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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Disclosures

Soukaïna Mouallif and François Blanchette are employees of Novartis Pharmaceutical Canada Inc.

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Background

- 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 antibody therapies with respect to reducing relapse rates and disability progression[1]
- Ofatumumab has a favourable safety profile that is similar to the widely used first-line disease modifying therapy (DMT), teriflunomide[2]
- It is important to assess the cost effectiveness of ofatumumab compared to currently available DMTs for RRMS

DMT: disease modifying therapy; NMA: network meta-analysis; RRMS: relapsing-remitting multiple sclerosis.

1. Samjoo et al. *J Comp Eff Res.* 2021;10(6):495-507; 2. Hauser et al. *N Engl J Med.* 2020; 383(6):546-557.

Objectives

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

DMT: disease modifying therapy; RRMS: relapsing-remitting multiple sclerosis.

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[2]
  - Each year, patients could transition between EDSS states, experience a relapse, discontinue therapy, or die (**Figure 1; next slide**)

EDSS: Expanded Disability Status Scale.

2. Hauser et al. *N Engl J Med.* 2020; 383(6):546-557

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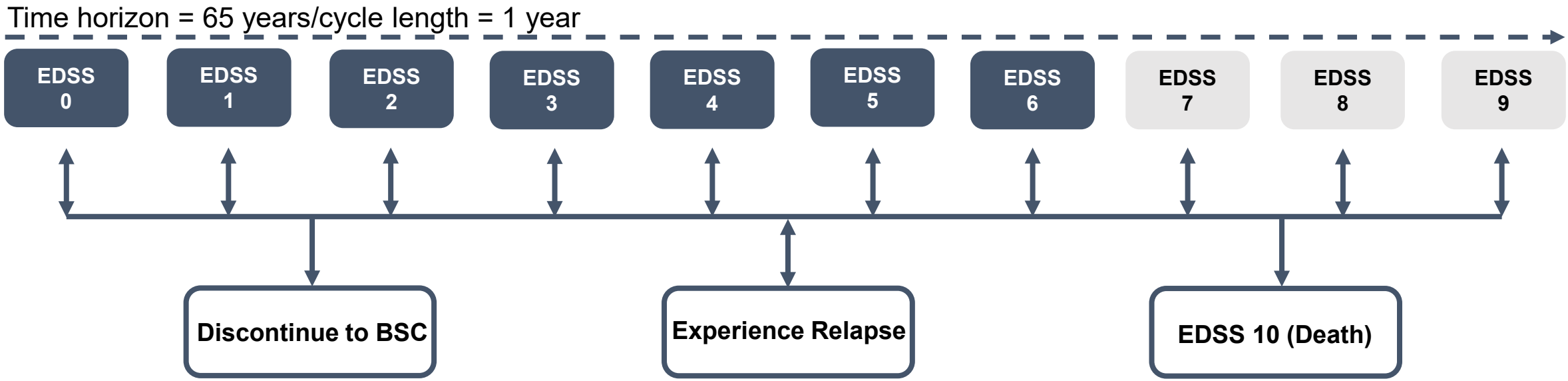
Figure 1. Model Structure



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

- ***Natural history data***
  - Transition probabilities between EDSS states were informed by the British Columbia MS database[3]
  - Annualized relapse rates (ARR) were EDSS-dependent[4-6]
  - Relapse severity was defined as mild (47%), moderate (35%) or severe (18%)[7]
  - Mortality rates were adjusted for the MS population using an EDSS-dependent MS-specific hazard ratio[8]

ARR: annualized relapse rates; EDSS: Expanded Disability Status Scale; MS: multiple sclerosis.

3. Palace et al. *BMJ Open.* 2014;4(1):e004073; 4. Mauskopf et al. *J Med Econ.* 2016;19(4):432-42; 5. Patzold and Pocklington, *Acta Neurol Scand.* 1982;65(4):248-66; 6. Orme et al. *Value in health.* 2007;10(1):54-60; 7. Mowry et al. *PLoS One.* 2013;8(10):e75416; 8. Pokorski. *J Insur Med.* 1997;29(2):101-6.

Methods

- ***Treatment-specific model inputs***
  - Treatment effects for each DMT were modelled using hazard ratios for 6-month confirmed disability progression and ARR from an NMA[1]
  - Discontinuation rates for each DMT were calculated using the relative effect estimates from the NMA using ofatumumab as a reference arm[1]
  - Discontinuation rates for first-line DMTs were constant for 9 years, followed by 100% discontinuation at 10 years based on clinician opinion; the discontinuation rate for cladribine was adjusted to 16% after 2 years[9]
  - Adverse event 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

ARR: annualized relapse rates; DMT: disease modifying therapy; NMA: network meta-analysis.

1. Samjoo et al. *J Comp Eff Res.* 2021;10(6):495-507; 9. CADTH. CDR Pharmacoeconomic Review Report for Lemtrada. 2015.

Methods

- ***Cost inputs***
  - Direct medical costs for EDSS 1 to 6 were sourced from Grima et al.[10], while EDSS 7 to 9 costs were extrapolated based on Patwardhan et al.[11]
  - Professional care costs were added to the total health state costs[12]
  - Mild/moderate relapse costs ($7,275) were informed by Karampampa et al.[12]
  - Severe relapse costs ($17,459) were extrapolated based on Patwardhan et al.[11]

EDSS: Expanded Disability Status Scale.

10. Grima et al. Multiple sclerosis. 2000;6(2):91-8; 11. Patwardhan et al. Multiple sclerosis. 2005;11(2):232-9; 12. Karampampa et al. J Popul Ther Clin Pharmacol. 2012; 19(1):e11-25.

Methods

- ***Cost inputs - continued***
  - Drug acquisition costs (**Table 1; next slide**) were sourced from Ontario formularies[13,14] and manufacturer anticipated list price for ofatumumab
  - Administration and monitoring costs (**Table 1; next slide**) were sourced from the Ontario Schedule of Benefits[15,16], Ontario Case Costing Initiative[17], formularies[13,14], published literature[18], and clinician opinion
  - Costs for a physician visit and an MS Day Case admission were assumed for non-serious adverse events ($84)[16] and serious adverse events ($363)[17], respectively

MS: multiple sclerosis.

13. Government of Ontario. Ontario Drug Benefit Formulary. 2021; 14. Ontario Exceptional Access Program Formulary. 2021; 15. Ontario Ministry of Health. Schedule of Benefits, Lab Services. 2020; 16. Ontario Ministry of Health. Schedule of Benefits, Physician Services. 2021; 17. Ontario Case Costing Initiative. 2018;18. Tam et al. Curr Oncol. 2013; 20(2):e90-e106.

Methods

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

Drug	Drug cost (Year 1)	Drug cost (Year 2)	A&M cost (Year 1)	A&M cost (Year 2+)
Base case analysis (first-line therapies)				
Ofatumumab[a]	$30,917	$26,500	$1,136	$38
Ocrelizumab[14]	$32,600	$32,600	$3,374	$1,581
Teriflunomide[14]	$22,005	$22,005	$1,196	$38
Dimethyl fumarate[14]	$26,606	$26,863	$1,141	$74
Glatiramer acetate[13]	$11,834	$11,834	$1,125	$38
Avonex[14]	$24,886	$24,886	$1,261	$84
Rebif 22[14]	$23,610	$23,610	$1,261	$84
Rebif 44[14]	$28,743	$28,743	$1,261	$84
Betaseron[14]	$20,089	$20,089	$1,631	$70
Extavia[14]	$19,119	$19,119	$1,631	$70
Best supportive care	$0	$0	$0	$0
Scenario analysis (second-line therapies)				
Cladribine[b,14]	$44,968	$44,968	$1,158	$82
Natalizumab[14]	$46,911	$46,911	$6,397	$3,681
Fingolimod[13]	$26,996	$26,996	$1,682	$84

*Canadian dollars. [a]Manufacturer's submitted price; [b]Cost for cladribine was only applied in Year 2 unless a patient was treated with a third dose, in which case the cost would also be applied to Year 3; Year 2+: year 2 and beyond. A&M = administration and monitoring.
[13]Ontario Drug Benefit Formulary. 2021; [14]Ontario Exceptional Access Program Formulary. 2021.

Methods

- ***Utilities and Disutilities***
  - Mean utility values were derived from normative utility data for the Canadian population (EDSS 0)[19] and a Canadian study of MS patients (EDSS 1 to 9)[20]
  - Relapse disutilities distinguished between mild or moderate and severe relapses and have been used in previous economic models[21-23]
  - Disutilities for adverse events were based on assumptions and aligned with previous MS economic models[4]

EDSS: Expanded Disability Status Scale; MS: multiple sclerosis.

4. Mauskopf et al. *J Med Econ*. 2016;19(4):432-42; 19. Guertin et al. *CMAJ.* 2018;190(6):E155-E161; 20. Tappenden et al. *Value in health.* 2009;12(5):657-65; 21. Chirikov et al. *Value in health*. 2019;22(2):168-176; 22. CADTH therapeutic review. 2013; 23. Prosser et al. *Value in health*. 2004;7(5):554-68.

Results

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- Considering DMTs with a first-line indication in pair-wise analyses, ofatumumab was dominant (more efficacy, lower costs) vs. teriflunomide, interferons, dimethyl fumarate, and ocrelizumab
- Ofatumumab 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. best supportive care (**Table 2; next slide**)
- Considering dominance in an incremental analysis resulted in only ofatumumab and best supportive care on the efficiency frontier; ofatumumab had an ICER of $28,034 vs. best supportive care
- At a willingness to pay threshold of $50,000/QALY gained, ofatumumab had the highest probability of being cost effective at 63.3%
- Scenario analysis results against DMTs with a second-line indication are presented in **Table 2** (**next slide**); at a willingness to pay threshold of $50,000/QALY gained, ofatumumab had the highest probability of being cost effective at 40.9%

DMT: disease modifying therapy; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year.

Results

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Table 2. Results of the base case and scenario probabilistic analyses (pair-wise comparisons)*

			Ofatumumab vs. Comparator		
Drug	**Total cost**	**QALY**	**Incremental cost**	**Incremental QALY**	**ICER ($ per QALY)**
Base case analysis (first-line therapies)					
Ofatumumab	$743,015	9.261	-	-	-
Ocrelizumab	$784,832	9.131	-$41,817	0.130	Dominant†
Teriflunomide	$761,998	7.933	-$18,983	1.328	Dominant†
Dimethyl fumarate	$771,029	8.327	-$28,014	0.934	Dominant†
Glatiramer acetate	$713,474	8.039	-$29,541	1.222	$24,177
Avonex	$770,188	8.102	-$27,173	1.159	Dominant†
Rebif 22	$756,048	8.072	-$13,033	1.189	Dominant†
Rebif 44	$781,810	7.978	-$38,795	1.283	Dominant†
Betaseron	$759,927	8.025	-$16,911	1.236	Dominant†
Extavia	$755,037	8.021	-$12,022	1.240	Dominant†
Best supportive care	$689,506	7.352	$53,509	1.909	$28,034
Scenario analysis (second-line therapies)					
Cladribine	$715,734	8.725	$27,282	0.536	$50,899
Natalizumab	$869,833	9.123	-$126,818	0.138	Dominant†
Fingolimod	$772,790	8.410	-$29,775	0.851	Dominant†

*Canadian dollars.†Ofatumumab dominant vs. comparator; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year.

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

DMT: disease modifying therapy; QALY: quality-adjusted life-year; RRMS: relapsing-remitting multiple sclerosis.

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