Cost-effectiveness Analysis of Treatment Sequence Initiating With Etanercept Compared With Leflunomide in Rheumatoid Arthritis: Impact of Reduced Etanercept Cost With Patent Expiration in South Korea

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ABSTRACT

Purpose: In south Korea, the price of biologics has been decreasing owing to patent expiration and the availability of biosimilars. This study evaluated the cost-effectiveness of a treatment strategy initiated with etanercept (ETN) compared with leflunomide (LFN) after a 30% reduction in the medication cost of ETN in patients with active rheumatoid arthritis (RA) with an inadequate response to methotrexate (MTX-IR).

Methods: A cohort-based Markov model was designed to evaluate the lifetime cost-effectiveness of treatment sequence initiated with ETN (A) compared with 2 sequences initiated with LFN: LFN-ETN sequence (B) and LFN sequence (C). Patients transited through the treatment sequences, which consisted of sequential biologics and palliative therapy, based on American College of Rheumatology (ACR) responses and the probability of discontinuation. A systematic literature review and a network meta-analysis were conducted to estimate ACR responses to ETN and LFN. Utility was estimated by mapping an equation for converting the Health Assessment Questionnaire-Disability Index score to utility weight. The costs comprised medications, outpatient visits, administration, dispensing, monitoring, palliative therapy, and treatment for adverse events. A subanalysis was conducted to identify the influence of the ETN price reduction compared with the unreduced price, and sensitivity analyses explored the uncertainty of model parameters and assumptions.

Findings: The ETN sequence (A) was associated with higher costs and a gain in quality-adjusted life years (QALYs) compared with both sequences initiated with LFN (B, C) throughout the lifetime of patients with RA and MTX-IR. The incremental cost-effectiveness ratio (ICER) for strategy A versus B was ₩13,965,825 (US$1726) per QALY and that for strategy A versus C was ₩9,587,983 (US$8050) per QALY. The results indicated that strategy A was cost-effective based on the commonly cited ICER threshold of ₩20,000,000 (US$16,793) per QALY in South Korea. The robustness of the base-case analysis was confirmed using sensitivity analyses. When the unreduced medication cost of ETN was applied in a subanalysis, the ICER for strategy A versus B was ₩20,909,572 (US$17,556) per QALY and that for strategy A versus C was ₩22,334,713 (US$18,753) per QALY.

Implications: This study indicated that a treatment strategy initiated with ETN was more cost-effective in patients with active RA and MTX-IR than 2 sequences initiated with LFN. The results also indicate that the reduced price of ETN affected the cost-effectiveness associated with its earlier use. (*Clin Ther.* 2016;38:2430–2446)

Key words: cost-effectiveness, early biologics use, etanercept, reduced price, rheumatoid arthritis.

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INTRODUCTION

The goal of rheumatoid arthritis (RA) treatment is to control the progression, symptoms, and signs of disease and to achieve a maximum quality of life.[1] It is believed that the treatment goal could be achieved by initiating the right treatment at the appropriate time.[2] Previous studies have found that aggressive and earlier treatment of RA is associated with better efficacy,[2,3] which might have been attributable to the treatment preventing the progression of irreversible joint damage during early RA.[4,5] In particular, biologic disease-modifying antirheumatic drugs (bDMARDs) were found to be superior to conventional disease-modifying antirheumatic drugs (cDMARDs).[2,6]

Despite the better clinical efficacy with earlier bDMARD use, the cost-effectiveness of early and aggressive bDMARDs remains uncertain because of higher medication costs for bDMARDs compared with those of cDMARDs.[7–9] Kvamme et al[9] reported that treatment with bDMARDs resulted in greater total RA-related costs, including medication costs that were approximately 80 times higher than those of cDMARDs. The cost-effectiveness of bDMARDs was assessed to evaluate whether the high medication costs are offset by improved quality of life and reduced health care use in patients with RA.[7] In most previous studies, the high medication costs of bDMARDs were not compensated with gain in quality-adjusted life years (QALYs) and reduced all-cause health care costs, excluding the medication costs, so the cost-effectiveness remained uncertain.[7,8,10]

Owing to the doubtful cost-effectiveness of earlier bDMARD use, bDMARDs are restricted to patients who have experienced inadequate responses (IRs) to at least 2 cDMARDs in several European countries, Taiwan, and South Korea.[11–14] However, the medication costs for bDMARDs are decreasing owing to the expiration of bDMARD patents and the introduction of biosimilars worldwide.[15] A lower price might reduce the economic burden for both payers and patients and allow for earlier bDMARDs use.[14] In addition, because of the reduced medication cost, there is a greater probability that earlier bDMARD use is cost-effective. Previously, the high cost for bDMARDs was the leading reason for the uncertainty surrounding the cost-effectiveness of earlier bDMARD use.

The price of etanercept (ETN), which has been used to treat RA since 2005, decreased by 30% in South Korea after its patent expired in 2016. The reduction in the price of ETN made it reasonable to reconsider the cost-effectiveness of earlier ETN use, which was previously uncertain because of the high price of ETN. This study aimed to evaluate the cost-effectiveness of earlier ETN use, compared with the use of leflunomide (LFN), followed by bDMARDs for patients with RA and an IR to methotrexate (MTX-IR). LFN is a cDMARD that is often used after a failed response to methotrexate (MTX),[16] and the combination of LFN with MTX has produced the greatest efficacy among the available cDMARDs in patients with MTX-IR.[17] Therefore, treatment sequences initiated with LFN were used as comparators and represented the current clinical practice for patients with RA and MTX-IR.

METHODS

Overview of Cost-utility Analysis

Cost-utility analysis was performed to compare the cost-effectiveness of earlier ETN use with the use of LFN followed by bDMARDs for patients with RA and MTX-IR after the cost of ETN decreased by 30%. Two treatment sequences initiated with LFN (B and C) were considered and compared with a sequence initiated with ETN (A). Sequence B involved the use of ETN after a failure of LFN and was defined as the LFN-ETN sequence. The LFN-ETN sequence was to identify the cost-effectiveness of starting ETN use earlier. Sequence C was defined as the LFN sequence and involved the use of LFN in place of ETN. The LFN sequence was used to determine the cost-effectiveness of the alternatively used ETN instead of LFN.

A cohort-based Markov model, commonly used to evaluate the cost-effectiveness of RA treatment, was designed using MS Excel 2010 (Microsoft Inc., Redmond, Washington).[18] In this model, the cohort progressed through the treatment sequences, taking into account that RA guidelines suggest that patients are continuously treated with sequential treatment.[19,20] However, the preferences for determining bDMARD treatment were not presented in the RA guidelines. Therefore, the treatment sequences were constructed considering the biologics' mechanism of action and actual clinical practice conditions (Figure 1).[19,20] Sequences A and C were made up of 5-phase treatments with an identical 4-phase treatment after the first-order treatment as follows: first-order treatment