Cost-utility of First-line Disease-modifying Treatments for Relapsing–Remitting Multiple Sclerosis

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ABSTRACT

Purpose: This study evaluated the cost-effectiveness of first-line treatments of relapsing–remitting multiple sclerosis (RRMS) (dimethyl fumarate [DMF] 240 mg PO BID, teriflunomide 14 mg once daily, glatiramer acetate 20 mg SC once daily, interferon [IFN]-β1a 44 μg TIW, IFN-β1b 250 μg EOD, and IFN-β1a 30 μg IM QW) and best supportive care (BSC) in the health care payer setting in Finland.

Methods: The primary outcome was the modeled incremental cost-effectiveness ratio (ICER; €/quality-adjusted life-year [QALY] gained, 3%/y discounting). Markov cohort modeling with a 15-year time horizon was employed. During each 1-year modeling cycle, patients either maintained the Expanded Disability Status Scale (EDSS) score or experienced progression, developed secondary progressive MS (SPMS) or showed EDSS progression in SPMS, experienced relapse with/without hospitalization, experienced an adverse event (AE), or died. Patients' characteristics, RRMS progression probabilities, and standardized mortality ratios were derived from a registry of patients with MS in Finland. A mixed-treatment comparison (MTC) informed the treatment effects. Finnish EuroQol Five-Dimensional Questionnaire, Three-Level Version quality-of-life and direct-cost estimates associated with EDSS scores, relapses, and AEs were applied. Four approaches were used to assess the outcomes: cost-effectiveness plane and efficiency frontiers (relative value of efficient treatments); cost-effectiveness acceptability frontier, which demonstrated optimal treatment to maximize net benefit; Bayesian treatment ranking (BTR); and an impact investment assessment (IIA; a cost-benefit assessment), which increased the clinical interpretation and appeal of modeled outcomes in terms of absolute benefit gained with fixed drug-related budget. Robustness of results was tested extensively with sensitivity analyses.

Findings: Based on the modeled results, teriflunomide was less costly, with greater QALYs, versus glatiramer acetate and the IFNs. Teriflunomide had the lowest ICER (24,081) versus BSC. DMF brought marginally more QALYs (0.089) than did teriflunomide, with greater costs over the 15 years. The ICER for DMF versus teriflunomide was 75,431. Teriflunomide had >50% cost-effectiveness probabilities with a willingness-to-pay threshold of <€77,416/QALY gained. According to BTR, teriflunomide was first-best among the disease-modifying therapies, with potential willingness-to-pay thresholds of up to €68,000/QALY gained. In the IIA, teriflunomide was associated with the longest incremental quality-adjusted survival and time without cane use. Generally, primary outcomes results were robust, based on the sensitivity analyses. The results were sensitive only to large changes in analysis perspective or mixed-treatment comparison.

Implications: The results were sensitive only to large changes in analysis perspective or MTC. Based on the analyses, teriflunomide was cost-effective versus BSC or DMF with the common threshold values, was dominant versus other first-line RRMS treatments, and provided the greatest impact on investment. Teriflunomide is potentially the most cost-effective option among first-line treatments of

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Key words: cost-effectiveness, dimethyl fumarate, economic evaluation, glatiramer acetate, interferon-β, teriflunomide.

INTRODUCTION

Multiple sclerosis (MS)—a chronic progressive, autoimmune, inflammatory disease—affects >2 million people worldwide. Approximately 89% of cases are classified as relapsing–remitting MS (RRMS) at the time of diagnosis.[1] MS prevalence is particularly high in the United Kingdom, the United States, Canada, Germany, and Scandinavia.[2,3] In Finland, MS prevalence varies regionally, from 100 to 200 per 100,000 inhabitants.[4–7]

In young adults with MS, prognosis is based on an individual's factors.[1] The progression and accumulating disability cause a significant human and economic burden[8–15] and the need for support.[16]

The risk for death among Finnish patients with MS is 2.8-fold compared with that in the general population, being 3.4-fold in women and 2.2-fold in men as early as 2 to 10 years after diagnosis.[17] Relapse, MS progression, and disability level (eg, higher Expanded Disability Status Scale [EDSS] score[18]) are associated with a higher risk for mortality,[17,19,20] additional costs,[9–14] and quality of life (QoL) losses.[9,10,12,14,21–24]

MS treatment with disease-modifying therapies (DMTs) is aimed at decreasing the inflammatory activity leading to relapses, stopping or slowing progression of residual disability, and, eventually, delaying the progression to the secondary progressive phase. However, long-term prognosis among treated patients is largely unknown. Based on Finnish drug reimbursement and sales data,[25] commonly used first-line DMTs include injectable DMTs, namely glatiramer acetate (GA), interferon (IFN)-β1a IM, IFN-β1a SC, and IFN-β1b SC.

Dimethyl fumarate (DMF) and teriflunomide are new oral DMTs reimbursed as the first-line treatment of RRMS in Finland. The efficacy and safety of DMF 240 mg BID for established MS have been studied in the Phase III CONFIRM (Comparator and an Oral Fumarate in Relapsing-Remitting Multiple Sclerosis)[26,27] and DEFINE (Determination of the Efficacy and Safety of Oral Fumarate in Relapsing–Remitting MS)[28,29] trials (ClinicalTrials.gov identifiers: NCT00451451 and NCT00420212, respectively). The efficacy and safety of teriflunomide 14 mg once daily for established MS have been demonstrated in the Phase III TEMSO (Teriflunomide Multiple Sclerosis Oral Teriflunomide for Relapsing Multiple Sclerosis)[30–33] and TOWER (Teriflunomide Oral in People With Relapsing Multiple Sclerosis)[34,35] trials (NCT00134563 and NCT00751881, respectively), and in patients with a first clinical episode suggestive of MS in the TOPIC (Oral Teriflunomide for Patients with a First Clinical Episode Suggestive of Multiple Sclerosis)[36] trial (NCT00622700). Effectiveness of teriflunomide compared with IFN-β1b SC has been demonstrated in the Phase III TENERE (Teriflunomide and Rebif® in Patients with Relapsing Multiple Sclerosis)[37] trial (NCT00883337).

We evaluated the cost-utility of injectable and oral first-line DMTs in the Finnish population of patients with RRMS, based on a decision-analytical model. To our knowledge, there are no previously published journal articles on the cost-utility of first-line oral DMTs in a European setting or on oral and injectable DMTs for first-line treatment of RRMS. In addition, progression of RRMS in Finnish patients has not been assessed before, and the 4 different approaches elaborating the key results from MS cost-utility analysis have not been previously reported.

MATERIALS AND METHODS

The cost-utility of the first-line DMTs in the Finnish RRMS population was assessed in a decision-analytical modeling framework[38] by implementing a Markov cohort model with mutually exclusive health states in Excel 2007, including Visual Basic for Applications (Microsoft Corporation, Redmond, Washington). The modeling approach followed the Finnish guidance for health economic analyses.[39]

The primary outcome of analysis was the modeled incremental cost-effectiveness ratio (ICER), reported as Euros per quality-adjusted life-year (€/QALY) gained. The interpretation of ICER is challenging in Finland because the decision maker's willingness-to-pay (WTP) threshold per QALY gained has not been publicly declared,[40] and significant variation in