Cost-effectiveness Of Ofatumumab In Comparison With Other Disease Modifying Therapies And Best Supportive Care For The Treatment Of Relapsing-Remitting Multiple Sclerosis In Canada

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Introduction

- Ofatumumab is the first fully human monoclonal anti-CD20 antibody approved in Canada for the initial treatment of relapsing-remitting multiple sclerosis (RRMS) with active disease
- A network meta-analysis (NMA) demonstrated that ofatumumab has similar effectiveness to other highly efficacious monoclonal antibodies with respect to reducing relapse rates and disability progression

Method Overview

- Objective: To evaluate the cost effectiveness of ofatumumab against other DMTs and best supportive care (BSC) for the treatment of adult patients with RRMS from a Canadian public healthcare system perspective

Methods

- Model Overview
  - A Markov cohort model with 10 total health states representing disability status defined by the Expanded Disability Status Scale (EDSS) levels 0 to 9 and a single state for death (EDSS 10) was constructed
  - Run over 65-years using annual cycle lengths
  - Costs and effects discounted at 1.5% per annum
  - 100% treatment discontinuation imposed at 10 years
  - Analyses conducted probabilistically using an incremental analysis considering dominance
  - Baseline patient distribution was informed by a pooled analysis of the ASCLEPIOS trials
  - Each year, patients could transition between EDSS states, experience a relapse, discontinue therapy, or die (Fig 1)

Natural history data:
- Transition probabilities between EDSS states were informed by British Columbia data
- Annualized relapse rates (ARR) were EDSS-dependent1-4; relapse severity was defined as mild (47%), moderate (35%) or severe (18%)5
- Mortality rates were adjusted for the MS population using an EDSS-dependent MS-specific hazard ratio6

Treatment-specific model inputs:
- Treatment effects for each DMT were modelled using hazard ratios for 6-month confirmed disability progression and AHR from an NMA
- Discontinuation rates for each DMT were calculated using the relative effect estimates from the NMA using ofatumumab as a reference arm
- Discontinuation rates for first-line DMTs were constant for 9 years, followed by 100% discontinuation at 10 years based on clinician opinion; discontinuation rate for cladribine was adjusted to 16% after 2 years8
- Adverse event (AE) probabilities were modelled as non-serious and serious, sourced from each of the treatments’ pivotal trials, or from a pivotal trial where the treatment was a comparator

Figure 1. Model Structure

Rounded squares: health states; rounded rectangles: events that patients could experience at any time. Patients who reached an EDSS score of ≥7 while on treatment would discontinue and receive BSC; BSC: best supportive care; EDSS: Expanded Disability Status Scale.

Methods – cont.

Cost inputs:
- Direct medical costs for EDSS 1 to 6 were sourced from Grima et al.9, while EDSS 7 to 9 costs were extrapolated based on Patwardhan et al.10
- Professional care costs were added to the total health state costs
- Mild/moderate relapse costs ($7,275) were included12; severe ($17,459) relapse costs were extrapolated based on Patwardhan et al.11
- Drug acquisition costs (Table 1) were sourced from Ontario formularies13,14 and manufacturer anticipated list price for ofatumumab
- Administration and monitoring costs (Table 1) were sourced from the Ontario Schedule of Benefits15-17, Ontario Case Costing Initiative10, published literature18, and clinician opinion
- Costs for a physician visit and an MS Day Case admission were assumed for non-serious AEs ($84)19 and serious AEs ($363)11, respectively

Utilities and Disutilities:
- Mean utility values were derived from normative utility data for the Canadian population (EDSS 0-9)20 and a Canadian study of MS patients (EDSS 1 to 9)21
- Relapse disutilities distinguished between mild or moderate severe relapses and have been used in previous economic models22
- Disutilities for AEs were derived based on assumptions and are aligned with previous MS economic models23

Results

- Considering DMTs with a first-line indication in pair-wise analyses, ofatumumab was dominant (more efficacy, lower costs) vs. teriflumide, interferons, dimethyl fumarate, and ocrelizumab; and resulted in incremental cost-effectiveness ratios (ICERs) of $24,177 CAD per quality-adjusted life-year (QALY) gained vs. glatiramer acetate and $28,034 vs. BSC (Table 2)
- Considering dominance in an incremental analysis resulted in only ofatumumab and BSC on the efficiency frontier; ofatumumab had an ICER of $28,034 vs. BSC
- At a WTP threshold of $50,000/QALY gained, ofatumumab had the highest probability of being cost effective at 63.3%
- Scenario analyses against DMTs with a second-line indication are presented in Table 2; at a WTP threshold of $50,000/QALY gained, ofatumumab had the highest probability of being cost effective at 40.9%

Table 1. Drug acquisition, administration, and monitoring (A&M) costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost (CAD)</th>
<th>Drug cost (YD)</th>
<th>A&amp;M cost (CAD)</th>
<th>A&amp;M cost (YD)</th>
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<td>Ofatumumab</td>
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<td>Ocrelizumab</td>
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<td>Finglizomd</td>
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Scenario analyses (second-line therapies)

<table>
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<tr>
<th>Drug</th>
<th>Cost (CAD)</th>
<th>Cost (YD)</th>
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<tr>
<td>Cladribine</td>
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<td>Natalizumab</td>
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</table>

Costs for a physician visit and an MS Day Case admission were assumed for non-serious AEs ($84)16 and serious AEs ($363)11, respectively

Conclusions:

- Ofatumumab is cost effective against all comparators and dominant compared to all currently approved and reimbursed DMTs with a first-line indication, except glatiramer acetate, from a Canadian public healthcare system perspective
- Cost savings associated with ofatumumab suggest greater disease management, reflected by increased QALYs gained, at a lower cost
- Ofatumumab’s cost effectiveness, alongside its high-efficacy and favourable safety profile, demonstrate its value as an early treatment option in RRMS

References:

14. Ontario Case Costing Initiative. 2015

Disclosures

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