The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb):
A Systematic Literature Review

Miptah Farid Thariqulhaq¹, Tri Yunis Miko Wahyono²
¹,²Universitas Indonesia

ARTICLE INFO

Objective: MDR-TB is a life-threatening infectious disease. In recent years, RR/MDR TB sufferers have increased by 10% from 186,883 patients in 2018 to 206,030 in 2019. The success rate of treatment for RR/MDR-TB patients only reaches 57% globally. WHO has recommended bedaquiline for treatment of MDR-TB as the first drug in an all-oral regimen designed to maximize treatment outcomes. Purpose: to describe the efficacy and safety of a bedaquiline-containing regimen for the treatment of MDR-TB.

Methods: Pubmed, Science Direct, and Embase online databases were used to obtain data published in the last five years where literature searches were carried out independently by researchers. The keywords used in this search are combined with the Boolean operator "AND", namely (bedaquiline) AND (multidrug resistant) AND (effectiveness). Results: Eight studies met the inclusion criteria, demonstrating a higher conversion rate of sputum cultures on the bedaquiline containing regimen between 74%-95.8% with a mean time to culture conversion between 39 days-3 months. The majority of studies reported an adverse effect of QT prolongation in patients treated with bedaquiline. Conclusion: This systematic review showed that bedaquiline is effective and safe for use in the treatment of MDR-TB. However, serious side effects of QT prolongation occurred in some respondents who were treated with bedaquiline, so an effective and efficient monitoring and surveillance system is needed to ensure best practice in the treatment of MDR-TB.

Keywords: bedaquiline, tuberculosis, multidrug resistant, effectiveness, safety

Email : miptah2384@gmail.com

Copyright © 2023 Journal Eduhealt. All rights reserved is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License (CC BY-NC 4.0)

1. INTRODUCTION

A total of 5.8 million new Tuberculosis (TB) cases were diagnosed and reported in 2020, which decreased by 18% compared to 7.1 million cases in 2019, attributed to the COVID-19 pandemic. As a consequence, the number of TB-related deaths increased from 1.2 million in 2019 to 1.3 million in 2020. Geographically, in 2020, the highest number of TB cases occurred in Southeast Asia (43% of cases) and Africa (25%). Globally, in 2019, nearly half a million TB patients developed Rifampicin-resistant TB (TB-RR), of which 78% had Multi-Drug Resistant Tuberculosis (TB-MDR) with resistance to several first-line drugs. In recent years, the number of TB-RR/MDR patients increased by 10%, from 186,883 patients in 2018 to 206,030 in 2019. The success rate of treating RR/MDR-TB patients globally was only 57%.

TB-MDR is a form of tuberculosis where there is resistance to isoniazid (INH) and rifampicin (RIF), with or without resistance to other first-line drugs. Drug resistance occurs due to chromosomal mutations, genetic coding of drug target, or drug-activating enzymes, as a response to antibiotic selection pressure [1][2]. Currently, WHO recommends treating TB-MDR with four or more combinations of second-line TB drugs. The TB-MDR therapy consists of two regimens, long-term and short-term treatment. For most patients, the recommended total treatment duration for the long-term regimen is 18-20 months, but it can be adjusted based on the patient's response to treatment. The short-term regimen is recommended for TB MDR patients who have not used second-line drugs for more than one month, are not resistant to fluoroquinolones or second-line injectable drugs, and it...
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review

Miptah Farid Thariqulhaq, et.al

involves four or more second-line drugs with a treatment duration of 9-12 months [3]. Factors contributing to treatment failure include the lack of effective drugs for MDR-TB and XDR-TB treatment. Additionally, MDR-TB treatment is time-consuming and costly, leading to efforts to shorten the treatment duration and develop more effective drugs with new mechanisms of action, such as bedaquiline [4].

WHO has recommended bedaquiline as the first-line treatment for MDR-TB in an all-oral regimen designed to maximize treatment outcomes while minimizing the toxicity of injectable agents. Bedaquiline is classified as Group A in the WHO guidelines (WHO, 2019). It is a diarylquinoline that works by inhibiting mycobacterial ATP synthase as the first antituberculosis drug in 40 years approved for MDR-TB patients [5] [6]. Over the past few years, several studies have been conducted to evaluate bedaquiline [7] [8] [9]. However, a comprehensive analysis has not been performed. Therefore, the aim of this study is to evaluate the effectiveness and safety of bedaquiline-based regimens in TB-MDR patients.

2. METHOD

The selection of articles for this critical review was conducted using the PRISMA method (Preferred Reporting Items for Systematic Review and Meta-Analyses), following each instruction and step outlined in the PRISMA checklist [10]. The article search was independently performed by the researcher using online databases such as PubMed, ScienceDirect, and Embase, focusing on articles published within the last five years. The search terms used in this study were combined using the Boolean operator "AND," namely (bedaquiline) AND (multidrug resistant) AND (effectiveness). The selected articles were open-access and only studies published in English were included in the final review.

Articles identified through the database search were merged, and duplicates were removed. Articles were screened based on title and abstract relevance to exclude those that did not meet the criteria. The inclusion criteria for research articles were as follows: 1) patients diagnosed with MDR-TB based on WHO criteria (2020); 2) patients treated with a regimen containing bedaquiline; 3) reporting the effectiveness and/or safety of bedaquiline in combination therapy for MDR-TB. Conference abstracts, reviews, experimental studies in animal models, laboratory studies, case series/case reports, and articles describing tuberculosis patients recruited without bacteriological confirmation of diagnosis were excluded.

Data extracted from each published article for this systematic review included: 1) article details (researcher names and publication year), 2) methodology, 3) country setting of the study, 4) sample size, 5) type of intervention provided, 6) research outcomes. The primary outcome assessed in this systematic review was the rate of conversion from positive sputum culture to negative sputum culture in patients diagnosed with MDR-TB treated with a regimen containing bedaquiline. Secondary outcomes examined included the time to conversion from positive sputum culture to negative sputum culture, percentage of recovery, mortality, and side effects.
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review. Miptah Farid Thariqulhaq, et.al

3. RESULTS AND DISCUSSION

Based on the search results for scientific articles using the keywords or terminology above, eighteen articles were selected from various countries with subjects originating from health facilities and populations with varying study periods. The summaries of the eight journals are described systematically in table 1.

Identification results through database searches for the last 5 years: PubMed (212), Sciedirect (241), Embases (133)

Identification results N = 586

Articles after Duplication removed N = 509

Text articles with title suitability = 89

Articles that match the title and review abstract N = 53

Total articles included N = 8

Inappropriate article after the full text review was issued with the reasons:
- Reviews = 4
- Does not explain the outcome of therapy = 9
- There is no control group = 10
- Inappropriate research design = 8
- Inaccessible = 11
- Not speaking English = 1
- Laboratory studies = 3

Figure 1. PRISMA flowchart of literature search
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review. Miptah Farid Thariqulhaq, et.al

Table 1. Results of data analysis in the final review article related to effectiveness

<table>
<thead>
<tr>
<th>Author, research location</th>
<th>Research design</th>
<th>Sample</th>
<th>Intervention</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dooley et al, 2021 (South Africa &amp; Peru)</td>
<td>RCT</td>
<td>84 Adult participants (mean age 34 years) with MDR/RR-TB, of which 28 in each bedaquiline, delamanid or Bedaquiline+ delamanid group</td>
<td>Bedaquiline was given at a dose of 400 mg daily for 14 days, followed by 200 mg three times weekly, for 24 weeks plus a regimen of at least 4-5 active drugs except clofazimine and levofloxacin, compared to delamanid or delamanid + bedaquiline</td>
<td>Cumulative culture conversion at 8 weeks in the bedaquiline group was 88% (21/24) with last positive cultures seen at a median of 5 weeks and cumulative culture conversion at 24 weeks in the bedaquiline group was 92%, whereas in the delamanid group it was 83% (20/24), P=0.480 at second month and at four months 93.6% vs. 95.8%, P=1.000 with HR= 1.208 (95% CI, 0.733-1991) p=0.459 with an average time for culture conversion of 2 months</td>
</tr>
<tr>
<td>Fu et al, 2021 (China)</td>
<td>prospective nonrandomized controlled trial</td>
<td>103 MDR-TB patients diagnosed with pulmonary MDR-TB in Shenzhen, China with a mean age of 38 years</td>
<td>Patients prescribed linezolid, fluoroquinolone (FQ), clofazimine, cycloserine, and pyrazinamide compared to a regimen in which clofazimine was replaced with bedaquiline</td>
<td>The culture conversion rate in the groups without bedaquiline to those containing bedaquiline was 79.5% vs. 90.5%, P=0.480 at second month and at four months 93.6% vs. 95.8%, P=1.000 with HR= 1.208 (95% CI, 0.733-1991) p=0.459 with an average time for culture conversion of 2 months</td>
</tr>
<tr>
<td>Ndjeka et al, 2022</td>
<td>retrospective cohort</td>
<td>1387 rifampicin-resistant TB patients</td>
<td>A brief regimen containing bedaquiline consists of</td>
<td>Treatment success in the</td>
</tr>
</tbody>
</table>
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review. Miptah Farid Thariqulhaq, et.al

The treatment regimen for the bedaquiline-treated patients was pyrazinamide (98.3%), levofloxacin (91.0%), terizidone (87.5%), linezolid (78.7%), clofazimine (69.7%), ethionamide (64.3%) and moxifloxacin (52.6%), and for patients who were not treated bedaquiline were pyrazinamide (97.5%), terizidone (93.1%), moxifloxacin (86.9%), ethionamide (81.5%) and kanamycin (64.7%) duration of MDR-TB treatment during the study period was at least 18-24 months. Bedaquiline is recommended for a duration of 6 months.
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review. Miptah Farid Thariqulhaq, et.al

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patients Information</th>
<th>Treatment Details</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shim et al, 2023 (South Korea)</td>
<td>Prospective cohort</td>
<td>The 172 patients overall had a mean age of 48-50 years, of which 88 were treated with bedaquiline and 84 were not treated with bedaquiline.</td>
<td>Of the patients receiving bedaquiline, 68 (77.3%) received cycloserine, 63 (71.6%) linezolid, and 62 prothionamide (70.5%). And those who did not receive bedaquiline 75 (89.3%) received prothionamide, 74 (88.1%) cycloserine, 72 (85.7%) pyrazinamide, 59 (70.2%) kanamycin, and 44 (52.4%) levofloxacin. MDR-TB therapy 18-24 months, including bedaquiline for up to 6 months on label when prescribed</td>
<td>(83.9%) and 868/1358 (63.9%), respectively, achieved culture conversion with a median time to culture conversion of 102 (95% CI: 98, 106) and 83 (95% CI: 78.88) days</td>
</tr>
<tr>
<td>Taune et al, 2019 (Papua New Guinea)</td>
<td>Retrospective cohort</td>
<td>277 MDR-TB patients mean age 33 years, 77 (39%) received BDQ, and 200 (61%) patients who did not receive BDQ.</td>
<td>The standard treatment regimen for MDR-TB in Daru includes at least five drugs that appear to be effective based on known resistance patterns: kanamycin, levofloxacin, linezolid, clofazimine, cycloserine and pyrazinamide (no)</td>
<td>Interim results The 6-month culture-negative rate was 92.2% for the BDQ group, whereas in the non-bedaquiline group it was</td>
</tr>
<tr>
<td>Study</td>
<td>Cohort Type</td>
<td>Patients Description</td>
<td>Intervention</td>
<td>Outcomes</td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Zhang et al, 2022 (East China)</td>
<td>Retrospective</td>
<td>Patients with refractory RR/MDR/XDR-TB receiving regimens containing BDQ (n=102) and BDQ-free regimens (n=100)</td>
<td>BDQ was administered for 24 weeks (with a loading dose of 400 mg once daily for the first 2 weeks, followed by 200 mg three times weekly for the remaining 22 weeks). The other regimen consisted of at least 4 anti-tuberculosis drugs likely to be effective in the intensive phase, including furoquinolones, injectable agents (capreomycin or amikacin), Cs, prothionamide, E, pyrazinamide, Cfz, Lzd, or para-aminosalicylate, drug doses the same as group non-BDQ.</td>
<td>Culture conversion rate 96.2% with a mortality of 6.5% vs. 8.5%. Culture conversion rate in BDQ group 3rd month (89.2% vs. 66.0%), 6th month (90.2% vs 72.0%), 9th month (91.2% vs. 66.0%), and 12th month (94.1% vs. 65.0%) significantly higher than the non-BDQ group (p&lt;0.001) with a mean time of culture conversion in the BDQ group was 3.0 months (IQR, 3.0–3.0), and the non-BDQ group (5.8 months [IQR, 3.0–12.0]). Treatment success 92.2% vs 63.0%, with OR=7.4, 95% CI: 2.9–18.5, p&lt;0.001 87.4% (95% CI, 81.1%–92.4%) in the bedaquiline group achieved sputum culture conversion within 6 months versus 78.3% (95% CI, 71.0%–85.0%).</td>
</tr>
<tr>
<td>Zhao et al, 2019 (South Africa)</td>
<td>Retrospective</td>
<td>162 patients received bedaquiline substitution and 168 controls</td>
<td>Bedaquiline was administered for a minimum of 24 weeks (at a loading dose of 400 mg once daily for the initial 2 weeks, followed by 200 mg 3 times per week for 22 weeks). Other drugs in the MDR regimen include levofloxacin, pyrazinamide, ethionamide, high-dose isoniazid, ethambutol, and terizidone.</td>
<td>92.2% vs 63.0%, with OR=7.4, 95% CI: 2.9–18.5, p&lt;0.001 87.4% (95% CI, 81.1%–92.4%) in the bedaquiline group achieved sputum culture conversion within 6 months versus 78.3% (95% CI, 71.0%–85.0%).</td>
</tr>
</tbody>
</table>
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review. Miptah Farid Thariqulhaq, et al

Table 2. Results of data analysis in the final review articles related to security

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Year</th>
<th>Security</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dooley et al</td>
<td>2021</td>
<td>The maximum change from baseline in the Bdq group was 72 ms at week 18 with the mean (95% CI) QTc value on treatment (in ms) was 409.7 (402.5–416.8). The mean change in QTc (ms) from baseline, at 95% CI was 12.3 (7.8-16.7). There were no Grade 3 or 4 QTc prolongation events and no deaths during study treatment.</td>
</tr>
<tr>
<td>Fu et al</td>
<td>2021</td>
<td>The bedaquiline-containing group experienced more hyperuricemia (65.71% vs. 39.71%, P=0.012) and palpitations (40.00% vs. 19.12%, P=0.022).</td>
</tr>
<tr>
<td>Ndjeka et al</td>
<td>2022</td>
<td>Tidak dijelaskan</td>
</tr>
<tr>
<td>Pai et al</td>
<td>2022</td>
<td>Serious TEAE (severity 3–5) was reported in 1491/3747 (39.8%) patients treated with bedaquiline and 581/2234 (26.0%) patients not treated with bedaquiline. The most common serious TEAEs for patients treated with bedaquiline (reported in ≥ 2.0% of patients) were ototoxicity, anemia, optic neuritis, ECG QT prolongation, peripheral neuropathy, decreased hemoglobin, vomiting, and psychotic disorders. Diarrhea and nausea were the most frequently reported treatment-related adverse effects (TEAEs) in the bedaquiline group (27.3% [24/88] and 22.7% [20/88], respectively). The most common TEAE associated with bedaquiline were QT prolongation (10.2%; 9/88), and diarrhea and nausea (9.1%; 8/88 respectively). and no deaths associated with bedaquiline</td>
</tr>
<tr>
<td>Shim et al</td>
<td>2023</td>
<td>Of 277 MDR-TB patients, 77 (39%) received BDQ with a total of 8 serious adverse events including 5 (6.5%) death, of which 1 (1.3%) QTcF</td>
</tr>
<tr>
<td>Taune et al</td>
<td>2019</td>
<td></td>
</tr>
</tbody>
</table>
completed according to the WHO 2013 treatment outcome definition, as 172 MDR
linea among 277 MDR. Other studies reported longer conversion times, namely 102 days and 3 months
conversion time. Based on four study outcomes, the average conversion times ranged from 39 days to
Discussion
studies were 1.5 months and 2 months, respectively
90.5% for the non-
74%, respectively, with death rates of 15% and 17% in the groups treated with bedaquiline
achieved in 56.3% of patients treated with bedaquiline and 45.2% of patients without
outcomes compared to those without bedaquiline. In the study by
well as deaths during treatment in the group containing a bedaquiline regimen, demonstrated better
rates were 66.9% and 74%, respectively, with death rates of 15% and 17% in the groups treated with bedaquiline-containing
regimens. [14] reported treatment success rates of 92.2% vs. 63.0% in the bedaquiline group compared to the non-bedaquiline group, with an OR = 7.4, 95% CI: 2.9–18.5, p < 0.001 [14]
Experimental Study Outcomes
The sputum culture conversion rate after bedaquiline therapy was found to be superior compared to the group not receiving bedaquiline. [11] showed a sputum culture conversion rate of 83.9% compared to the non-bedaquiline-treated group (63.95%), and [12] also significantly demonstrated a sputum culture conversion rate of 87.4% (95% CI = 81.1-92.4) within 6 months of therapy [11] [12]. Similar results were observed in other studies. In the study by [13] in South Korea, among 172 MDR-TB patients, the sputum conversion rate in the bedaquiline-treated group was 90.4% [13]. [14] in East China showed a sputum culture conversion rate of 89.2% at month 3, 91.2% at month 9, and 94.1% at month 12 in the bedaquiline group, all significantly higher compared to the SLI group (p < 0.001) [14]. However, a different outcome was observed in the study by [9] in Papua New Guinea among 277 MDR-TB patients, where the negative conversion rate at 6 months was 92.2% for the bedaquiline group and 96.2% for the non-bedaquiline group.
The average conversion time varied in the articles. [12] and [14] reported average conversion times of 2 months and 3 months, respectively [12] [14]. Other studies reported average conversion times ranging from 39 days to 102 days [13] [11]. Treatment success, defined as a combination of patients cured and treatment completed according to the WHO 2013 treatment outcome definition, as well as deaths during treatment in the group containing a bedaquiline regimen, demonstrated better outcomes compared to those without bedaquiline. In the study by [13], treatment success was achieved in 56.3% of patients treated with bedaquiline and 45.2% of patients without bedaquiline, with a death rate of 14.9% [13]. In the studies by [11] and [8], treatment success rates were 66.9% and 74%, respectively, with death rates of 15% and 17% in the groups treated with bedaquiline-containing
regimens. [14] reported treatment success rates of 92.2% vs. 63.0% in the bedaquiline group compared to the non-bedaquiline group, with an OR = 7.4, 95% CI: 2.9–18.5, p < 0.001 [14]

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Conversion Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang et al</td>
<td>2022</td>
<td>Not explained</td>
</tr>
<tr>
<td>Zhao et al</td>
<td>2019</td>
<td>Not explained</td>
</tr>
</tbody>
</table>

A total of 586 articles were identified based on the database search, as shown in Figure 1. Among these articles, 8 met the inclusion criteria and were selected for the final review. Based on the study design, 5 studies utilized a retrospective cohort design, 1 study employed a prospective cohort design, 1 study used a nonrandomized controlled trial design, and 1 study utilized a randomized controlled trial design, originating from various different countries. According to the findings of several studies, bedaquiline was administered at a dose of 400 mg once daily for 2 weeks, followed by 200 mg three times a week for 24 weeks in combination with other drug regimens.

Experimental Study Outcomes

The sputum culture conversion rate after bedaquiline therapy in the study by [7] was 88% at week 8 and 92% at week 24. The study by [15] reported sputum culture conversion rates of 79.5% vs. 90.5% for the non-bedaquiline group compared to the bedaquiline group, respectively, at the second month, and 93.6% vs. 95.8% at four months, with a p-value of 0.459 and an HR value of 1.208 (95% CI, 0.733-1991), indicating no statistically significant difference [15]. The conversion times in these studies were 1.5 months and 2 months, respectively [7] [15].

Discussion

In this systematic review, bedaquiline demonstrated a relatively short average sputum culture conversion time. Based on four study outcomes, the average conversion times ranged from 39 days to 2 months [7] [15] [13] [12]. Achieving sputum culture conversion within two months of therapy has been associated with a higher likelihood of treatment success in MDR-TB patients. However, two other studies reported longer conversion times, namely 102 days and 3 months [11] [14]. This
difference may be attributed to other factors that could impede the culture conversion process. Malnutrition or significant nutritional deficiency has been linked to treatment failure, including mortality and longer time to sputum culture conversion in MDR-TB patients [16]. In the study by [9] in Papua New Guinea involving 277 MDR-TB patients, the 6-month negative conversion rate was 92.2% for the bedaquiline group, which was lower than the 96.2% for the non-bedaquiline group. This could potentially be due to resource limitations in terms of monitoring, staffing, treatment quality, patient counseling, and patient selection criteria applied for bedaquiline, introducing potential bias toward favorable outcomes in the non-BDQ group due to the 6-month BDQ administration in the analysis.

The use of bedaquiline necessitates vigilance regarding its associated side effects. Several studies have reported serious side effects associated with bedaquiline use, including QT interval prolongation (Table 2). A meaningful QT interval prolongation is defined as an absolute value >450ms in males and >470ms in females, or >60ms from pre-therapy/baseline. In the study by [7], the maximum change from baseline in the Bdq group was 72 ms at week 18, although no Grade 3 or 4 QTc prolongation events were observed, and no deaths occurred during the study treatment [7]. In the study by [13], the most common side effects associated with bedaquiline were QT interval prolongation (10.2%), diarrhea, and nausea (9.1%), but no deaths were linked to bedaquiline use [13]. In the study by [9] involving 277 MDR-TB patients, 77 (39%) received BDQ, with a total of 8 serious adverse effects, including 5 (6.5%) deaths, where 1 (1.3%) QTcF prolongation of Grade 3 was attributed to bedaquiline [9].

Despite the effectiveness of bedaquiline in promoting culture conversion, most studies provide limited information about the side effect of QT interval prolongation. Hence, there remains a scarcity of safety data concerning patient QT intervals when administering higher doses of bedaquiline or when combining it with other medications known to cause QT interval prolongation. Therefore, monitoring and close observation of bedaquiline use are imperative. While our study provides evidence of bedaquiline effectiveness, it does have some limitations. Our study did not assess adherence to bedaquiline-containing treatment regimens. Additionally, there is variability and differences in patient characteristics across each study. Furthermore, the majority of selected studies had low-quality evidence with a limited number of participants in some studies, which may potentially introduce bias.

4. CONCLUSION

The rate of culture conversion and treatment success in MDR-TB with regimens containing bedaquiline demonstrated superior outcomes compared to the group without bedaquiline, with relatively short culture conversion times and improved culture conversion rates. The use of bedaquiline can be effectively implemented in tuberculosis programs if financial and procurement barriers are adequately addressed to ensure availability. However, several articles have reported serious side effects in the form of QT interval prolongation during bedaquiline therapy, with varying degrees of severity. Effective and efficient monitoring, along with a surveillance system, is necessary to gather data on patients receiving new drugs and regimens to ensure best practices in MDR-TB treatment. Furthermore, further research is needed to monitor the QT interval prolongation side effects associated with bedaquiline administration in MDR-TB therapy.

REFERENCES
The Effectiveness And Safety Of Bedaquiline-Containing Regimens In The Treatment Of Patients With Multi-Drug Resistant Tuberculosis (Mdr-Tb): A Systematic Literature Review. Miptah Farid Thariqulhaq, et al


