture conversion and improving treatment outcomes in patients with MDR-TB and XDR-TB. Common side effects include QT prolongation (requiring ECG monitoring), hepatic dysfunction, arthralgia, and headache. It is generally

Table 1: Summary of BPaLM Regimen for drug resistant TB

Drug	Indication	Dose	Age Criteria	Duration of Course	Side Effects	Contraindications	Other Relevant Information
Bedaquiline (B)	MDR/ RR-TB and pre-XDR-TB	400 mg daily for 2 weeks, then 200 mg three times a week	Adults and adolescents aged 14 years and above	6 months	Nausea, headache, chest pain, increased liver enzymes, QT prolongation	Known hypersensitivity to Bedaquiline, severe hepatic impairment	Monitor ECG regularly due to the risk of QT prolongation; avoid use with other QT-prolonging drugs.
Pretomanid (Pa)	MDR/ RR-TB and pre-XDR-TB	200 mg daily	Adults and adolescents aged 14 years and above	6 months	Peripheral neuropathy, nausea, vomiting, liver enzyme elevations	Known hypersensitivity to Pretomanid, severe hepatic impairment	Limited safety data for children under 14 years, pregnancy, and breastfeeding.
Linezolid (L)	MDR/ RR-TB and pre-XDR-TB	600 mg daily	Adults and adolescents aged 14 years and above	6 months	Myelosuppression, peripheral neuropathy, optic neuropathy GI disturbances	Known hypersensitivity to linezolid, uncontrolled hypertension, MAOI use	Adjust dose if severe adverse events occur; monitor blood counts regularly.
Moxifloxacin (M)	MDR/ RR-TB	400 mg daily	Adults and adolescents aged 14 years and above	6 months	Nausea, diarrhea, QT prolongation, tendonitis, liver enzyme elevations	Known hypersensitivity to moxifloxacin, history of tendon disorders	Use with caution in patients with a history of QT prolongation or electrolyte imbalances

well-tolerated, but caution is advised in patients with pre-existing QT interval prolongation or electrolyte imbalances.[7] Approved by the FDA in 2012, Bedaquiline is indicated for use in adults and adolescents aged 14 years and older. The recommended dosing regimen starts with 400 mg once daily for 2 weeks, followed by 200 mg three times per week. It typically forms part of a 6-month treatment regimen for multidrug-resistant tuberculosis under specific treatment guidelines.[1,3]

Pretomanid (Pa)

Pretomanid (trade name Pa) is a medication used to treat multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). Chemically known as (S) -6-Nitro-2,3-dihydroimidazo[2,1-b][1,3]oxazole-5-carboxamide, it belongs to the nitroimidazole class of compounds. Pretomanid interferes with mycolic acid biosynthesis in Mycobacterium tuberculosis, disrupting cell wall integrity and leading to bacterial death.[8] After oral administration, Pretomanid is well-absorbed, with peak plasma concentrations achieved within 2–4 hours. It undergoes hepatic metabolism primarily via CYP1A2 and FMO3 enzymes, and is eliminated through urine and feces. The drug has a half-life of approximately 16–18 hours, allowing for once-daily dosing.[1,9] Resistance to Pretomanid can develop through mutations in genes involved in mycolic acid synthesis pathways, and cross-resistance with other nitroimidazoles may occur. Although resistance testing is not widely available, monitoring for treatment outcomes and relapse is crucial during therapy.[10]

Clinical trials, including the Nix-TB trial, have demonstrated Pretomanid's efficacy in treating MDR-TB and XDR-TB, particularly when used in combination with other anti-TB drugs such as Bedaquiline and Linezolid. Common side effects include peripheral neuropathy and hepatotoxicity. Due to limited safety data, Pretomanid is not recommended during pregnancy and breastfeeding.[11] Approved by the FDA in 2019, Pretomanid is indicated for adults and adolescents aged 14 years and older. The recommended dose is 200 mg once daily, typically as part of a 6-month treatment regimen like BPaL (Bedaquiline, Pretomanid, and Linezolid), following specific treatment guidelines for drug-resistant tuberculosis.[10]

Linezolid (L)

Linezolid (trade name L) is a vital medication employed in combating multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). Chemically known as (S)-N-[[3-[3-Fluoro-4-(morpholin-4-yl) phenyl]-2-oxooxazolidin-5-yl] methyl] acetamide, it belongs to the oxazolidinone class of antibiotics. Linezolid exerts its therapeutic effect by inhibiting bacterial protein synthesis, specifically binding to the 23S ribosomal RNA of the 50S subunit and disrupting the formation of the initiation complex.[12] Following oral administration, Linezolid is well-absorbed, achieving peak plasma concentrations within 1–2 hours. It undergoes hepatic metabolism primarily through oxidation and subsequent glucuronidation, with excretion mainly occurring via urine.[13] With a half-life of approximately 5–7 hours, Linezolid permits once-daily dosing, facilitating adherence to treatment regimens. Resistance to Linezolid may emerge due to mutations in the 23S rRNA gene or ribosomal proteins, potentially leading to reduced drug binding. Cross-resistance with other oxazolidinones is also possible, underscoring the importance of resistance testing and employing combination therapies to mitigate resistance risks effectively.[14]

Clinical trials have demonstrated Linezolid's efficacy when used in combination with drugs like Bedaquiline and Pretomanid, showing improvements in treatment outcomes, faster sputum culture conversion, and favorable clinical responses in patients with drug-resistant TB strains. However, its use is associated with common side effects such as myelosuppression (e.g. thrombocytopenia, anemia), neuropathy (particularly with prolonged use), and gastrointestinal disturbances, necessitating regular monitoring of blood counts during treatment.[11] Approved for use in adults and adolescents aged 14 years and above, Linezolid is typically prescribed at a dose of 600 mg once daily, with adjustments based on individual tolerability and renal function. It forms a critical component of 6-month treatment regimens tailored for managing MDR-TB and XDR-TB.[12]

Moxifloxacin (M)

Moxifloxacin, marketed under the trade name M, is an essential antibiotic used in the treatment of multidrug-resistant tuberculosis (MDR-TB), forming a crucial component of the BPaLM regimen. Structurally identified as 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b] pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, it belongs to the fluoroquinolone class of antibiotics. Moxifloxacin exerts its therapeutic effect by inhibiting bacterial DNA gyrase and topoisomerase IV, pivotal enzymes involved in DNA replication, repair, and recombination within Mycobacterium tuberculosis.[15] Upon oral administration, Moxifloxacin is well-absorbed, achieving peak plasma concentrations within 1–4 hours. It undergoes hepatic metabolism primarily through glucuronidation and sulfation processes, with subsequent elimination occurring predominantly via urine and feces. With a half-life of approximately 12 hours, Moxifloxacin supports convenient once-daily dosing, enhancing patient compliance during treatment.[16] Resistance to Moxifloxacin can develop due to mutations in genes encoding DNA gyrase or topoisomerase IV, potentially leading to reduced efficacy. Cross-resistance with other fluoroquinolones is also a concern, necessitating resistance testing to guide treatment strategies and advocating for combination therapy to mitigate resistance risks effectively.[17]

Clinical trials have validated Moxifloxacin's efficacy within the BPaLM regimen, alongside Bedaquiline, Pretomanid, and Linezolid, showcasing its role in improving treatment outcomes and shortening therapy durations for drug-resistant tuberculosis. However, caution is warranted regarding its use due to common

adverse effects such as QT prolongation (mandating ECG monitoring), gastrointestinal disturbances (e.g. nausea, vomiting, diarrhea), and potential central nervous system effects, especially in patients with a history of QT prolongation or tendon disorders.[18] Approved for use in adults and adolescents aged 14 years and above, Moxifloxacin is typically prescribed at a dose of 400 mg once daily for a duration of 6 months as part of comprehensive multidrug-resistant TB treatment protocols.[19]

However, the high costs of new drugs like Bedaquiline hinder their widespread use, especially in developing countries. There is also a risk of developing resistance to these new drugs, emphasizing the need for careful and responsible use.

Implementation Considerations of BPaLM Regimen

The BPaLM/BPaL regimen represents a significant advancement in treating multidrug-resistant tuberculosis (MDR-TB), but several critical considerations and limitations influence its clinical application. Firstly, the safety and efficacy of Pretomanid, a pivotal component of this regimen, have not been extensively studied in children under 14 years old, leading to restricted use in adults and adolescents aged 14 years and above until more data is available. Furthermore, limited safety data for Pretomanid in pregnant and breastfeeding women underscores the need for alternative treatment options with established safety profiles during pregnancy and lactation.[20,21]

Patients with a history of QT prolongation or electrolyte imbalances are at higher risk of developing QT interval prolongation when treated with medications like Moxifloxacin. Bedaquiline, and Moxifloxacin have been associated with QT prolongation—a condition that can potentially lead to serious cardiac arrhythmias. Regular monitoring of electrocardiograms (ECGs) is essential to detect any abnormalities early. Additionally, concurrent use of other medications known to prolong the QT interval should be avoided to mitigate the risk of adverse cardiac effects.[22]

Medications like Linezolid can cause severe adverse effects such as myelosuppression (reduced blood cell production). Regular monitoring of blood counts allows healthcare providers to detect and manage these adverse events promptly. Adjustments in medication dosage may be necessary based on individual patient responses to treatment to balance therapeutic efficacy with tolerability.[3,23]

Special caution is advised for patients with low CD4 counts (<100 cells/mm^3), (e.g., Person with HIV infection) as compromised immune function may impact tolerance and increase the risk of adverse effects of BPaLM/BPaL regimen, necessitating careful assessment and potentially additional monitoring or treatment adjustments.[1,24] Additionally, while effective for most forms of TB, the BPaLM/BPaL regimen is not recommended for severe cases such as extrapulmonary TB involving the central nervous system, osteoarticular TB, or disseminated (miliary) TB, highlighting the importance of precise diagnostic and treatment planning tailored to the specific clinical presentation of each TB case.[25] These considerations collectively guide healthcare providers in optimizing treatment outcomes while navigating the complexities and limitations associated with the BPaLM/BPaL regimen in managing challenging forms of tuberculosis.

Advancements in Tuberculosis Diagnostics, Vaccines, and Therapeutics

According to WHO Global Tuberculosis Report-2023 in recent advancements, the tuberculosis (TB) diagnostic pipeline has expanded significantly, featuring molecular tests for disease and drug resistance, interferon-gamma release assays (IGRA) for infection detection, biomarker-based assays, computer-aided detection (CAD) for digital chest radiography TB screening, and new aerosol-capture technologies. WHO endorsed three M.TB. antigen-based skin tests in 2022, improving specificity over tuberculin tests. Targeted next-generation sequencing for drug-resistant TB from sputum was recommended for enhanced drug susceptibility testing. By August 2023, 16 vaccine candidates were in clinical trials, targeting TB prevention and treatment enhancement. Additionally, 28 drugs were in various trial phases, including new entities and repurposed options, with ongoing trials focusing on TB preventive treatment regimens and delivery models.[2]

Conclusion

The BPaLM/BPaL regimen has shown high efficacy in treating drug-resistant TB, with an 89% success rate for MDR/RR-TB cases. However, safety concerns, especially for vulnerable populations such as children and pregnant women, necessitate cautious implementation and monitoring. The expanded diagnostic pipeline, including molecular tests, IGRA assays, CAD, and aerosol-capture technologies, enhances detection and drug susceptibility testing. Ongoing clinical trials for new vaccines and drug candidates offer hope for better preventive and therapeutic options. Addressing these challenges through rigorous safety protocols, patient monitoring, and tailored treatment strategies is crucial for optimizing TB control efforts and improving global health outcomes.

Acknowledgement

AIIMS Bibinagar Supportive system.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ignatius EH, Dooley KE. New drugs for the treatment of tuberculosis. Clin Chest Med 2019;40:811-27.
2. World Health Organization (WHO). Global tuberculosis report 2023. [Updated on 27 Nov 2023]. Available form: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023. [Last accessed on 2024 Jul 15].
3. Udwadia ZF, Patel JM. New treatments for drug resistant TB: Past imperfect, future bright. Lung India 2023;40:1-3.
4. Pym AS, Diacon AH, Tang SJ, Conradie F, Danilovits M, Chuchottaworn C, *et al.*; TMC207-C209 Study Group. Bedaquiline in the treatment of multidrug- and extensively drug-resistant tuberculosis. Eur Respir J 2016;47:564-74.
5. Field SK. Bedaquiline for the treatment of multidrug-resistant tuberculosis: Great promise or disappointment? Ther Adv Chronic Dis 2015;6:170-84.
6. Deshkar AT, Shirure PA. Bedaquiline: A novel diarylquinoline for multidrug-resistant pulmonary tuberculosis. Cureus 2022;14:e28519.
7. Deoghare S. Bedaquiline: A new drug approved for treatment of multidrug-resistant tuberculosis. Indian J Pharmacol 2013;45:536-7.
8. PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 456199, Pretomanid. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Pretomanid. [Last accessed on 2024 Jul 15].
9. Ignatius EH, Abdelwahab MT, Hendricks B, Gupte N, Narunsky K, Wiesner L, *et al.* Pretomanid pharmacokinetics in the presence of rifamycins: Interim results from a randomized trial among patients with tuberculosis. Antimicrob Agents Chemother 2021;65:e01196-20.
10. Stancil SL, Mirzayev F, Abdel-Rahman SM. Profiling pretomanid as a therapeutic option for TB infection: Evidence to date. Drug Des Devel Ther 2021;15:2815-30.
11. Solans BP, Imperial MZ, Olugbosi M, Savic RM. Analysis of dynamic efficacy endpoints of the Nix-TB trial. Clin Infect Dis 2023;76:1903-10.
12. Singh B, Cocker D, Ryan H, Sloan DJ. Linezolid for drug-resistant pulmonary tuberculosis. Cochrane Database Syst Rev 2019;3:CD012836.
13. Schecter GF, Scott C, True L, Raftery A, Flood J, Mase S. Linezolid in the treatment of multidrug-resistant tuberculosis. Clin Infect Dis 2010;50:49-55.
14. Long KS, Vester B. Resistance to linezolid caused by modifications at its binding site on the ribosome. Antimicrob Agents Chemother 2012;56:603-12.
15. Naidoo A, Naidoo K, McIlleron H, Essack S, Padayatchi N. A review of moxifloxacin for the treatment of drug-susceptible tuberculosis. J Clin Pharmacol 2017;57:1369-86.
16. Moise PA, Birmingham MC, Schentag JJ. Pharmacokinetics and metabolism of moxifloxacin. Drugs Today (Barc) 2000;36:229-44.
17. Xia H, Zheng Y, Liu D, Wang S, He W, Zhao B, *et al.* Strong increase in moxifloxacin resistance rate among multidrug-resistant mycobacterium tuberculosis isolates in China, 2007 to 2013. Microbiol Spectr 2021;9:e0040921.
18. Cevik M, Thompson LC, Upton C, Rolla VC, Malahleha M, Mmbaga B, *et al.*; SimpliciTB Consortium. Bedaquiline-pretomanid-moxifloxacin-pyrazinamide for drug-sensitive and drug-resistant pulmonary tuberculosis treatment: A phase 2c, open-label, multicentre, partially randomised controlled trial. Lancet Infect Dis 2024;24:1003-14.
19. Radtke KK, Hesseling AC, Winckler JL, Draper HR, Solans BP, Thee S, *et al.* Moxifloxacin pharmacokinetics, cardiac safety, and dosing for the treatment of rifampicin-resistant tuberculosis in children. Clin Infect Dis 2022;74:1372-81.
20. Ali MZ, Dutt TS, MacNeill A, Walz A, Pearce C, Lam H, *et al.* A Modified BPaL Regimen for Tuberculosis Treatment replaces Linezolid with Inhaled Spectinamides. bioRxiv [Preprint]. 2024 Jun 11:2023.11.16.567434. doi: 10.1101/2023.11.16.567434.
21. Haley CA, Schechter MC, Ashkin D, Peloquin CA, Peter Cegielski J, Andrino BB, *et al.*; BPaL Implementation Group. Implementation of bedaquiline, pretomanid, and linezolid in the united states: experience using a novel all-oral treatment regimen for treatment of rifampin-resistant or rifampin-intolerant tuberculosis disease. Clin Infect Dis 2023;77:1053-62.
22. Dooley KE, Rosenkranz SL, Conradie F, Moran L, Hafner R, von Groote-Bidlingmaier F, *et al.*; AIDS Clinical Trials Group (ACTG) A5343 DELIBERATE Study Team. QT effects of bedaquiline, delamanid, or both in patients with rifampicin-resistant tuberculosis: A phase 2, open-label, randomised, controlled trial. Lancet Infect Dis 2021;21:975-83.
23. Li MM, Shen WC, Li YJ, Teng J. Linezolid-induced pancytopenia in patients using dapagliflozin: A case series. Infect Drug Resist 2022;15:5509-17.
24. Onyebujoh PC, Ribeiro I, Whalen CC. Treatment options for HIV-associated tuberculosis. J Infect Dis 2007;196(Suppl 1):S35-45.
25. Nyang'wa BT, Berry C, Kazounis E, Motta I, Parpieva N, Tigay Z, *et al.* A 24-week, all-oral regimen for rifampin-resistant tuberculosis. N Engl J Med 2022;387:2331-43.