Cost-effectiveness analysis of efgartigimod versus chronic intravenous immunoglobulin (IVIg) for treatment of acetylcholine receptor antibody positive (AChR-Ab+) generalized myasthenia gravis (gMG) in Canada

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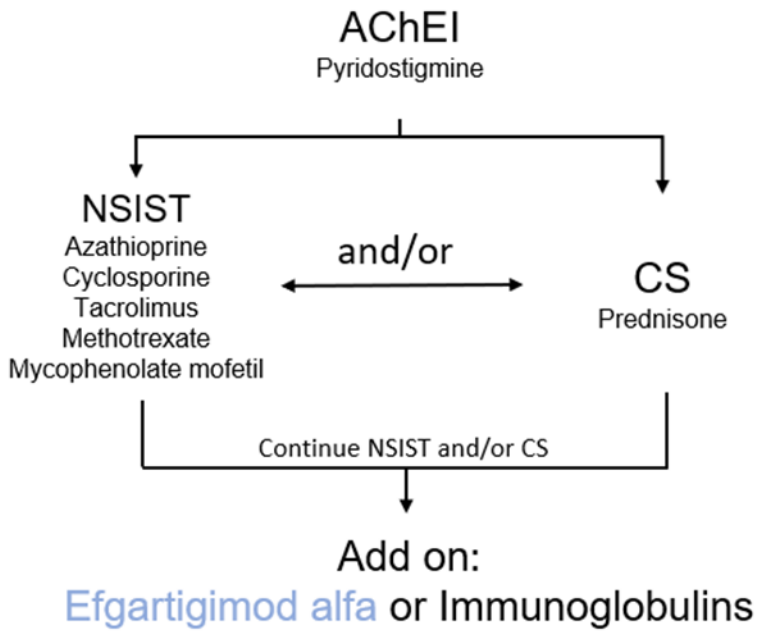
Background

- Generalized myasthenia gravis (gMG) is a chronic neuromuscular disease that causes muscle weakness and fatigue, severely impairing quality of life.[1]
- Immunoglobulins are used off-label for treating gMG in Canada and can be administered intravenously or subcutaneously (IVIg or SCIg, respectively). However, there is limited evidence for its efficacy.[2]
- Efgartigimod is an efficacious and well-tolerated treatment for gMG. The efficacy and safety of efgartigimod was studied in the ADAPT trial.[3]
- Canadian clinicians from seven academic centers and Canadian Agency for Drugs and Technologies in Health (CADTH) noted that chronic immunoglobulins are the main comparator for efgartigimod based on anticipated place in therapy.[4,5]
- Although C5 inhibitors (ravulizumab, eculizumab) are approved in Canada, they are not funded by public payers and clinicians/CADTH did not consider them as comparators.[4,5]

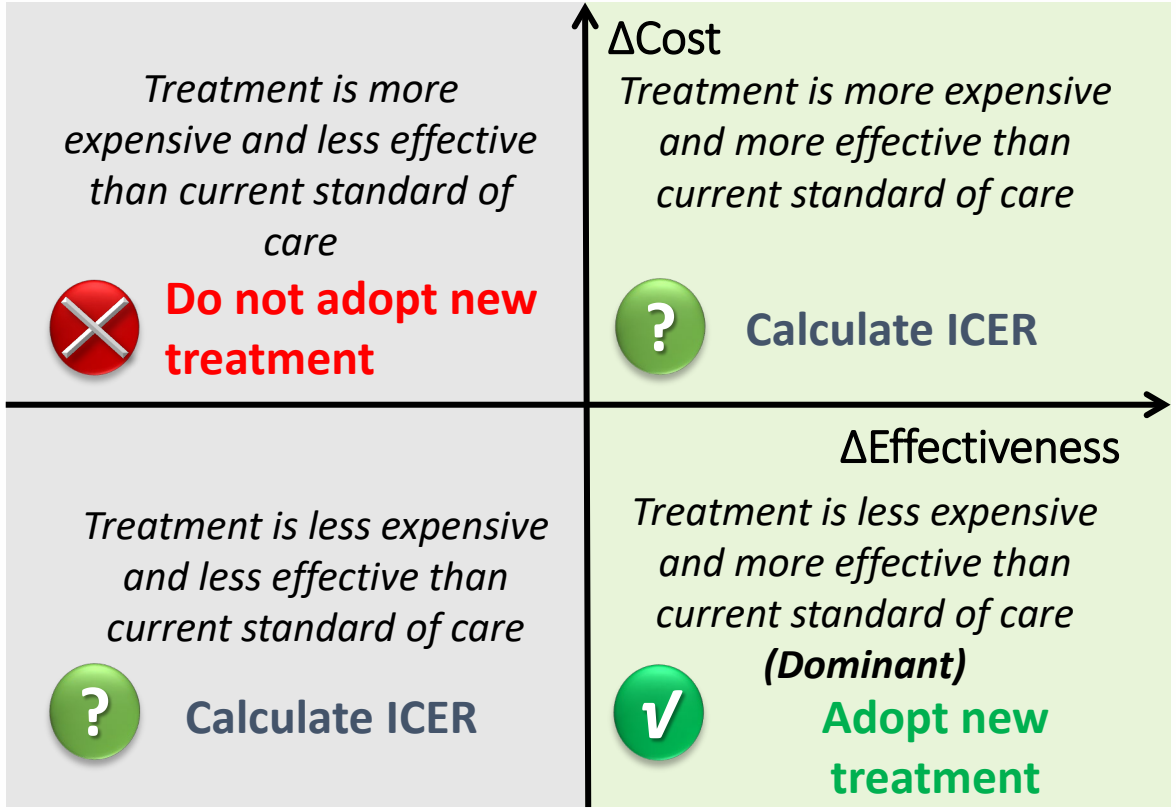
Figure 1: Anticipated place in therapy for efgartigimod



Objective

- A cost-utility analysis (CUA) model was developed to assess the cost-effectiveness of efgartigimod versus IVIg from a healthcare system perspective.
- A CUA is an economic analysis that compares the relative costs and health outcomes in quality-adjusted life years (QALYs) of different treatments.[6]
- It is required in Canada to determine the value of new treatments to inform reimbursement decisions; CADTH is the lead agency providing these recommendations.[6]

Figure 2: Interpretation of CUA results

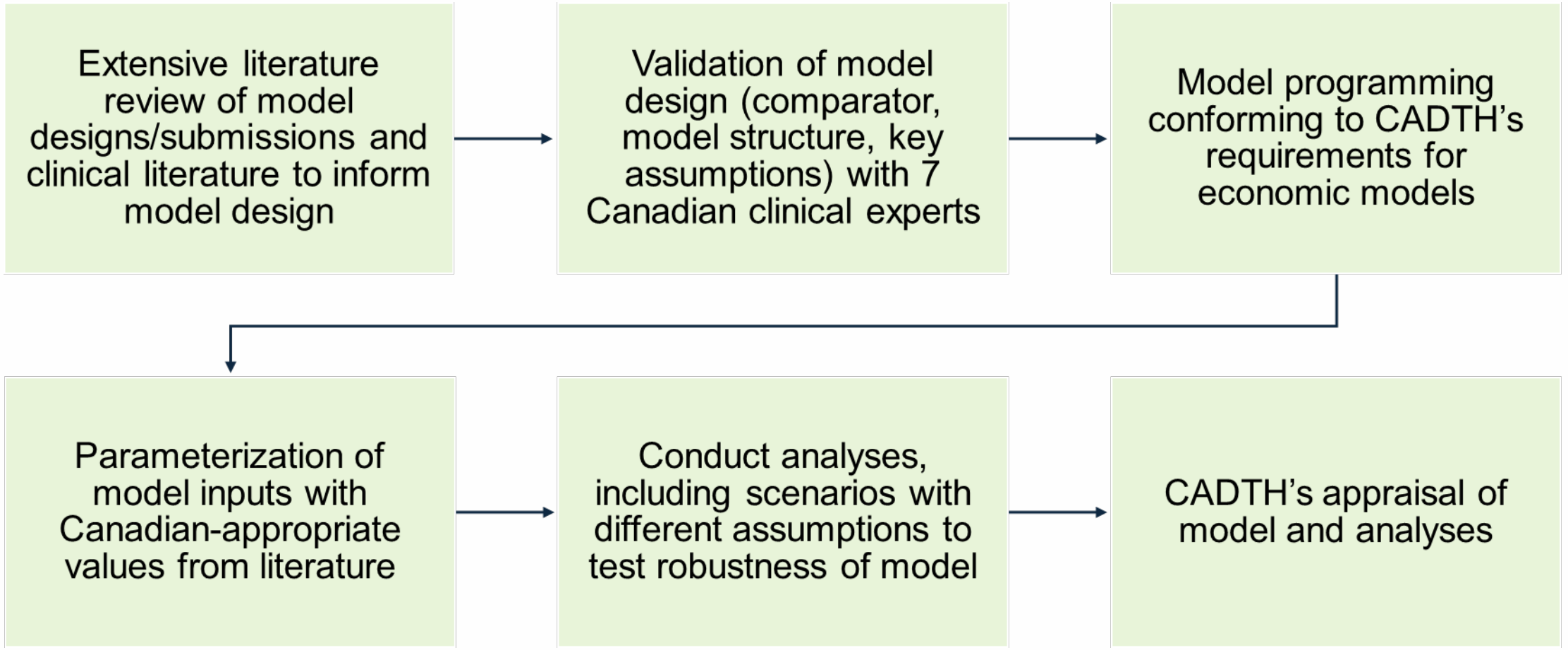


Methods - Model Overview

- **Target population**: AChR-Ab+ patients with gMG whose symptoms persist despite adequate treatment with acetylcholinesterase inhibitors, corticosteroids, and/or nonsteroidal immunosuppressants
- **Main comparator**: chronic immunoglobulins
- **Time horizon:** lifetime

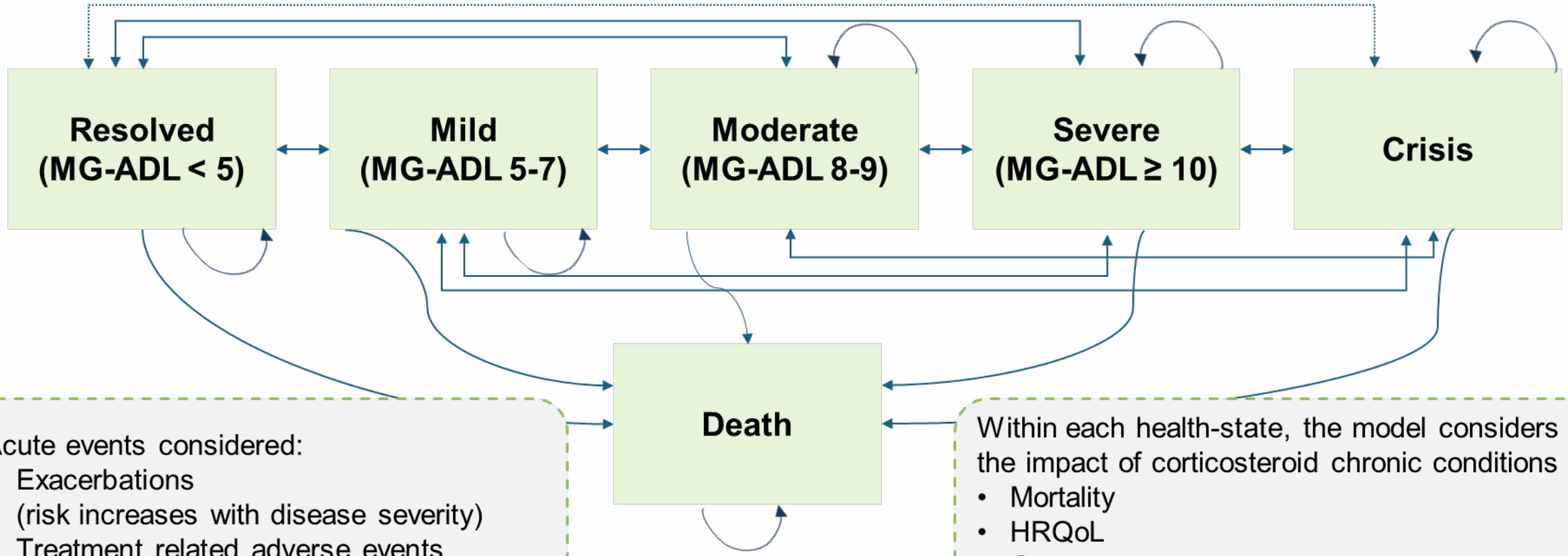
Methods - Model Development Process

Figure 3: Model development process



Methods - Model Structure

Figure 4: Model structure featuring six health states



Methods - Overview of Model Inputs

Table 1: Overview of model inputs

	Details / Unit Cost / Source
Efficacy inputs	• Efgartigimod: ADAPT/ADAPT+ pooled[3] • IVIg/SCIg: indirect treatment comparison analysis
Dosing schedule	• Efgartigimod: 10 mg/kg weekly for 4 weeks on, then off for 4 weeks or while MG-ADL <5[3] • IVIg: 2 g/kg loading dose, 1 g/kg every 3 weeks maintenance[7]; SCIg: 0.4 g/kg weekly maintenance[4] • Discontinuation rates based on ADAPT/ADAPT+ data and IVIg trial[3,8]
Drug costs (CAD)	• Efgartigimod: $7,900.00 / 400 mg • IVIg/SCIg: $73.88 / 1 g
Disease monitoring costs	• Canadian schedule of fees
Exacerbation & crisis costs	• Prior CADTH submission for eculizumab
Cs-related chronic complication costs	• Literature, assumptions validated with clinicians
Adverse event costs	• Canadian hospital database (Canadian Institute for Health Information)
Terminal care costs	• Literature
Utility inputs	• Real-world study

Efficacy Data: Efgartigimod vs. Comparator

- Given lack of head-to-head evidence on efgartigimod vs. chronic IVIg, a network meta-analysis (NMA) was conducted to derive comparative difference in MG-ADL between efgartigimod vs. key comparators

Figure 5: NMA inputs and results

Input data

Study ID	Treatment	N	Change from Baseline MG-ADL		
			Mean	SE	Timepoint (weeks)
ADAPT	Efgartigimod	65	-4.60	0.40	4
	Placebo	64	-1.80	0.31	4
Howard 2019	Efgartigimod	12	-3.50	1.10	11
	Placebo	12	-1.80	1.20	11
NCT02473952	IVIG	30	-3.31	0.58	24
	Placebo	32	-2.22	0.58	24
Wolfe 2002	IVIG	6	-0.30	0.82	6
	Placebo	9	-2.60	0.80	6
CHAMPION MG	Ravulizumab	86	-3.12	0.38	26
	Placebo	89	-1.42	0.35	26

Modeled data

Mean Differences for Change From Baseline in MG-ADL

EFG			
-1 (-2.38 to 0.41)	RAV		
-2.7 (-3.64 to -1.75)	-1.7 (-2.72 to -0.69)	PBO	
-2.79 (-4.4 to -1.14)	-1.77 (-3.43 to -0.11)	-0.08 (-1.4 to 1.25)	IVIG

Methods - Model Assumptions

- **Individualized dosing:** Efgartigimod patients assumed to remain off-treatment for at least 4 weeks between treatment cycles; stayed off-treatment if MG-ADL <5 (same assumption was applied to IVIg)[3]
- **Discontinuation:** Efgartigimod non-responders after 2 consecutive initial treatment cycles were assumed to discontinue efgartigimod[3]; 33% of IVIg patients assumed to discontinue after 1 month based on literature[8]; patients who did not discontinue are assumed to receive the treatment continuously till the end of time horizon
- **Quantifying steroid impact:** Assumed chronic steroid use resulted in additional mortality, utility decrement, and costs based on literature[9,10]; patients with MG-ADL < 5 assumed to receive low-dose steroid (lower magnitude of impact)
- **75% IVIg and 25% SCIg use**: Based on consultation with Canadian clinicians from 7 academic centers[4]
- **Chronic IVIG administered every 3 weeks:** Based on frequencies in literature[7]
- **IVIg efficacy:** Assumed to remain the same after cycle 1 with no worsening or improvement for the rest of time horizon
- **Adverse events for IVIg:** Assumed to be equivalent to the placebo arm of ADAPT study[a]

[a] Patients in the placebo arm of the ADAPT study received background gMG medications, though this did not include immunoglobulins. This was a conservative assumption as there is limited safety data for chronic IVIg in gMG.

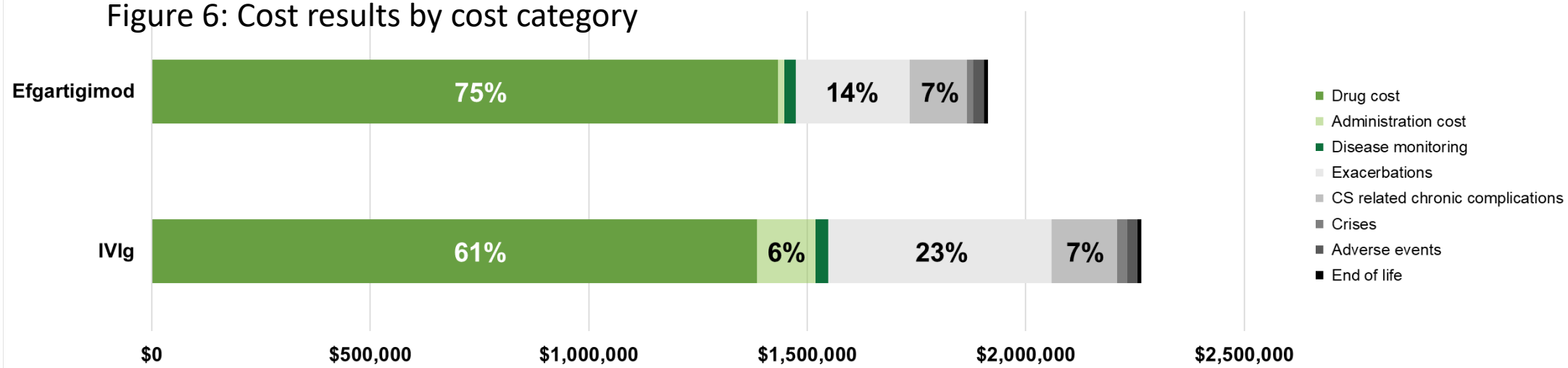
Results - Base Case

- Over a lifetime horizon, efgartigimod dominated chronic IVIg/SCIg, with higher total QALYs and lower total costs

Table 2: Base case results

	Efgartigimod	Chronic IVIg/SCIg
Total Costs	$1,913,294	$2,263,906
Total QALY	16.80	13.35
ICER (Efgartigimod vs. comparator)		**Dominant**

Figure 6: Cost results by cost category



Results - Scenario Analyses

Table 3: Scenario analysis results

Scenario	Efgartigimod cost	IVIg/SCIg cost	Efgartigimod QALY	IVIg/SCIg QALY	ICER
IVIg every 4 weeks	$1,913,294	$1,992,976	16.80	13.35	Dominant
100% IVIg every 3 weeks	$1,913,294	$2,238,148	16.80	13.35	Dominant
100% SCIg weekly	$1,913,294	$2,340,630	16.80	13.35	Dominant
CADTH re-analysis[a]	$1,969,893	$2,210,045	16.38	15.47	Dominant
Societal perspective	$1,952,520	$2,332,699	16.80	13.35	Dominant

[a] CADTH adjusted some assumptions for their re-analysis. Changes included not associating MG-ADL <5 with reduced corticosteroid use, alternative health state utility values, and allowing patients to transition to any health state after a crisis instead of only MG-ADL ≥10.

Model Limitations

1) **Variability around IVIg dosing**: real-world dosing may be less than every 3 weeks; tested a scenario with dosing every 4 weeks
2) **Assumptions around mortality**: impact of chronic steroid use was informed based on literature; CADTH modified these assumptions in their re-analysis
3) **Uncertainty around efficacy and safety of chronic IVIg**: there is limited evidence available on efficacy, utilization, and adverse events of chronic IVIg use in MG patients, where IVIg is used off-label

Discussion and Conclusions

- Efgartigimod was cost-effective vs chronic immunoglobulins, being dominant in the base case and all scenario analyses
- This represents more efficient use of healthcare resources at lower cost with efgartigimod
- A strength of the analysis was validation of the model and assumptions by Canadian clinicians across seven academic centers

References

1. Dresser L, Wlodarski R, Rezania K, Soliven B. Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. J Clin Med. 2021;10(11).
2. CADTH. CADTH Rapid Response Report: Off-Label Use of Intravenous Immunoglobulin for Neurological Conditions: A review of Clinical Effectiveness. 2018.
3. Howard JF, Jr., Bril V, Vu T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. Lancet Neurol. 2021;20(7):526-536.
4. EVERSANA Canada Inc. Canadian Clinician Survey: Current and Future Treatment Landscape of gMG. 2023.
5. CADTH. Efgartigimod alfa. 2024. cadth.ca/efgartigimod-alfa
6. CADTH. Procedures for CADTH Reimbursement Reviews. 2024. cadth.ca/cadth-procedures-reimbursement-reviews
7. Bril V, Szczudlik A, Vaitkus A, et al. Randomized Double-Blind Placebo-Controlled Trial of the Corticosteroid-Sparing Effects of Immunoglobulin in Myasthenia Gravis. Neurology. 2023;100(7):e671-e682.
8. Wolfe GI, Barohn RJ, Foster BM, et al. Randomized, controlled trial of intravenous immunoglobulin in myasthenia gravis. Muscle Nerve. 2002;26(4):549-552.
9. Dalal AA, Duh MS, Gozalo L, et al. Dose-Response Relationship Between Long-Term Systemic Corticosteroid Use and Related Complications in Patients with Severe Asthma. J Manag Care Spec Pharm. 2016;22(7):833-847.
10. Chen SY, Choi CB, Li Q, et al. Glucocorticoid Use in Patients With Systemic Lupus Erythematosus: Association Between Dose and Health Care Utilization and Costs. Arthritis Care Res (Hoboken). 2015;67(8):1086-1094.