Poster
EE15

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

Fatine Farhane[1], Virender Bhan[2], Fraser Clift[3], Moogeh Baharnoori[4], Kimberly Thomas[5], Barkha P. Patel[5], François Blanchette[1], Nicholas Adlard[6], Umakanth Vudumula[7], Kapil Gudala[8], Nikkita Dutta[5], Daniel Grima[5], Soukaïna Mouallif[1]

[1]Novartis Canada Inc., QC, Canada; [2]Dept. of Medicine, Queen's University, ON, Canada; [3]Dept. Of Neurology, Memorial University of Newfoundland, NL, Canada; [4]Dept. Of Medicine, Division of Neurology, Queen's University, ON, Canada; [5]CRG-EVERSANA, ON, Canada; [6]Novartis Pharma AG, Basel, Switzerland; [7]Novartis Ireland Inc., Dublin, Ireland; [8]Novartis Healthcare Pvt. Ltd., Hyderabad, India

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 antibody therapies with respect to reducing relapse rates and disability progression, as well as a favourable safety profile[1,2]
- Given patients with RRMS may experience deteriorating physical and mental wellbeing, as well as economic instability, it is important to assess the costs and consequences of treatment with ofatumumab versus other first-line and second-line disease modifying therapies (DMTs) and best supportive care (BSC) in patients with RRMS

Objective

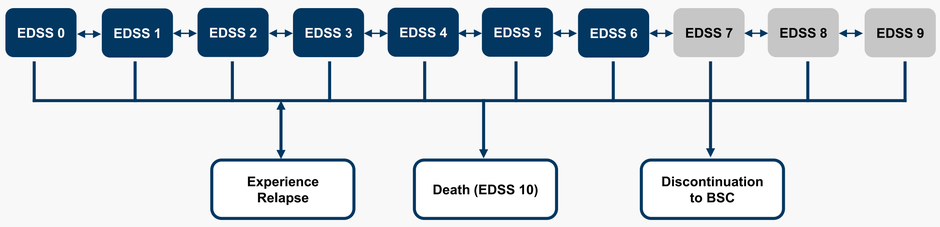
- To evaluate the costs and consequences of ofatumumab as an initial therapy versus other DMTs and BSC in adults with RRMS with active disease from a Canadian healthcare system perspective
- A scenario analysis also examined the impact of administering ofatumumab as a first-line therapy versus delaying ofatumumab (3 years vs. 5 years) until after treatment with commonly administered first-line therapies

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
- The model used a 10-year time horizon with annual cycles and 1.5% discounting
- 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**)

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.

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 was adjusted for the MS population using an EDSS-dependent MS-specific hazard ratio[8]
- MS-specific disability weights were informed by Cho et al.[9] and linear interpolation, while hospitalization days were EDSS-dependent and based on clinician-validated assumptions
- Productivity loss due to disability and retirement were EDSS-dependent and informed by Grima et al.[10] and Karampampa et al.[11], respectively, and modified based on clinician input

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[12]

Cost inputs:

- Direct medical costs were informed by Grima et al.[10], Karampampa et al.[11], and Patwardhan et al.[13]
- Mild/moderate relapse costs ($7,275) were included[11]; severe ($17,459) relapse costs were extrapolated based on Patwardhan et al.[13]
- Administration and monitoring costs were sourced from the Ontario Schedule of Benefits[14,15], Ontario Case Costing Initiative[16], formularies[17,18], published literature[19], and clinician opinion
- Costs for a physician visit and an MS Day Case admission were assumed for non-serious adverse events (AEs) ($84)[15] and serious AEs ($363)[16], respectively

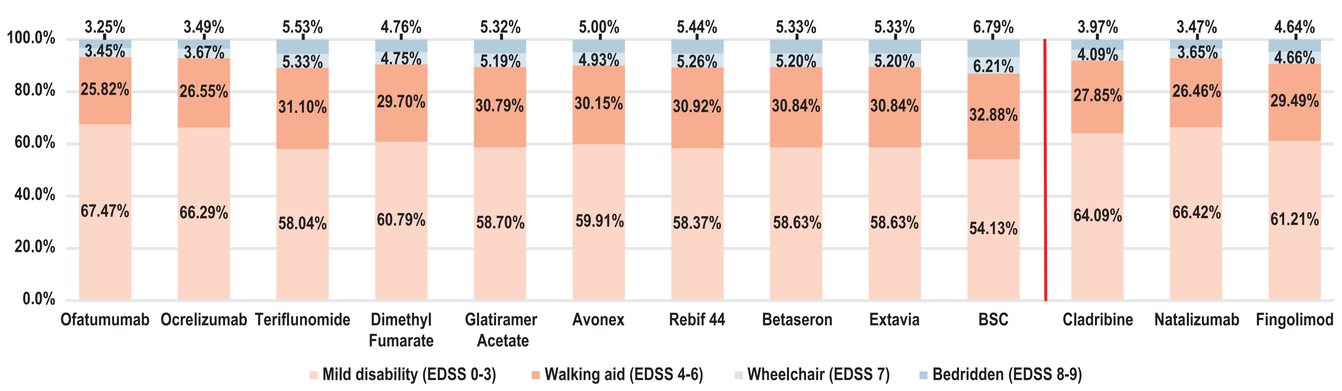
Outcomes:

- Clinical outcomes included patient distribution and time spent in each EDSS health state, number of relapse events, and risk of wheelchair use or confinement to bed (percent of patients progressing to EDSS 7 or higher over time)
- Burden of disease was assessed using the disability-adjusted life year (DALY), which combines years of life lost due to premature mortality (YLLs) and years of life lost due to disability or due to living in states of less than full health (YLDs)
- Economic outcomes included administration and monitoring and non-DMT costs (direct medical, relapse, and AEs)
- Productivity outputs included the percent of patients employed and working full time

Results

- Patients treated with ofatumumab versus a comparator had a lower degree of disability, as indicated by a greater percentage of patient time (67.47%) spent in the mild disability health states, and lower percentage of patient time (3.25%) spent in the health states associated with greater disability (**Figure 2**)

Figure 2. Percent of patient time spent in each health state in the base case over a 10-year horizon for first-line and second-line treatments without treatment switching or delay



Bars to the left and right of the red line represent first-line and second-line therapies, respectively. Values within the bars represent the percent of patient time spent in each respective health state severity grouping. Abbreviations: BSC: best supportive care; EDSS: Expanded Disability Status Scale.

- Patients treated with ofatumumab versus a comparator had less YLL, YLD and DALYs
- Treatment with a comparator resulted in greater incremental administration and monitoring costs compared to ofatumumab, except for glatiramer acetate (-$27) and cladribine (-$58). Incremental non-DMT costs were greater for all comparators versus ofatumumab and ranged from $3,606 (ocrelizumab) to $32,096 (Avonex)
- Patients treated with ofatumumab resulted in a greater percent of patients employed and working full time at 10 years compared to patients initially treated with a comparator
- Patients initially treated with ofatumumab versus switching to ofatumumab after 3 or 5 years with another commonly used first-line DMT had a lower degree of disability, a lower number of relapse events, less DALYs, slower progression to EDSS 7 or higher, and higher percent of patients employed at 10 years (**Table 1**)
- Non-DMT costs were greater in patients who switched to ofatumumab after 5 versus 3 years; both treatment delay scenarios resulted in greater non-DMT costs than patients initially treated with ofatumumab

Table 1. Delayed treatment scenario results for clinical outcomes over a 10-year time horizon for ofatumumab provided initially versus switching to ofatumumab after 3 and 5 years of treatment with another commonly used first-line DMT

Treatment	% Patient time spent in health state at 10 years				Relapse events at 10 years	DALY at 10 years	% Patients at EDSS 7+ at 10 years	% Employed at 10 years
	Mild Disability (EDSS 0-3)	Walking Aid (EDSS 4-6)	Wheelchair (EDSS 7)	Bedridden (EDSS 8-9)				
Ofatumumab (initially)	67.47%	25.82%	3.45%	3.25%	3.82	2.30	14.62%	35.60%
3-year delay								
Teriflunomide + Ofatumumab	61.03%	29.69%	4.66%	4.62%	4.52	2.63	18.39%	32.40%
Dimethyl Fumarate + Ofatumumab	62.99%	28.56%	4.28%	4.17%	4.22	2.53	17.20%	33.40%
Glatiramer Acetate + Ofatumumab	61.65%	29.37%	4.53%	4.45%	4.43	2.60	17.85%	32.90%
Rebif 44 + Ofatumumab	61.06%	29.62%	4.67%	4.65%	4.56	2.63	18.60%	32.20%
5-year delay								
Teriflunomide + Ofatumumab	59.19%	30.60%	5.06%	5.14%	4.83	2.74	20.06%	30.90%
Dimethyl Fumarate + Ofatumumab	61.66%	29.28%	4.56%	4.51%	4.41	2.60	18.34%	32.30%
Glatiramer Acetate + Ofatumumab	59.88%	30.27%	4.91%	4.94%	4.71	2.70	19.38%	31.50%
Rebif 44 + Ofatumumab	59.36%	30.48%	5.04%	5.13%	4.85	2.73	20.21%	30.80%

Abbreviations: DALY: disability-adjusted life years; EDSS 7+: Expanded Disability Status Scale 7 or above.

Conclusions:

- Treatment with ofatumumab resulted in improved clinical, economic, and productivity outcomes versus other first-line and second-line DMTs in Canada
- Early adoption of a high efficacy DMT such as ofatumumab had beneficial effects compared to patients who delayed treatment initiation for up to 3- or 5-years. Patients switching to ofatumumab earlier in their disease course achieved greater outcomes, with reduced costs
- Given its high efficacy, favourable safety profile, and ability for patients to self-administer treatment at home, ofatumumab is the first treatment option that may shift the treatment paradigm towards early high-efficacy treatment for all patients with RRMS

References:

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; **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; **9.** Cho et al. *Mult Scler* 2014;20(9):1217-1223; **10.** Grima et al. *Multiple sclerosis.* 2000;6(2):91-8; **11.** Karampampa et al. *J Popul Ther Clin Pharmacol.* 2012;19(1):e11-25; **12.** CADTH. CDR Pharmacoeconomic Review Report for Lemtrada. 2015; **13.** Patwardhan et al. *Multiple sclerosis.* 2005;11(2):232-9; **14.** Ontario Ministry of Health. Schedule of Benefits, Lab Services. 2020; **15.** Ontario Ministry of Health. Schedule of Benefits, Physician Services. 2021; **16.** Ontario Case Costing Initiative. 2018; **17.** Government of Ontario. Ontario Drug Benefit Formulary. 2021; **18.** Ontario Exceptional Access Program Formulary. 2021; **19.** Tam et al. *Curr Oncol.* 2013;20(2):e90-e106.

Disclosures:

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