Cost-effectiveness of Bedaquiline for the Treatment of Multidrug-resistant Tuberculosis in the Republic of Korea

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ABSTRACT

Purpose: Bedaquiline is a new drug used for the treatment of multidrug-resistant tuberculosis (MDR-TB). This study aimed to evaluate the cost-effectiveness of adding bedaquiline to a standard regimen (SR) for treating patients with MDR-TB, including extensively drug-resistant (XDR)-TB, in the Republic of Korea.

Methods: A cohort-based decision-analytic model developed in a previously published study from the United Kingdom was used, with a 20-year time horizon and a 5% discount rate for cost and effectiveness, to evaluate the incremental cost-effectiveness ratios of bedaquiline + SR and SR only. The key parameters regarding the clinical data were available via the published Phase II trial of bedaquiline. Additional parameters for recurrence, cure status, loss to follow-up, surgery, death, cost, and health utility were based on Korean data if available; otherwise the international literature data were applied. Univariate and probabilistic sensitivity analyses were conducted.

Findings: Based on the analysis, a patient on bedaquiline + SR would gain 1.20 quality-adjusted life-years (QALYs) at 13,961,659 Korean won (KRW) (1100 KRW = US $1) of additional cost compared with a patient administered SR only, with an incremental cost/utility ratio of 11,638,656 KRW/QALY. Bedaquiline + SR had an 80% probability of being cost-effective, at a willingness-to-pay threshold of 26 million KRW, compared with SR only.

Implications: The results of this study suggest that, in the Republic of Korea, bedaquiline, as a part of combination therapy with SR, is a cost-effective option for the treatment of MDR-TB (including XDR-TB) compared with SR only. (*Clin Ther*. 2016;38:655–667)

Key words: bedaquiline, cost-effectiveness, multidrug-resistant tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a global epidemic, and ~9 million people are estimated to be infected, resulting in ~1.5 million deaths/y as of 2013. The World Health Organization (WHO) has reported that the incidence of TB has been on a downward trend since 2000; the proportion of new cases of multidrug-resistant (MDR)-TB was 3.5% and has not changed in recent years. In 2013, the estimated number of new MDR-TB cases was 480,000 (range, 350,000–610,000), with extensively drug-resistant (XDR)-TB constituting ~9% of MDR-TB cases.[1] The burden of incidence, prevalence, and mortality caused by TB or MDR-TB varies by country. In the Republic of Korea (ROK) in 2013, the number of patients registered as having TB was 45,292, of whom 1064 had MDR-TB, including 113 with XDR-TB (11.3% of MDR-TB cases).[2]

MDR-TB is defined as TB resistant to isoniazid and rifampicin (the most effective TB drugs) and needs to

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be treated with a complex regimen that contains second-line, injectable drugs. The treatment success rate of MDR-TB is only 48% compared with that of drug-susceptible (DS)-TB, which exceeds 85% of new cases in most settings. The low treatment success rate is a result of the longer treatment period, low drug susceptibility, increased risk for adverse reactions to drugs, and high rates of discontinuation.[1,3] In addition, the economic burden at the individual and societal levels is high owing to expensive second-line anti-TB drugs, repeated hospitalizations, the long-term treatment period, and productivity losses.

Health-related quality of life (HRQOL) research involving MDR-TB is very limited. However, MDR-TB is generally assumed to result in an HRQOL substantially lower than that of DS-TB, given that MDR-TB patients need to take multiple drugs (including injectable ones) continuously for at least 2 years with or without accompanied hospitalization.

Improvements in TB diagnosis and drugs have increased treatment success and contributed to a decreased TB burden, but unmet needs are still high. Bedaquiline is a new anti-TB agent in the diarylquinoline group developed primarily to treat MDR-TB. It has antimycobacterial activity that specifically inhibits the ATP synthase enzyme of *Mycobacterium tuberculosis*.[4] Bedaquiline received marketing approval in Korea after approval in the United States and Europe based on efficacy and safety data from pivotal Phase II trials.[5,6] MDR-TB affects individual HRQOL and social productivity significantly. Therefore, a cost-effectiveness evaluation of this new MDR-TB treatment agent is urgent and of high priority for MDR-TB control in the ROK.

The cost-effectiveness of bedaquiline has been assessed and the results published in the United Kingdom. However, an analysis of the cost-effectiveness of bedaquiline in the ROK is necessary because the ROK has a different disease burden and medical circumstances from those of UK. Cost-effectiveness analyses in the ROK could then be referred to by other countries with incidences of MDR-TB and XDR-TB (including pre–XDR-TB) that are similar to those in the ROK. Therefore, the objective of this study was to compare the cost-effectiveness of bedaquiline + the standard regimen (SR) to that of SR only for the treatment of MDR-TB or XDR-TB patients. The results from this analysis will assist health care providers in selecting the optimal therapeutic strategy for managing MDR-TB.

PATIENTS AND METHODS

Target Population, Comparator, and Settings

This study targeted patients with MDR-TB or XDR-TB in the ROK based on the approved indication of bedaquiline. MDR-TB patients co-infected with HIV were excluded because the rate of TB/HIV co-infection in the ROK is very low.[2] The currently practiced SR for the treatment of MDR-TB was used as the comparator. The drugs used in the SR were aligned with the Korean tuberculosis treatment guidelines[7] and WHO guidelines[8] (see **Supplemental Table I** in the online version at http://dx.doi.org/10.1016/j.clinthera.2016.01.023). The dosage and administration were set as the approved label in the ROK, and the proportions of drugs in the SR were based on the pivotal study on bedaquiline, clinical study C208.[9] In clinical practice, proportions of drugs in the SR are diverse according to physician or institution, and the effect of regimen difference was evaluated through a sensitivity analysis by varying the proportions of the SR based on consultation with experts. A health-service perspective horizon of 20 years and a 5% discount rate for cost and benefits were applied to the base-case analysis.

Model

The model for this study was based on the previous bedaquiline cost-effectiveness study in the United Kingdom[10] and modified in accordance with Korean clinical practice. The UK model applied a cohort-based Markov state transition model to evaluate the long-term economic and health benefits of achieving sputum culture conversion in patients with MDR-TB. We added XDR-TB patients to the starting population because they constitute a relatively large number of patients in the ROK (**Figure 1**). One cycle was set as 28 days in order to reflect the sputum culture conversion over time. The model had 9 mutually exclusive core health states: active MDR-TB, active XDR-TB, active secondary MDR-TB, sputum culture conversion, treatment completion, cured, surgery (lung resection), loss to follow-up, and death. *Sputum culture conversion* was defined as maintaining negative results for more than 2 consecutive sputum culture conversion tests spaced over 25 days apart after 6 months. If patients were not transferred to surgery or lost to follow-up or to death, they had to be treated for 18 months after they achieved sputum culture conversion. If they relapsed to a culture-positive status before