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REVIEW

Therapeutic strategies in multidrug-resistant pulmonary tuberculosis: impact of bedaquiline as a pharmacological innovation

Estrategias terapéuticas en la tuberculosis pulmonar multirresistente: impacto de la bedaquilina como innovación farmacológica

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ABSTRACT

MDR-TB is a considerable challenge for global public health given the growing resistance to conventional drugs. This article evaluates the efficacy and safety of bedaquiline, an inhibitor of Mycobacterium tuberculosis ATP synthase, in the pharmacotherapy of multidrug-resistant pulmonary tuberculosis. Using the PRISMA method, 20 investigations from international data were selected with the objective of evaluating therapeutic efficacy, adverse effects and clinical improvement in patients undergoing treatments with regimens that incorporate bedaquiline. The findings indicate that these interventions achieve success rates exceeding 80 %, with accelerated bacteriological conversion during the first weeks of treatment. Although adverse effects such as QTc interval prolongation, hepatotoxicity, peripheral neuropathy, myelosuppression, and hematologic toxicity were documented, these were manageable with appropriate follow-up. The article concludes that bedaquiline constitutes an essential progress in the treatment of MDR-TB, although its high cost and monitoring restrict its accessibility.

Keywords: MDR-TB; Bedaquiline; Therapeutic Efficacy; Adverse Effects and Clinical Improvement.

RESUMEN

La TB - MDR es un reto considerable para la salud pública mundial dado por la creciente resistencia a los fármacos convencionales. Este artículo evalúa la eficacia y seguridad de la bedaquilina, un inhibidor de la ATP sintasa del *Mycobacterium tuberculosis*, en la farmacoterapia de la tuberculosis pulmonar multidrogorresistente. Mediante el empleo del método PRISMA, se seleccionaron 20 investigaciones procedentes de datos internacionales con el objetivo de evaluar la eficacia terapéutica, efectos adversos y mejora clínica en los pacientes sometidos a tratamientos con esquemas que incorporan la bedaquilina. Los hallazgos indican que estas intervenciones logran tasas de éxito que superan el 80 %, con una conversión bacteriológica acelerada durante las primeras semanas del tratamiento. A pesar de que se documentaron efectos adversos como la prolongación del intervalo QTc, hepatotoxicidad, neuropatía periférica, mielosupresión y toxicidad hematológica, estos fueron gestionables mediante un seguimiento apropiado. El artículo concluye que la bedaquilina constituye un progreso esencial en el tratamiento de la TB - MDR, aunque su elevado costo y la monitorización restringen su accesibilidad.

Palabras clave: TB - MDR; Bedaquilina; Eficacia Terapéutica; Efectos Adversos y Mejora Clínica.

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INTRODUCTION

Multidrug-resistant tuberculosis caused by strains of Mycobacterium tuberculosis remains one of the most significant challenges in public health, complicating healthcare prevention strategies where rifampicin and isoniazid, two of the first-line anti-tuberculosis drugs, compromise their effectiveness and synergy in the fight against this infection, making its management increasingly complex.[1,2,3,4,5,6]

According to global estimates, in 2024, 410 000 people contracted multidrug-resistant or rifampicin-resistant tuberculosis. Although the therapeutic efficacy rate has shown sustained improvement (50 % in 2012, 60 % in 2019, and 63 % in 2020), these figures still reflect a considerable challenge.[2,7,8,9,10]

In 2019, Argentina recorded 325 cases of drug-resistant tuberculosis, 73,5 % of which were new cases, while the rest had received previous treatment. Of these, 140 cases of multidrug resistance (43,5 %) and 7 cases of extensively drug-resistant tuberculosis (3 %) were reported.[3,11,12,13,14] On the other hand, in 2021, in the central jungle of Peru, a high rate of TB (134 cases) was reported, mainly in patients who had previously received treatment (rate of 4,71 per 100 000 inhabitants) than in those undergoing initial treatment (rate of 3,61 per 100 000 inhabitants), thus evidencing therapeutic failure in 58,97 % of cases.[4,15,16,17,18,19]

Given this situation, the study focuses on analyzing the efficacy and safety of bedaquiline in the treatment of multidrug-resistant tuberculosis. Bedaquiline is an ATP synthase inhibitor of Mycobacterium tuberculosis. This potent bactericidal agent avoids the need for continuous use of injectable drugs, offering safer and more effective oral treatments. These findings could have a significant impact on the development of therapeutic strategies, as well as occupational and public health standards and guidelines.[5,6,19,20,21,22,23]

In this context, the question arises: How effective and safe is bedaquiline as a treatment strategy for multidrug-resistant pulmonary tuberculosis?[24,25,26,27,28] This led to the primary objective of this study: to determine the therapeutic efficacy,[29,30,31] adverse effects, and clinical improvement of patients with multidrug-resistant pulmonary tuberculosis who received the drug "Bedaquiline" as part of their therapeutic regimen, considering the most up-to-date scientific evidence to strengthen initiatives against antimicrobial resistance.[32,33,34,35,36,37,38]

METHOD

The research was conducted using the PRISMA methodology to analyze reviews that assess the efficacy, effect, and clinical improvement of bedaquiline in the treatment of multidrug-resistant tuberculosis. This approach was based on a structured strategy, informed by the investigation, selection, and examination of relevant scientific literature.

Four database systems were selected: "Scopus," "PubMed," "Web of Science," and "Europe PMC," recognized for their excellence and accessibility in the field of medical research. These were subjected to a search strategy focused on key terms combined with the Boolean operator "AND," which facilitated the generation of equations that optimized the results obtained. The terminology used included: "tuberculosis AND pulmonary AND multidrug-resistant AND bedaquiline AND treatment AND efficacy," which facilitated the identification of a total of 1394 articles, specifically 116 in Scopus, 91 in PubMed, 72 in Web of Science, and 1115 in Europe PMC.

The inclusion criteria applied in the study included publications made between 2020 and 2024, available in free full text, and classified as clinical trials, to ensure the relevance and usefulness of the selected research; on the other hand, duplicate research and research that did not align with the study objective or whose content did not comply with the proposed analytical approach were discarded.

A total of 1394 publications were identified, of which 116 were from Scopus, 91 from PubMed, 72 from Web of Science, and 1115 from Europe PMC. Then, 535 publications were excluded because they were outside the analysis period, distributed among 62 publications from Scopus, 51 from PubMed, 35 from Web of Science, and 711 from Europe PMC, leaving a total of 859 valid publications.

Three hundred sixty-eight publications were excluded in the next phase due to a lack of full text or failure to meet the document's criteria. Subsequently, 491 publications were selected for more detailed evaluation, excluding 414 articles from Europe PMC, seven from PubMed, 28 from Scopus, and 22 from Web of Science. Ultimately, 20 studies were relevant for the review after excluding 471 publications due to duplication or thematic inconsistency. The final distribution of the included studies consisted of 7 studies from Scopus, seven from PubMed, two from Web of Science, and four from Europe PMC.

This selection phase ensured the relevance and scientific excellence of the studies included in the review through a comprehensive evaluation of the identified articles, in which the information collected was organized into essential categories: therapeutic efficacy, adverse effects, and profile of patients treated with bedaquiline, performing a qualitative synthesis of the data to identify trends and patterns using computer tools.

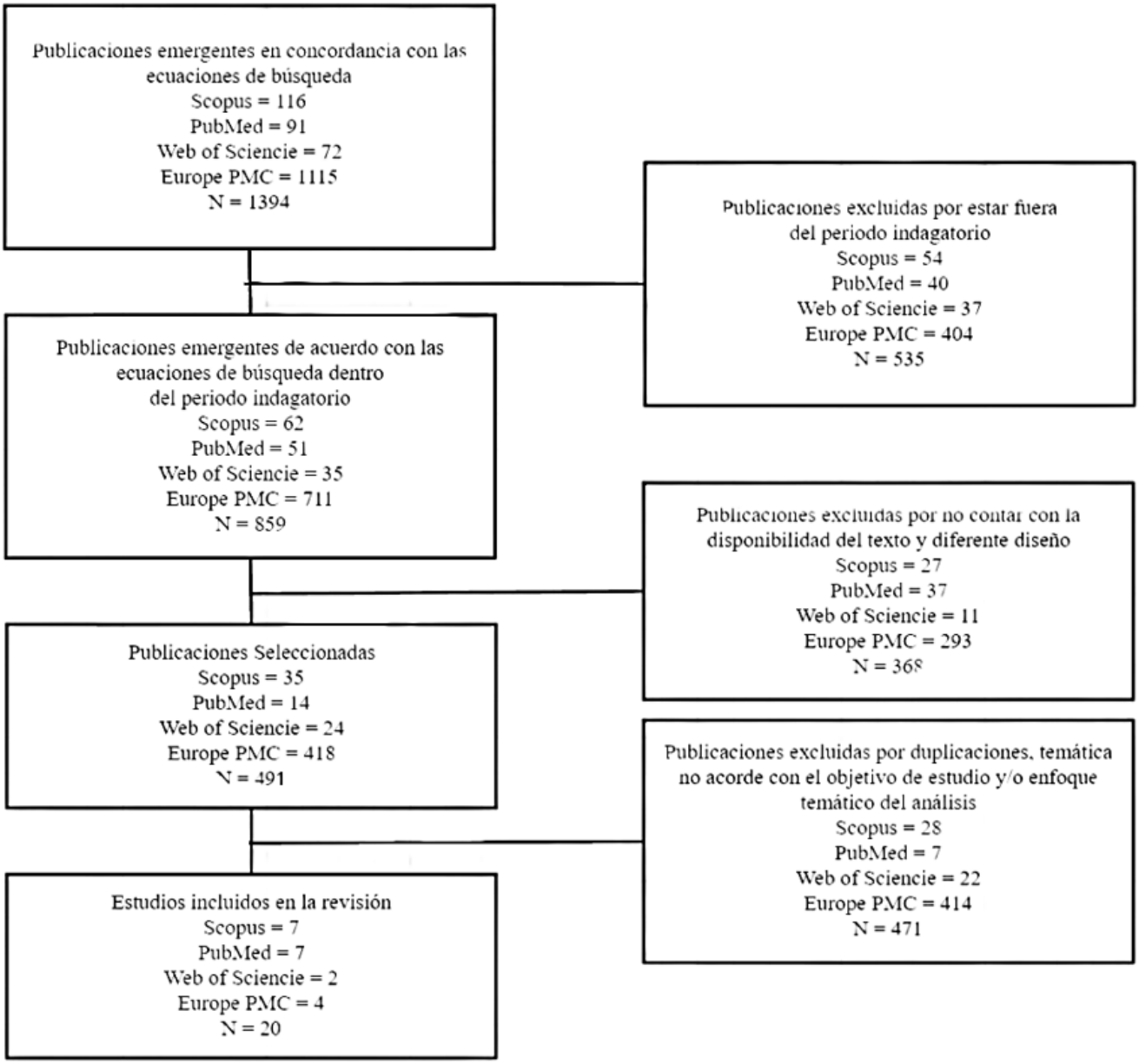

Figure 1. PRISMA flow chart of the systematization process

RESULTS AND DISCUSSION

In the context of the systematic review, a synthesis matrix was developed to structure the key findings from the selected studies. This procedure, implemented in accordance with the PRISMA methodology guidelines, involved the systematization of 1394 initial articles identified in Scopus, PubMed, Web of Science, and Europe PMC. Subsequently, by following the criteria outlined in the "Materials and Methods" section, 20 studies were selected and subjected to critical analysis to ensure their consistency with the study's objectives.

Multidrug-resistant pulmonary tuberculosis represents a significant global challenge due to the limited efficacy and serious side effects associated with conventional treatments. In this context, bedaquiline, an ATP synthase inhibitor of Mycobacterium tuberculosis, has emerged as a key therapeutic advance, with growing evidence supporting its efficacy and safety in various populations and therapeutic regimens. This has been demonstrated in several studies, which have shown superior bacteriological conversion rates and a significant reduction in mortality, thereby consolidating bedaquiline as a pillar in the treatment of multidrug-resistant pulmonary tuberculosis.[7,8]

This is evident in the results achieved in Chinese pediatric populations, where regimens containing bedaquiline exhibited a significantly higher cure rate ($p = 0,03$), revealing a significant decrease in the mean time to sputum culture conversion. Although the incidence of adverse effects was lower in the control group, these data indicate that bedaquiline is better tolerated in the pediatric population, reaffirming its usefulness in this susceptible population.[8]

Table 1. Synthesis Matrix

No.	Author(s)	Year	Title	Country of Publication	Population	Intervention	Main Results	DOI
1	Song Y, Shu W, Pei Y, et al	2024	Nine months of bedaquiline, linezolid, levofloxacin, clofazimine, and cycloserine chemotherapy for rifampicin/multidrug-resistant tuberculosis: a multicenter, randomized, open-label non-inferiority trial in China	United Kingdom	264 participants randomly assigned and 231 included in the final analysis (116 for the standard regimen and 115 for the short regimen)	Short 9-month regimen based on bedaquiline, linezolid, levofloxacin, clofazimine, and cycloserine, and standard 18-month regimen based on 6 months of the short regimen followed by 12 months of levofloxacin and three potentially active drugs among clofazimine, cycloserine, pyrazinamide, ethambutol, and protionamide	83,5 % achieved therapeutic efficacy on the short regimen and 77,6 % on the standard regimen in combination with bedaquiline, resulting in QTc prolongation, hematological events, and liver disorders	10.1186/s12916-024-03633-3
2	Martínez J, Aznar M, Zacarías A, et al	2024	A non-randomized pragmatic historically controlled trial evaluating the effectiveness and safety of a bedaquiline or a linezolid-based short regimen for rifampicin-resistant tuberculosis	Netherlands	69 participants received the treatment regimen containing bedaquiline and 52 received the regimen containing linezolid	First regimen based on bedaquiline, levofloxacin, clofazimine, and cycloserine, and second regimen based on linezolid, levofloxacin, clofazimine, and cycloserine	Therapeutic efficacy of 81 % in the regimen containing bedaquiline with consequent gastrointestinal, cardiac, and nervous system adverse effects	10.1016/j.jinf.2024.106291
3	Cevik M, Thompson L, Upton C, et al	2024	Bedaquiline-pretomanid-moxifloxacin-pyrazinamide for drug-sensitive and drug-resistant pulmonary tuberculosis treatment: a phase 2c, open-label, multicenter, partially randomized controlled trial	United Kingdom	1059 participants, of whom 303 had DS-TB and 152 had DR-TB, assigned to treatment regimens	Regimen of bedaquiline, pretomanid, moxifloxacin, and pyrazinamide for 4 months for DS-TB and 6 months for DR-TB	Conversion to negative culture at 8 weeks, with 84 % for the DS-TB group receiving the regimen and 86 % for the DR-TB group, with side effects such as hepatotoxicity	10.1016/S1473-3099(24)00223-8
4	Chandrasekaran P, Vikram V, Anuj B, et al	2023	Bedaquiline, Delamanid, Linezolid, and Clofazimine for Treatment of Pre-extensively Drug-Resistant Tuberculosis	United States	165 participants, of whom 158 had MDR-TB	Therapeutic regimen based on bedaquiline, delamanid, linezolid, and clofazimine for 24 to 36 weeks	Efficacy of the bedaquiline-containing treatment regimen was 91 %, with adverse effects such as myelosuppression and peripheral neuropathy	10.1093/cid/ciac528

5	Padmapriyadarsini C et al.[37]	2024	Effectiveness and Safety of Varying Doses of Linezolid With Bedaquiline and Pretomanid in Treatment of Drug-Resistant Pulmonary Tuberculosis: Open-Label, Randomized Clinical Trial	India	103 participants subjected to bedaquiline, pretomanid, and linezolid regimens	Combinations of bedaquiline and pretomanid with different doses of linezolid	Treatment effectiveness of 91 % in the group that received bedaquiline, pretomanid, and 600 mg daily of linezolid for 26 weeks, with consequent adverse effects such as peripheral neuropathy and bone marrow suppression	10.1093/cid/ciae388
6	Rashitov M, Franke MF, Trevisi L, et al	2024	Safety and Effectiveness of 3 Novel All-Oral Shortened Regimens for Rifampicin- or Multidrug-Resistant Tuberculosis in Kazakhstan	USA	510 participants enrolled, of whom 452 were included in the effectiveness analyses due to baseline drug resistance	3 shortened oral regimens over 9 months: cycloserine with clofazimine, delamanid with pyrazinamide, and delamanid with clofazimine; each of these regimens featured bedaquiline, linezolid, and levofloxacin	Success rates of 92 %, 89 %, and 100 % for the first, second, and third regimens, respectively, with adverse effects such as hepatotoxicity, peripheral neuropathy, optic neuritis, QTc prolongation, myelosuppression, seizures, and psychosis	10.1093/cid/ciae305
7	Conraide F, Diacon A, Ngubane N, et al	2020	Treatment of Highly Drug-Resistant Pulmonary Tuberculosis	USA	109 participants, of whom 38 had MDR-TB	Bedaquiline, pretomanid, and linezolid	Therapeutic efficacy of 92 % for MDR-TB with adverse effects such as peripheral neuropathy, hematologic toxicity, and death (1 in the MDR-TB group)	10.1056/NEJMoa1901814
8	Goodall R et al.[26]	2022	Evaluation of two short standardized regimens for the treatment of rifampicin-resistant tuberculosis (STREAM stage 2): an open-label, multicenter, randomized, non-inferiority trial	United Kingdom	202 participants in the control regimen, 211 in the oral regimen, and 143 in the 6-month treatment regimen followed by 8 weeks of second-line injections	Control regimen consisting of moxifloxacin, clofazimine, ethambutol, pyrazinamide, kanamycin, isoniazid, and protionamide; oral regimen consisting of bedaquiline replacing kanamycin and levofloxacin replacing moxifloxacin, and 6-month regimen including bedaquiline, clofazimine, pyrazinamide, levofloxacin, isoniazid, and kanamycin (during the 8-week phase)	83 % favorable results in the oral regimen containing bedaquiline followed by adverse effects such as grade 3 or 4 hearing loss and death (7 participants who pursued the oral regimen)	10.1016/S0140-6736(22)02078-5

9	Goodall R et al.[27]	2024	Long-term efficacy and safety of two short standardized regimens for the treatment of rifampicin-resistant tuberculosis (STREAM stage 2): extended follow-up of an open-label, multicenter, randomized, non-inferiority trial	Netherlands	1436 patients evaluated, of whom 202 were assigned to the control regimen, 211 to the oral regimen, 143 to the 6-month regimen, and 32 to the long regimen (with early termination of recruitment)	Control regimen based on standard injections, oral regimen containing bedaquiline, pretomanid, linezolid, and moxifloxacin, 6-month regimen containing bedaquiline and other anti-tuberculosis drugs	51 % efficacy in the 6-month regimen demonstrated at 24 months with adverse effects such as grade 3 or 4 hearing loss and resistance to study drugs in low proportions	10.1016/S2213-2600(24)00186-3
10	Fu et al.[28]	2021	Insignificant difference in culture conversion between bedaquiline-containing and bedaquiline-free all-oral short regimens for multidrug-resistant tuberculosis	Netherlands	103 participants analyzed after loss to follow-up of 31 individuals	First regimen comprising r bedaquiline, linezolid, latest-generation fluoroquinolones, cycloserine, clofazimine, and pyrazinamide, and second regimen not including bedaquiline	Therapeutic efficacy of 83,1 % and 94,4 % at the second and fourth months of the bedaquiline-containing regimen with adverse effects such as liver damage, anemia, arthralgia, and myalgia	10.1016/j.ijid.2021.08.055
11	Nyang'wa BT, Berry C, Kazounis E, et al	2024	Short oral regimens for pulmonary rifampicin-resistant tuberculosis (TB-PRACTECAL): an open-label, randomized, controlled, phase 2B-3, multi-arm, multicenter, non-inferiority trial	Netherlands	275 participants, of whom 137 belong to the standard care group and 138 to the BPaLM group	Standard care group regimen: rifampicin, isoniazid, pyrazinamide, ethambutol, and clofazimine; BPaLM group regimen: bedaquiline, pretomanid, and moxifloxacin	The BPaLM regimen showed a risk difference of -37,2 percentage points compared with the standard care group, suggesting a reduction in serious adverse events ≥ 3 for BPaLM.	10.1016/S2213-2600(23)00389-2
12	Conradie et al.[30]	2022	Bedaquiline-Pretomanid-Linezolid Regimens for Drug-Resistant Tuberculosis	USA	181 participants intervened	200 mg daily of bedaquiline for 8 weeks, then 100 mg daily for 18 weeks, pretomanid (200 mg daily for 26 weeks) and linezolid at doses of 1200 mg and 600 mg for 9 weeks and 26 weeks	Those who received the bedaquiline, linezolid, and pretomanid regimen showed favorable results ranging from 84 % to 93 %, followed by adverse effects such as peripheral neuropathy, myelosuppression, and optic neuropathy	10.1056/NEJMoa2119430
13	Kim JH et al.[31]	2020	Bedaquiline in multidrug-resistant tuberculosis treatment: Safety and efficacy in a Korean subpopulation	Netherlands	20 participants included in the efficacy analysis population	Bedaquiline for 24 weeks in combination with linezolid and fluoroquinolones	Therapeutic success rate in culture conversion at 120 weeks of 75 % with adverse effects such as arthralgia and nausea	10.1016/j.resinv.2019.08.004
14	Paton N et al.[38]	2023	Treatment Strategy for Rifampin-Susceptible Tuberculosis	USA	670 participants intervened	Therapeutic regimen based on bedaquiline and linezolid for the initial 8 weeks	5,8 % reported primary outcome (death, treatment, or ongoing disease) with category 3 or 4 side effects	10.1056/NEJMoa2212537

15	Berry C et al.[39]	2022	A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis	United States	404 participants	24-week oral regimen with bedaquiline, linezolid, moxifloxacin, and clofazimine	79 % success rate with side effects such as hepatotoxicity and peripheral neuropathy	10.1056/NEJMoa2117166
16	Dawson R et al.[32]	2024	Quabodepistat in combination with delamanid and bedaquiline in participants with drug-susceptible pulmonary tuberculosis: protocol for a multicenter, phase 2b/c, open-label, randomized, dose-finding trial to evaluate safety and efficacy	United Kingdom	120 participants	Quabodepistat, delamanid, and bedaquiline regimen for 4 months compared with standard 6-month treatment including rifampicin, isoniazid, ethambutol, and pyrazinamide	Observation in participants experiencing grade 3 or higher adverse events	10.1186/s13063-024-07912-5
17	Afifi M et al.[33]	2024	Impact of bedaquiline regimen on the treatment success rates of multidrug-resistant tuberculosis patients in Egypt.	India	100 patients diagnosed with MDR-TB	Bedaquiline, in combination with other second-line anti-tuberculosis drugs	Treatment success rate of 74 % with adverse effects related to QT prolongation on electrocardiogram	10.1038/s41598-024-65063-8
18	Fadeyi MO et al.[34]	2024	A four-drug standardized short regimen for highly resistant TB in South-West Nigeria.	France	20 participants	9-month treatment regimen including bedaquiline, delamanid, linezolid, and clofazimine	70 % of patients achieved treatment success with adverse effects such as grade 1 or 2 peripheral neuropathy	
19	Moodliar R et al.[35]	2021	Bedaquiline for multidrug-resistant TB in pediatric patients.	France	First group of 15 patients (aged 12 to under 18) and second group of 15 patients (aged 5 to under 12)	24 weeks of treatment with bedaquiline in combination with a background treatment regimen	Efficacy defined as 75 % conversion in the first group and 100 % conversion in the second group, with side effects mainly focused on arthralgia	10.5588/ijtld.21.0022
20	Yao G et al.[36]	2023	Improved outcomes following addition of bedaquiline and clofazimine to a treatment regimen for multidrug-resistant tuberculosis.	United Kingdom	68 participants	Experimental regimen mainly based on bedaquiline and clofazimine followed by a regimen without bedaquiline for the following 12 months, and control group regimen that included bedaquiline and protionamide for the first 6 months followed by a regimen without bedaquiline for the following 12 months	The cure rate was significantly higher in the experimental group at 82 % compared to 56 % in the control group, with 6 adverse events in the experimental group (18 %) and 15 in the control group (44 %)	10.1177/03005221148416

However, prior exposure to new anti-tuberculosis drugs presents additional challenges, as it is associated with adverse clinical outcomes and acquired resistance. In fact, research has shown that sputum culture conversion rates and positive outcomes were significantly lower in previously exposed patients (65,9 % versus 98,0 %, p < 0,001; 41,0 % versus 82,3 %, p < 0,001), emphasizing the need to optimize the administration of new drugs to prevent the development of resistance.[9]

In this regard, one study demonstrated that sputum culture conversion rates were significantly lower among patients exposed to new or complementary anti-tuberculosis drugs, at 65,9 % compared to 98,0 % in those not exposed (p < 0,001); In addition, significant differences were observed in favorable outcome rates (41,0 % vs. 82,3 %, p < 0,001), which intensifies the need to prevent early exposure to these treatments to avoid resistance.[10]

Compared with other drugs such as moxifloxacin, bedaquiline demonstrated a higher culture conversion rate at 8 weeks (78 % vs. 65 %, p < 0,05) and greater therapeutic success at the end of treatment (82 % vs. 72 %). However, adverse events in the bedaquiline-treated group, such as QTc prolongation and mild hepatotoxicity, were observed, emphasizing the importance of continuous clinical monitoring during treatment.[11]

On the other hand, the combined therapeutic regimen of bedaquiline with other drugs has been shown to improve treatment success by 23,9 % (95 % CI: 4,8 %–43,0 %), reducing the treatment duration by 64 days (95 % CI: 18–109 days). This approach has therefore proven to be more effective than other treatments; however, it is essential to note that the cost of treatment is significantly higher, which could limit its accessibility in certain contexts.[12]

It is worth mentioning that a notable example of the effectiveness of combinations is the BPaL regimen, a scheme that includes pretomanid, bedaquiline, and linezolid, which has been shown to have both a high therapeutic success rate (89 %–92 %) and rapid bacteriological conversion at 8 weeks. However, the most common adverse effects include peripheral neuropathy, myelosuppression, and mild hepatic toxicity, highlighting the need for adequate monitoring during administration.[13]

Globally, regimens incorporating bedaquiline have demonstrated an early bacteriological conversion rate of 75 % and a therapeutic success rate of 80 %, with minor side effects affecting fewer than 10 % of patients. These results confirm the drug's overall good tolerability, reinforcing its favorable profile as a treatment for multidrug-resistant tuberculosis.[14]

In studies of modified treatments for rifampicin-resistant pulmonary tuberculosis, 82,7 % of participants achieved successful treatment outcomes. However, some adverse events were reported; most were manageable, underscoring the efficacy of regimens that include bedaquiline in these complicated cases.[15]

However, a meta-analysis that included 29 articles and 23,358 individuals showed that bedaquiline significantly improved bacteriological conversion rates at 24 weeks (RR = 1,27) and during subsequent follow-up (RR = 1,33), thereby consolidating its position as a practical option for treating multidrug-resistant tuberculosis.[16]

In prolonged treatments, bedaquiline has shown high success rates (89,6 %–90 %) with no significant differences between groups; however, some adverse effects such as anemia and liver dysfunction were reported, reinforcing the need for continuous monitoring during prolonged treatments; on the other hand, the combination of bedaquiline and delamanid in children and adolescents with MDR-TB has achieved a 100 % success rate, underscoring the superior efficacy of this combination in this vulnerable population. Reinforcing a broader analysis, regimens that included bedaquiline showed significant improvements in clinical cure rates (OR = 4,15) and reductions in mortality (OR = 5,22), without a notable increase in adverse effects, reinforcing its overall effectiveness and safety.[17,18,19]

Finally, a study conducted in China reported 1,563 adverse events related to bedaquiline, most of which were minor, with QTc prolongation being the most frequent adverse effect (24,7 %). This highlights the importance of clinical monitoring during treatment, especially in individuals with comorbidities that may predispose them to certain complications.[40]

CONCLUSIONS

Bedaquiline has proven to be a key innovation in the treatment of multidrug-resistant pulmonary tuberculosis, achieving efficacy rates ranging from 75 % to 93 % in combination with other drugs. These treatments offer significant benefits, such as rapid bacteriological conversion and a reduction in treatment duration. However, their use requires careful monitoring due to adverse effects such as QTc prolongation (14–15 %), hepatotoxicity (8–10 %), peripheral neuropathy (18 %), myelosuppression (12 %), gastrointestinal disorders, arthralgia, myalgia, optic neuritis, and psychiatric disorders to a lesser degree. Despite these advantages, the high cost of the drug and the need for specialized follow-up limit its accessibility in specific contexts, making it crucial to develop strategies that promote access and ensure continuous monitoring of resistance, thereby maximizing its impact on public health.

BIBLIOGRAPHIC REFERENCES

1. Tuberculosis. World Health Organization. 2024. https://www.who.int/es/news-room/fact-sheets/detail/tuberculosis

2. Tuberculosis multirresistente. World Health Organization. 2024. https://www.who.int/es/news-room/questions-and-answers/item/tuberculosis-multidrug-resistant-tuberculosis-(mdr-tb)

3. Palmero DJ, Lagrutta L, Inwentarz SJ, Vescovo M, Aidar OJ, Montaner PJG. Tratamiento de la tuberculosis drogorresistente en adultos y niños. Revisión narrativa. 2022.

4. Distribución geográfica y factores de riesgo de tuberculosis multidrogorresistente en el centro de Perú. 2024. http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-00112020000200245

5. Edith N, Marin M, Eugenia M. Bedaquilina en el tratamiento de tuberculosis multirresistente en pediatría. 2024;24.

6. Palmero DD. Tuberculosis 2024: ¿hemos avanzado? 2024.

7. Sun WW, Yang M, Chen XH, Fan LC, Wu HY, Zhang SJ, et al. Efficacy and safety of the all-oral bedaquiline-containing regimen as treatment for pediatric multidrug/rifampicin-resistant tuberculosis: a multicenter, retrospective, cohort study. Expert Rev Anti Infect Ther. 2024 Apr;22(4):219-27.

8. Deshkar AT, Shirure PA. Bedaquiline: A Novel Diarylquinoline for Multidrug-Resistant Pulmonary Tuberculosis. Cureus. 2022 Aug;14(8):e28519.

9. Ahmad A, Akhtar J, Ahmad M, Khan MI, Wasim R, Islam A, et al. Bedaquiline: An Insight Into its Clinical Use in Multidrug-Resistant Pulmonary Tuberculosis. Drug Res. 2024 Jul;74(6):269-79.

10. Mikiashvili L, Kempker RR, Chakhaia TS, Bablishvili N, Avaliani Z, Lomtadze N, et al. Impact of Prior Tuberculosis Treatment With New/Companion Drugs on Clinical Outcomes in Patients Receiving Concomitant Bedaquiline and Delamanid for Multidrug- and Rifampicin-Resistant Tuberculosis. Clin Infect Dis. 2024 Apr 10;78(4):1043-52.

11. Desai G, Purohit G, Borana H, Deokar K, Yogi S. Comparison of efficacy of bedaquiline and moxifloxacin in drug resistant pulmonary tuberculosis. A prospective observational study. Monaldi Arch Chest Dis. 2022 May 4;93(1).

12. Geng X, Yang Y, Wen XT, Long HF, Li YX, Liu YX, et al. Comprehensive clinical evaluation of bedaquiline in the treatment of multidrug-resistant tuberculosis. Zhonghua Jie He He Hu Xi Za Zhi. 2023 Jun 12;46(6):572-9.

13. Oelofse S, Esmail A, Diacon AH, Conradie F, Olayanju O, Ngubane N, et al. Pretomanid with bedaquiline and linezolid for drug-resistant TB: a comparison of prospective cohorts. Int J Tuberc Lung Dis. 2021 Jun 1;25(6):453-60.

14. Gao M, Gao J, Xie L, Wu G, Chen W, Chen Y, et al. Early outcome and safety of bedaquiline-containing regimens for treatment of MDR- and XDR-TB in China: a multicentre study. Clin Microbiol Infect. 2021 Apr;27(4):597-602.

15. Korotych O, Achar J, Gurbanova E, Hovhannesyan A, Lomtadze N, Ciobanu A, et al. Effectiveness and safety of modified fully oral 9-month treatment regimens for rifampicin-resistant tuberculosis: a prospective cohort study. Lancet Infect Dis. 2024;24(10):1151-61.

16. Tong E, Wu Q, Chen Y, Liu Z, Zhang M, Zhu Y, et al. The Efficacy and Safety of Bedaquiline in the Treatment of Pulmonary Tuberculosis Patients: A Systematic Review and Meta-Analysis. Antibiotics. 2023;12(9).

17. Ke H, Gui X, Sun W, Zhang S, Yang Y, Zhang Z, et al. The Safety and Efficacy of Prolonged Use of Bedaquiline for the Treatment of Patients with Pulmonary Multi-Drug Resistant/Rifampin-Resistant Tuberculosis: A Prospective, Cohort Study in China. Infect Drug Resist. 2023;16:5055-64.

18. Yu CH, Liu X, Shen LJ, Li HW, Li X, Wu RS, et al. Meta analysis of efficacy and safety of the treatment containing bedaquiline for multidrug-resistant pulmonary tuberculosis. Chin J Antituberc. 2022;44(7):660-8.

19. Sakhelashvili MI, Platonova IL, Sakhelashvili-Bil OI, Piskur ZI. Evaluation of the effectiveness of bedaquiline and delamanid treatment among children and adolescents with multi-drug-resistant pulmonary tuberculosis. Mod Pediatr Ukr. 2023;2(130):17-23.

20. Scopus - Document details - Nine months of bedaquiline, linezolid, levofloxacin, clofazimine, and cycloserine chemotherapy for rifampicin/multidrug-resistant tuberculosis: a multicenter, randomized, open-label non-inferiority trial in China. 2024. https://www.scopus.com/record/display.uri?eid=2-s2.0-85204358209&origin=resultslist&sort=plf-f&src=s&sot=b&sdt=cl&cluster=scosubtype%2C%22ar%22%2Ct&s=TITLE-ABS-KEY%28tuberculosis+AND+pulmonary+AND+multidrug-resistant+bedaquiline+AND+treatment+AND+efficacy%29&sessionSearchId=07589dbb8f5b8874adde7649473caf13&relpos=2

21. Scopus - Document details - A non-randomized pragmatic historically controlled trial evaluating the effectiveness and safety of a bedaquiline or a linezolid-based short regimen for rifampicin-resistant tuberculosis. https://www.scopus.com/record/display.uri?eid=2-s2.0-85206993517&origin=resultslist&sort=plf-f&src=s&sot=b&sdt=cl&cluster=scosubtype%2C%22ar%22%2Ct&s=TITLE-ABS-KEY%28tuberculosis+AND+pulmonary+AND+multidrug-resistant+bedaquiline+AND+treatment+AND+efficacy%29&sessionSearchId=07589dbb8f5b8874adde7649473caf13&relpos=1

22. Scopus - Document details - Bedaquiline-pretomanid-moxifloxacin-pyrazinamide for drug-sensitive and drug-resistant pulmonary tuberculosis treatment: a phase 2c, open-label, multicentre, partially randomised controlled trial. https://www.scopus.com/record/display.uri?eid=2-s2.0-85194578486&origin=resultslist&sort=plf-f&src=s&sot=b&sdt=cl&cluster=scosubtype%2C%22ar%22%2Ct&s=TITLE-ABS-KEY%28tuberculosis+AND+pulmonary+AND+multidrug-resistant+bedaquiline+AND+treatment+AND+efficacy%29&sessionSearchId=07589dbb8f5b8874adde7649473caf13&relpos=7

23. Scopus - Document details - Bedaquiline, Delamanid, Linezolid, and Clofazimine for Treatment of Pre-extensively Drug-Resistant Tuberculosis. 2024. https://www.scopus.com/record/display.uri?eid=2-s2.0-85151838124&origin=resultslist&sort=plf-f&src=s&sot=b&sdt=cl&cluster=scosubtype%2C%22ar%22%2Ct&s=TITLE-ABS-KEY%28tuberculosis+AND+pulmonary+AND+multidrug-resistant+bedaquiline+AND+treatment+AND+efficacy%29&sessionSearchId=07589dbb8f5b8874adde7649473caf13&relpos=18

24. Scopus - Document details - Safety and Effectiveness of 3 Novel All-Oral Shortened Regimens for Rifampicin- or Multidrug-Resistant Tuberculosis in Kazakhstan. 2024. https://www.scopus.com/record/display.uri?eid=2-s2.0-85206595553&origin=resultslist&sort=plf-f&src=s&sot=b&sdt=cl&cluster=scosubtype%2C%22ar%22%2Ct&s=TITLE-ABS-KEY%28tuberculosis+AND+pulmonary+AND+multidrug-resistant+bedaquiline+AND+treatment+AND+efficacy%29&sessionSearchId=07589dbb8f5b8874adde7649473caf13&relpos=4

25. Conradie F, Diacon AH, Ngubane N, Howell P, Everitt D, Crook AM, et al. Treatment of Highly Drug-Resistant Pulmonary Tuberculosis. N Engl J Med. 2020 Mar 5;382(10):893-902.

26. Goodall RL, Meredith SK, Nunn AJ, Bayissa A, Bhatnagar AK, Bronson G, et al. Evaluation of two short standardised regimens for the treatment of rifampicin-resistant tuberculosis (STREAM stage 2): an open-label, multicentre, randomised, non-inferiority trial. Lancet. 2022 Nov 26;400(10366):1858-68.

27. Goodall RL, Nunn AJ, Meredith SK, Bayissa A, Bhatnagar AK, Chiang CY, et al. Long-term efficacy and safety of two short standardised regimens for the treatment of rifampicin-resistant tuberculosis (STREAM stage 2): extended follow-up of an open-label, multicentre, randomised, non-inferiority trial. Lancet Respir Med. 2024 Dec;12(12):975-87.

28. Fu L, Weng T, Sun F, Zhang P, Li H, Li Y, et al. Insignificant difference in culture conversion between bedaquiline-containing and bedaquiline-free all-oral short regimens for multidrug-resistant tuberculosis. Int J Infect Dis. 2021 Oct;111:138-47.

29. Nyang'wa BT, Berry C, Kazounis E, Motta I, Parpieva N, Tigay Z, et al. Short oral regimens for pulmonary rifampicin-resistant tuberculosis (TB-PRACTECAL): an open-label, randomised, controlled, phase 2B-3, multi-arm, multicentre, non-inferiority trial. Lancet Respir Med. 2024 Feb;12(2):117-28.

30. Conradie F, Bagdasaryan TR, Borisov S, Howell P, Mikiashvili L, Ngubane N, et al. Bedaquiline-Pretomanid-Linezolid Regimens for Drug-Resistant Tuberculosis. N Engl J Med. 2022 Sep 1;387(9):810-23.

31. Kim JH, Kwon OJ, Kim YS, Park MS, Hwang S, Shim TS. Bedaquiline in multidrug-resistant tuberculosis treatment: Safety and efficacy in a Korean subpopulation. Respir Investig. 2020 Jan;58(1):45-51.

32. Dawson R, Diacon AH, Takuva S, Liu Y, Zheng B, Karwe V, et al. Quabodepistat in combination with delamanid and bedaquiline in participants with drug-susceptible pulmonary tuberculosis: protocol for a multicenter, phase 2b/c, open-label, randomized, dose-finding trial to evaluate safety and efficacy. Trials. 2024 Jan 19;25(1):70.

33. Afifi M, Amin W, Helal D, Ashmawy R, El-Maradny YA, Khalifa N, et al. Impact of bedaquiline regimen on the treatment success rates of multidrug-resistant tuberculosis patients in Egypt. Sci Rep. 2024 Jul 1;14(1):16247.

34. Fadeyi MO, Decroo T, Ortuño-Gutiérrez N, Ahmed B, Jinadu A, El-Tayeb O, et al. A four-drug standardized short regimen for highly resistant TB in South-West Nigeria. Int Health. 2024 Jan 1;16(1):123-5.

35. Moodliar R, Aksenova V, Frias MVG, van de Logt J, Rossenu S, Birmingham E, et al. Bedaquiline for multidrug-resistant TB in paediatric patients. Int J Tuberc Lung Dis. 2021 Sep 1;25(9):716-24.

36. Yao G, Zhu M, Nie Q, Chen N, Tu S, Zhou Y, et al. Improved outcomes following addition of bedaquiline and clofazimine to a treatment regimen for multidrug-resistant tuberculosis. J Int Med Res. 2023 Jan;51(1):3000605221148416.

37. Padmapriyadarsini C, Oswal VS, Jain CD, Mariappan MV, Singla N, Kumar S, et al. Effectiveness and Safety of Varying Doses of Linezolid With Bedaquiline and Pretomanid in Treatment of Drug-Resistant Pulmonary Tuberculosis: Open-Label, Randomized Clinical Trial. Clin Infect Dis. 2024 Dec 17;79(6):1375-85.

38. Paton NI, Cousins C, Suresh C, Burhan E, Chew KL, Dalay VB, et al. Treatment Strategy for Rifampin-Susceptible Tuberculosis. N Engl J Med. 2023;388(10):873-87.

39. 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(25):2331-43.

40. Scopus - Document details - Bedaquiline-containing regimens in patients with pulmonary multidrug-resistant tuberculosis in China: focus on the safety. 2025.

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