VIEWPOINT

A Miracle Drug for Tuberculosis: Bedaquiline

Subakeerthi Venkataramanan[1], Renuka Kandasamy[2]

Abstract

A new tuberculosis (TB) medication includes the active ingredient bedaquiline. Sirturo is a brand name for a drug that belongs to the diarylquinoline class of drugs. Bedaquiline is a diarylquinoline antimycobacterial drug that works by blocking an enzyme within the bacteria that cause TB. It prevents the proton pump of mycobacterial adenosine 5′-triphosphate (ATP) synthase. Bedaquiline is metabolized in hepatic form and eliminated in the feces. Bedaquiline is effective and safe in treating multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) patients. This drug treatment regimen was well supported and tended to a good result in this clinically relevant patient associated with MDR-TB.

Keywords: Bedaquiline, Diarylquinolines, Extensively drug-resistant tuberculosis, Multidrug-resistant tuberculosis, Mycobacterial adenosine 5′-triphosphate synthase.

Pondicherry Journal of Nursing (2021): 10.5005/jp-journals-10084-12174

Introduction

Tuberculosis (TB) is characterized by associate degree infectious microorganism sickness by the expansion of nodules (tubercles) within the respiratory organ tissues.[1] Tuberculosis is one of the top 10 causes of death worldwide, as well as the leading cause of death from a single infectious agent. According to figures, 10 million people worldwide contracted TB in 2019. There were 5.6 million men, 3.2 million women, and 1.2 million children affected in total. There were cases in all age groups and from all over the world. The global incidence of TB is decreasing at a rate of about 2% per year. To reach the top TB Strategy's 2020 milestones, this needs to accelerate to a 4–5% annual decline. One of the health priorities of the Sustainable Development Goals is to end the TB epidemic by 2030.[2]

Tuberculosis–An Overview

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* (MTB) bacteria strains. The disease typically affects the lungs and additionally affects alternative components of the body.[3] Most affected patients have no signs of TB, which is referred to as latent TB. Around 10% of latent infections progress to active disease, which kills about half of those who are infected if they are not treated. A persistent cough with the blood-containing mucus secretion, night sweats, weight loss, and fever are all common symptoms of active TB. When people with active TB in their lungs cough, spit, talk, or sneeze, it passes through the air to the next person. A limited number of people are at high risk, including household, workplace, and social connections with people with active TB.[4]

Chest X-rays, as well as microscopic examination and culture of body fluids for active cases of TB and tuberculin skin test (TST) or blood tests for latent cases of TB, are used to diagnose TB. Prevention of TB involves vaccination with the bacillus Calmette–Guérin (BCG) vaccine, screening for those at high risk, and early identification and treatment of cases. Antibiotic resistance is becoming more of a concern, as rates of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) increase (XDR-TB). The use of several antibiotics over a long period is needed for treatment.[5]

[1]Department of Community Health Nursing, Kasturba Gandhi Nursing College, Puducherry, India

[2]Department of Medical Surgical Nursing, Kasturba Gandhi Nursing College, Puducherry, India

Corresponding Author: Subakeerthi Venkataramanan, Department of Community Health Nursing, Kasturba Gandhi Nursing College, Puducherry, India, Phone: +91 9841726659, e-mail: subakeerthiv@kgnc.ac.in

How to cite this article: Venkataramanan S, Kandasamy R. A Miracle Drug for Tuberculosis: Bedaquiline. Pon J Nurs 2021;14(1):23–24.

Source of support: Nil

Conflict of interest: None

A Miracle Drug for Tuberculosis–Bedaquiline

A new TB treatment contains the active ingredient bedaquiline. Sirturo is a brand name for a drug that belongs to the diarylquinoline class of drugs.[6]

Clinical Pharmacology

Mechanism of Action

Bedaquiline is a diarylquinoline antimycobacterial drug that works by blocking an enzyme within the bacteria that causes TB. It prevents the proton pump of mycobacterial adenosine 5′-triphosphate (ATP) synthase. Enzymes are molecules that speed up chemical reactions in the body, and they are crucial for MTB to generate energy. The death of microorganisms is caused by bedaquiline.[6,7]

Pharmacodynamics

Bedaquiline, in particular, undergoes oxidative metabolism, yielding the *N*-monodesmethyl metabolite (M2), which inhibits mycobacterial TB at the lowest inhibitory level.[6,7]

Pharmacokinetics

Following single doses of between 10 mg and 700 mg in healthy individuals and multiple doses of between 25 mg and 400 mg once daily in patients with drug-susceptible TB or MDR-TB, bedaquiline

rises proportionally with the oral dose administered, and it reaches its maximum plasma concentration once administration, irrespective of the dose.[6,7]

Metabolism

The hepatic form of bedaquiline is metabolized. Bedaquiline was metabolized into the N-monodesmethyl metabolite, which was a major issue for the CYP3A4 enzyme (M2). This material is 4 to 6 times less active in terms of antimycobacterial activity.[6,7]

Route of Elimination

The main form of elimination in the feces.[6,7]

Recommended Dosing

Dosage: Four 100 mg tablets once a day for 2 weeks (2:400 mg).

For 2–4 weeks, two 100 mg tablets 3 days a week (24:600 mg).

Bedaquiline is usually given at the prescribed dosage and duration. The medication's 6-month (26 weeks) dosing schedule, as well as week 26 (the start of month 7) to the end of treatment: only second-line anti-TB drugs should be used, according to WHO guidelines. In this stage of treatment, bedaquiline is not used.[6]

Important Precautions and Interactions

Bedaquiline can also be administered for pregnant women, children, HIV-infected persons, persons with extrapulmonary TB, and persons with comorbid conditions on concomitant medications. It is impossible to have an appropriate care regimen if they are not taken. A clinical trial is needed before bedaquiline is administered to these population groups.[8]

Drug–Drug Interactions

Inducers and Inhibitors of CYP3A4

Since it depends on drug exposure, bedaquiline is decreased when co-administered with CYP3A4 inducers and increased when co-administered with CYP3A4 inhibitors.

Inducers of CYP3A4

The therapeutic effect of bedaquiline can be reduced by co-administration of extreme CYP3A4 inducers such as rifamycin (i.e., rifampin, rifapentine, and rifabutin) or moderate CYP3A4 inducers with SIRTURO due to the decrease in systemic exposure.

Inhibitors of the CYP3A4 Enzyme

Extended co-administration of bedaquiline, powerful CYP3A4 inhibitors, and increased systemic exposure (ketoconazole or itraconazole) for >14 days should be avoided unless the benefit outweighs the risk. SIRTURO-related adverse reactions need close clinical supervision.

Other Antimicrobial Medications

During co-administration with SIRTURO, there is no need to change the dosage of isoniazid or pyrazinamide.[7,8]

About the Bedaquiline Clinical Trial

A randomized trial, placebo-controlled, double-blind was used to assess the efficacy of bedaquiline. A study of newly diagnosed pulmonary MDR MTB patients with sputum smear positivity. For the treatment of MDR-TB, both patients were given a combination of five additional antimycobacterial drugs for a total of 12 months after the first reported negative culture or at least 18–24 months. The samples were randomized to receive 24 weeks of therapy, which included SIRTURO 400 mg once daily for 2 weeks, followed by SIRTURO 200 mg three times a week for 22 weeks. In the same analysis, a placebo was given for the same period. A total of 81 patients were randomized to the placebo arm and 79 to the SIRTURO arm in this clinical trial. Finally, a 120-week assessment was completed.

Sixty-six and 67 randomized patients with placebo and SIRTURO had either reported MDR-TB based on susceptibility tests (pre-randomized) or no susceptibility findings were accessible in their medical history, and the efficacy analyzes also included. In this study, 63% of the participants were male, with a median age of 34 years, 35% of them were black, and 15% of them were HIV-positive (median CD4 cell count 468 cells/L). They had cavitation in both lungs in 18% of the cases, and cavitation in one lung in 62% of the cases.

During therapy, the conversion period to sputum culture was also obtained at least 25 days apart. The median time to culture for the SIRTURO treatment group was 83 days, compared to 125 days for the placebo treatment group. In this study, the SIRTURO® treatment group had a shorter time for culture conversion and higher culture conversion rates at week 24 compared to the placebo treatment group.[9,10]

Conclusion

Bedaquiline is effective and safe in treating MDR-TB and XDR-TB patients. It incorporates treatment regimens that succeed high conversion and success rates under different field trial conditions. This drug treatment regimen was well supported and tend to a good result in this clinically relevant patient associate with MDR-TB.

References

1. Basic TB Facts | TB | CDC. 27 Mar. 2020 https://www.cdc.gov/tb/topic/basics/default.htm.
2. Global Tuberculosis Report https://www.who.int/teams/global-tuberculosis-programme/tb-reports.
3. Tuberculosis. Wikipedia, https://en.wikipedia.org/w/index.php?title=Tuberculosis&oldid=1009354709.
4. Jakeman B, Gross B, Fortune D, Babb S, Tinker D, Bachyrycz A. Evaluation of a pharmacist-performed tuberculosis testing initiative in New Mexico. J Am Pharmac Assoc 2015;55(3):307–312.
5. Steingart KR, Flores LL, Dendukuri N, Schiller I, Laal S, Ramsay A, et al. Commercial serological tests for the diagnosis of active pulmonary and extrapulmonary tuberculosis: an updated systematic review and meta-analysis. PLoS Med 2011;8(8):e1001062.
6. "Sirturo (Bedaquiline Tablets): Uses, Dosage, Side Effects, Interactions, Warning." *RxList,* https://www.rxlist.com/sirturo-drug.htm.020.
7. Alberto M, Anna CC, Kelly DE, Afranio K. The first compound of a new class of potent anti-tuberculosis drugs. Chem Future Microbiol 2010;5:849–858.
8. Koul A, Dendouga N, Vergauwen K, Molenberghs B, Vranckx L, Willebrords R, et al. Diarylquinolines target subunit c of mycobacterial ATP synthase. Nat Chem Biol 2007;3(6):323–324.
9. Charan J, Reljic T, Kumar A. Bedaquiline versus placebo for management of multiple drug-resistant tuberculosis: a systematic review. Indian J Pharmacol 2016;48(2):186.
10. Van Heeswijk RP, Dannemann B, Hoetelmans RM. Bedaquiline: a review of human pharmacokinetics and drug–drug interactions. J Antimicrob Chemother 2014;69(9):2310–2318.