Cost-utility analysis (CUA) of first-line disease-modifying treatments (DMT) versus best supportive care (BSC) in Finnish relapsing-remitting multiple sclerosis (RRMS) patients

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Background
Multiple sclerosis (MS) is a chronic, progressive, immune-mediated, neurodegenerative disease of the central nervous system, accumulating patients' disability over time and causing significant human and economic burden. Approximately 80-90% of the incident MS cases are relapsing-remitting MS (RRMS) characterised by phases of remission and relapse. Important goals of the disease-modifying drug treatment (DMT) in MS are to arrest or slow the accumulation of disability (measured on the Expanded Disability Status Scale, EDSS) and delay progression of the disease to secondary progressive multiple sclerosis (SPMS).

Key study methods included a Finnish register study and Markov cohort modelling. A simplified presentation of the Markov model is given in Figure 1.

Methods
- The following outcomes were included in the base-case analysis: direct health care costs, societal costs and quality-adjusted life-years (QALY) based on EQ-5D.
- Local register data
- EDSS-related standardised mortality ratios (SMR) and RRMS-progression matrix

Decision analytic modelling
During the modelled 50-year time horizon, patients could stay in, or progress to, EDSS-related standardised mortality ratios (SMR) and RRMS-progression matrix.

Local register data
EDSS-related standardised mortality ratios (SMR) and RRMS-progression matrix were analysed from a Finnish MS-register (1359 patients from Tampere, Vaasa, Seinäjoki regions). Other health risks were based on literature. Cohort characteristics were estimated from a subgroup of the Finnish register patients who fulfilled the indication of modelled treatment comparators (713 patients applicable for 1st line DMTs: clinically confirmed RRMS, age, gender and EDSS 0-6.5 at first DMT initiation).

Health economic analysis
The following outcomes were considered in the base-case analysis: direct health care costs, quality-adjusted life-years (QALY) based on EQ-5D, incremental cost-effectiveness ratios (ICER, the primary outcome), cost-effectiveness efficiency frontier (CEF) and expected value of perfect information per patient (EVPI). Costs and QALYs were discounted with 3% per year.

The CEEF demonstrates the maximum monetary value of parameter uncertainty that can be resolved by acquiring perfect evidence for the model parameters or alternatively the expected monetary consequences related to wrong treatment acquisition decision. Quality of life estimates, which were derived from literature, and Finnish costs (health-care costs in year 2013 value, drug costs without VAT in Aug'2014 value) were associated with EDSS, relapses, and AIDS. Indirect treatment comparison informed treatment effects.

Results
Expected lifetime healthcare (base case) costs, societal costs and QALYs per patient were given in Table 1. From the payer or societal perspectives and over a 50 years' time horizon, teriflunomide 14 mg was dominant (less costly and more effective) compared to other first-line DMTs. Furthermore, teriflunomide 14 mg was cost-effective when compared to BSC with an ICER of 8,572 €/QALY gained for the payer perspective and dominant for the societal perspective.

Conclusion
A simplified presentation of the Markov model is given in Figure 1.

Figure 2 shows the CEEF from the payer perspective. The CEEF includes teriflunomide 14 mg and BSC.

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Sensitivity analysis
Caregiver disutility and Finnish productivity losses and informal care costs were included in sensitivity analysis (societal perspective).

The CEEF shows the ICERs of non-dominated treatments. The EVPI per patient care costs, quality-adjusted life-years (QALY) based on EQ-5D, incremental cost-utility analysis (CUA) of first-line disease-modifying treatments (DMT) versus best supportive care (BSC) in Finnish relapsing-remitting multiple sclerosis (RRMS) patients

<table>
<thead>
<tr>
<th>Outcome Costs (€)</th>
<th>QALYs</th>
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<tbody>
<tr>
<td>Teriflunomide*</td>
<td>801,306 €</td>
</tr>
<tr>
<td>Avonex® 30mcg</td>
<td>816,974 €</td>
</tr>
<tr>
<td>INFβ-1a-SC</td>
<td>780,301 €</td>
</tr>
<tr>
<td>INFβ-1b-IM</td>
<td>817,677 €</td>
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</tbody>
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Teriflunomide (Aubagio® 14mg) and other first-line DMTs glatiramer acetate (GA: Copaxone® 20mg), interferon-β-1a (INFβ-1a; intramuscular (IM) Avonex® 40mg, subcutaneous (SC) Rebif® 44mcg) or interferon-β-1b (INFβ-1b; Betaseron® 250mcg), compared to best supportive care (BSC) in Finnish RRMS-patients.