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SCAN ME

Cost-Effectiveness of Belimumab for the Treatment of Adults With Active Lupus Nephritis in Canada

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Disclosures

- Justin Riemer and Erin Arthurs are employees of GSK and hold financial equities in GSK
- Kelly Campbell and Chris Knight are employees of RTI Health Solutions, an independent nonprofit research institute retained by GSK for research services

Background

- In Canada, the prevalence of SLE is 90 per 100,000[1]
  - Up to 38% of patients with SLE have biopsy-proven LN, of whom 87% have active ISN/RPS LN Class III ± V, IV ± V, or V[2]
- LN treatment options include immunosuppressants (e.g. CYC, MMF, and AZA, among others), corticosteroids, and biologics (e.g. belimumab), and comprise induction and maintenance phases[3–5]
- The efficacy and safety of belimumab, a human, IgG1λ monoclonal antibody that selectively binds to soluble BLyS and inhibits its activity, were demonstrated for patients with LN in the Phase 3 BLISS-LN trial[6]
- Belimumab received notice of compliance from Health Canada for the treatment (in addition to ST) of active LN in July 2021 with a recommendation for reimbursement with conditions received from CDA-AMC in February 2023[7,8]

Objective

To evaluate the costs and health outcomes of belimumab plus ST versus ST alone for the treatment of adults with active LN in Canada

AZA, azathioprine; BLyS, B-lymphocyte stimulator; CDA-AMC, Canada's Drug Agency L'Agence des médicaments du Canada; CYC, cyclophosphamide; IgG1λ, immunoglobulin G lambda; ISN/RPS, International Society of Nephrology/Renal Pathology Society; IV, intravenous; LN, lupus nephritis; MMF, mycophenolate mofetil; ST, standard therapy, SLE, systemic lupus erythematosus

1. Fatoye F, et al. *Rheumatol Int.* 2018;38:1721–1726. 2. Hanly JG, et al. *Arthritis Rheumatol.* 2016;68:1932–1944. 3. Almaani S, et al. *Clin J Am Soc Nephrol.* 2017;12:825–835. 4. Fanouriakis A, et al. *Ann Rheum Dis.* 2024;83:15–29. 5. GSK. Benlysta Product Monograph. 2024. https://ca.gsk.com/media/6151/benlysta.pdf. 6. Furie R, et al. *N Engl J Med.* 2020;383:1117–1128. 7. Office of Regulatory Affairs - Biologic and Radiopharmaceutical Drugs Directorate (ORA-BRDD). Available at: Regulatory Decision Summary for Benlysta - Drug and Health Products Portal. Accessed April 2025. 8. CADTH Reimbursement Recommendation – Belimumab (Benlysta). *Canadian Journal of Health Technologies.* 2023;3(2).

Study design

Patient population was aligned with the BLISS-LN trial and the Health Canada indication[1,2]

Patients had a diagnosis of active LN* and clinically active renal disease at screening requiring induction therapy

Sex (female)
88.1%

Mean (SD) weight
Males: 77.1 (7.71) kg
Females: 61.4 (6.14) kg

Mean (SD) disease duration
SLE: 5.32 (6.1) years
LN: 2.31 (4.2) years

Mean (SD) age
33.4 (10.68) years

- Patients were categorized by baseline eGFR and percentage decline
- These categories corresponded to literature-reported risks of ESKD and death, including established surrogate endpoints of 30% and 40% decline in eGFR values over 2 years in clinical trials of kidney disease[3,4]
- Treatments administered in the BLISS-LN trial:

Treatment	Dosage and regimen
Belimumab	10 mg/kg IV at Week 0, 2, 4, and every 4 weeks thereafter
ST	• CYC: 500 mg IV every 2 weeks for 6 infusions followed by AZA 2 mg/kg/day until study end, *or* • MMF: 1 to 3 g/day until study end. After 6 months, the dose of MMF could be reduced to 1 g/day • HDCS: 0 to 3 IV pulses of methylprednisolone 500 mg to 1000 mg/pulse, followed by oral prednisone at a recommended dose of 0.5 to 1 mg/kg/day with total daily dose up to 60 mg/day. By Week 24 of the trial, the CS dose must have been at 10 mg/day of prednisone or the patient was considered a treatment failure

*Biopsy-confirmed diagnosis in the past 6 months in Class III or IV and/or V LN

AZA, azathioprine; CS, corticosteroids; CYC, cyclophosphamide; eGFR, estimated glomerular efficacy rate; ESKD, end-stage kidney disease; HDCS, high-dose corticosteroids; IV, intravenous; LN, lupus nephritis; MMF, mycophenolate mofetil; SD, standard deviation, ST, standard therapy

1. Furie R, et al. *N Engl J Med.* 2020;383:1117–1128. 2. CADTH Reimbursement Recommendation – Belimumab (Benlysta). *Canadian Journal of Health Technologies.* 2023;3(2). 3. Coresh J, et al. *JAMA.* 2014;311(24):2518–2531. 4. Levey AS, et al. *Am J Kidney Dis.* 2019;75(1):84–104.

Study design

Cost-effectiveness analysis: Cohort-level Markov model

- Population characteristics and treatment effects were based on the BLISS-LN trial (24 months) with long-term renal function based on eGFR slope during BLISS-LN
  - Yearly transition probabilities, resource use, costs, and utility data by eGFR health state were derived from the literature[1–4]
  - The literature-derived transition probabilities were adjusted to correspond with the risk of ESKD and death at key timepoints reported in the literature per baseline eGFR and % decline category (i.e. eGFR slope category)[5]
- The model utilized a publicly funded Canadian healthcare payer perspective, where direct costs were considered over a lifetime time horizon (70 years)
- Cost (2021/2022 $CAD) and health outcomes were discounted at 1.5%

Efficacy inputs

- The trajectory of eGFR decline was determined by baseline eGFR and percentage decline during the 2-year trial period

Uncertainty analyses

- One-way sensitivity and scenario analyses were performed to evaluate robustness of results
- The base-case analysis was probabilistic
- Pairwise comparisons were performed for belimumab plus CYC→AZA versus CYC→AZA and belimumab plus MMF versus MMF alone

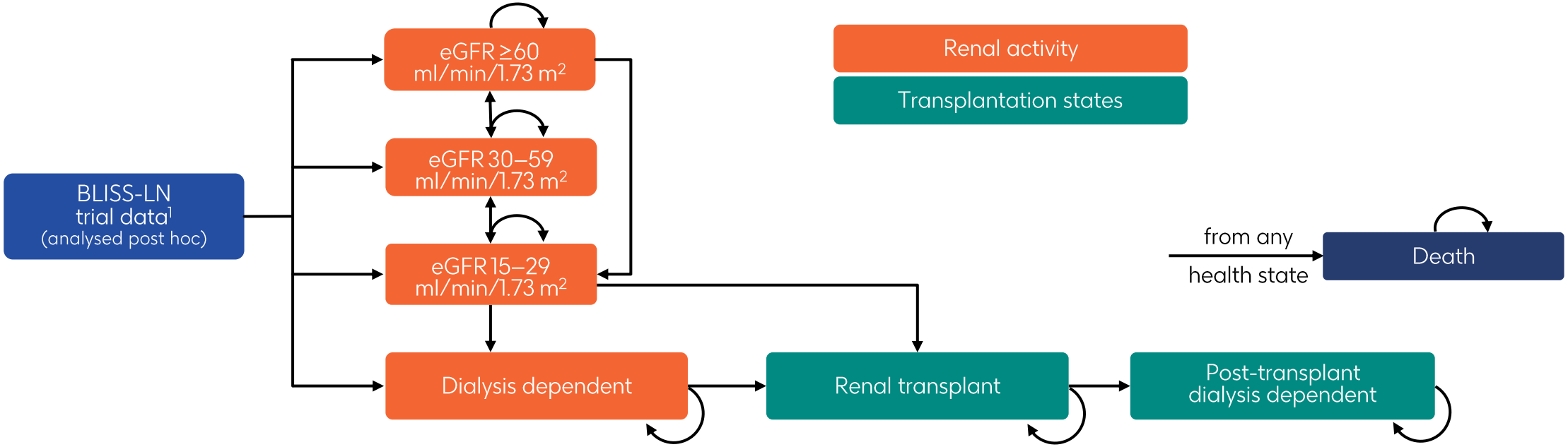
AZA, azathioprine; CAD, Canadian dollar; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; LN, lupus nephritis; MMF, mycophenolate mofetil

1. Hanly JG, et al. *Arthritis Rheumatol.* 2016;68(8):1932–1944. 2. Barber MRW, et al. *Arthritis Care Res.* 2018;70(9):1294–1302. 3. Ferguson TW, et al. *Kidney Med.* 2021;3(1):20–30. 4. Clarke AE, et al. *Arthritis Care Res.* 2015;67(3):431–436. *5.* Coresh J, et al. *JAMA.* 2014;311(24):2518–2531.

Study design

Cost-effectiveness analysis: Cohort-level Markov model (cont.)

- The cost-effectiveness model uses a Markov model structure with health states classified by eGFR (expressed as ml/min/1.73 m^2): eGFR ≥60, eGFR 30–59, and eGFR 15–29, and health states for patients who are "Dialysis dependent," undergoing "Renal transplant," and "Post-transplant dialysis dependent"



eGFR, estimated glomerular filtration rate

1. Furie R, et al. *N Engl J Med.* 2020;383:1117–1128.

Results: Belimumab therapy incurred lower costs

Probabilistic reference case results

- Patients receiving belimumab incurred lower health state costs (vs CYC→AZA and MMF), mainly due to a **reduction in hospitalizations and dialysis/renal transplants costs**, and lower costs of flare management

	CYC followed by AZA			MMF		
Outcome costs (CAD$)	BEL plus CYC→AZA	CYC→AZA	Incremental	BEL plus MMF	MMF	Incremental
Drug acquisition costs[1–3]	265,064	7,924	257,140	309,880	34,815	275,065
Administration costs	9,288	362	8,926	9,530	0	9,530
Health state costs	**579,492**	**637,402**	**-57,909**	**518,925**	**603,075**	**-84,151**
Flare costs	**11,147**	**13,701**	**-2,554**	**11,084**	**13,742**	**-2,658**
AE costs	9,462	1,480	7,982	19,039	19,915	-877
End of life costs	600	605	-5	595	603	-8
Total cost (CAD$)	**875,054**	**661,474**	**213,581**	**869,053**	**672,151**	**196,902**

AE, adverse event; AZA, azathioprine; BEL, belimumab; CAD, Canadian dollar; CYC, cyclophosphamide; MMF, mycophenolate mofetil

1. Ontario Ministry of Health. Drugs funded by Ontario Drug Benefit (ODB) program. Available at: https://www.ontario.ca/check-medication-coverage/. Accessed 2021. 2. IQVIA DeltaPA. Drug costs for Cyclophosphamide, powder for solution for IV infusion. Available at: https://www.iqvia.com/locations/canada/library/fact-sheets/iqvia-deltapa. Accessed 2022. 3. GSK. Data on file. Drug costs from IQVIA DeltaPA. 2022.

Results: Belimumab lowered flare disutility and steroid use

Probabilistic reference case results

- Overall, belimumab was associated with increased QALYs (vs CYC→AZA and MMF) due **to reduction in disease progression** (+0.28 and +0.47, respectively), **reduced flares,** and **steroid sparing** utilities

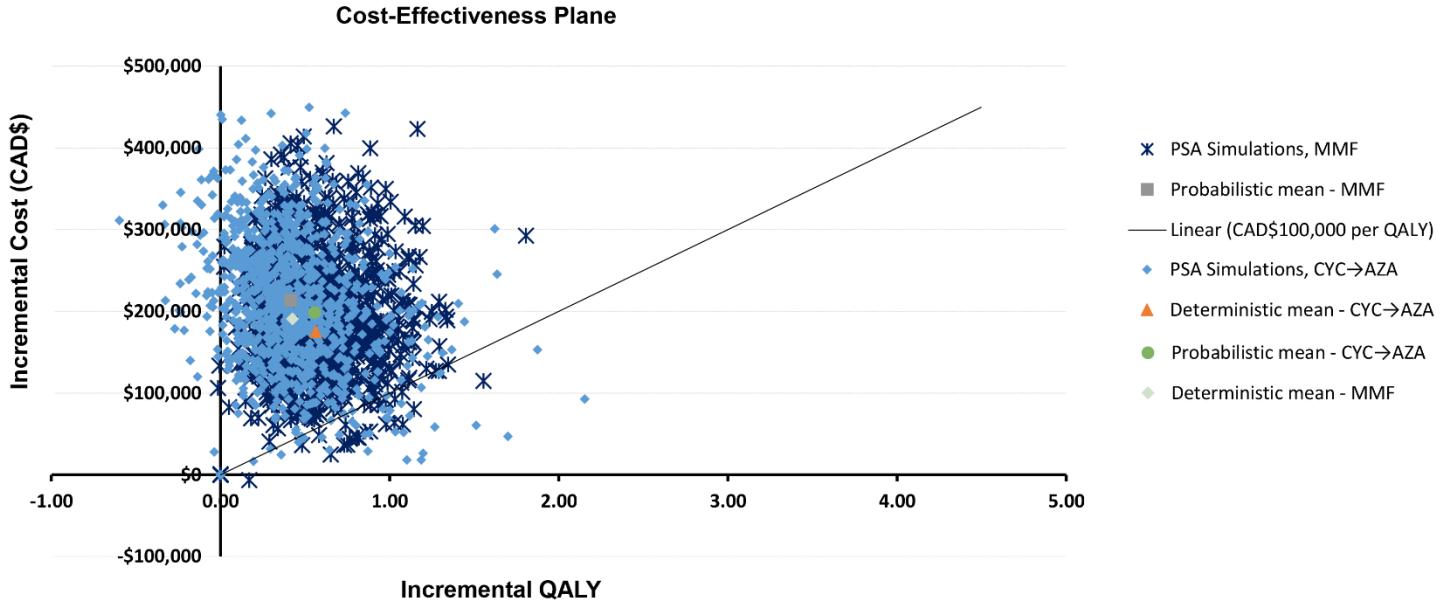
	CYC followed by AZA			MMF		
QALYs	BEL plus CYC→AZA	CYC→AZA	Incremental	BEL plus MMF	MMF	Incremental
eGFR ≥60 ml/min/1.73 m^2	5.27	5.26	0.01	5.67	4.86	0.81
eGFR 30–59 ml/min/1.73 m^2	8.22	7.17	1.04	8.65	8.04	0.61
eGFR 15–29 ml/min/1.73 m^2	6.07	5.82	0.25	6.75	6.07	0.68
Dialysis dependent	2.78	3.35	-0.56	2.17	3.00	-0.83
Renal transplant	1.24	1.49	-0.25	0.95	1.34	-0.39
Post-transplant dialysis dependent	1.29	1.51	-0.21	0.93	1.35	-0.42
Flare disutility	-0.35	-0.44	0.08	-0.35	-0.44	0.08
AE disutility	0.00	0.00	0.00	-0.01	-0.01	0.00
Steroid sparing utility increment	0.19	0.13	0.06	0.26	0.24	0.02
Total QALYs	24.71	24.30	0.41	25.02	24.45	0.57

AE, adverse event; AZA, azathioprine; BEL, belimumab; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; MMF, mycophenolate mofetil; QALY, quality-adjusted life year

Results: Belimumab therapy has additional benefit and cost

Probabilistic reference case results

- Belimumab plus CYC→AZA and belimumab plus MMF were more costly and more effective than CYC→AZA and MMF alone, with mean ICURs of $515,277 per QALY and $345,269 per QALY, respectively



- For both comparisons, PSA iterations were in the northeast quadrant of the cost-effectiveness plane (95.0% for belimumab plus CYC→AZA; 99.7% for belimumab plus MMF), indicating higher overall costs and higher effectiveness*

*The probabilistic iterations indicate belimumab plus CYC followed by AZA and belimumab plus MMF have a 3.3% and 2.4% probability of cost-effectiveness at a WTP threshold of CAD$ 100,000 per QALY

AZA, azathioprine; BEL, belimumab; CAD, Canadian dollar; CYC, cyclophosphamide; ICUR, incremental cost-utility ratio; MMF, mycophenolate mofetil; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; WTP, willingness-to-pay

Summary and conclusion

- Due to its confirmed safety and efficacy, belimumab has been approved and in clinical use for LN treatment in Canada since 2021, with a recommendation for reimbursement with conditions received from CDA-AMC in February 2023[1–3]
  - Belimumab treatment for SLE has been shown to be cost-effective in some studies and countries, including Canada[4,5]
  - Both IV and SC belimumab formulations are authorized by Health Canada[2]
- Patients receiving belimumab as an add-on to either CYC→AZA or MMF incurred lower health state costs and lower costs associated with managing disease flares
  - Belimumab add-on treatment was also associated with lower disutility due to flares and reduced steroid use, compared with ST alone

Given its known clinical benefit, and the lower health state costs demonstrated in this study, belimumab offers advantages over conventional LN therapies, thereby supporting its ongoing use in clinical practice in Canada

AZA, azathioprine; CAD, Canadian dollar; CDA-AMC, Canada's Drug Agency L'Agence des médicaments du Canada; CYC, cyclophosphamide; ICUR, incremental cost-utility ratio; IV, intravenous; MMF, mycophenolate mofetil; SC, subcutaneous; ST, standard therapy

1. Office of Regulatory Affairs - Biologic and Radiopharmaceutical Drugs Directorate (ORA-BRDD). Available at: https://dhpp.hpfb-dgpsa.ca/review-documents/resource/RDS00843. Accessed March 2025. 2. CADTH Reimbursement Recommendation – Belimumab (Benlysta). *Canadian Journal of Health Technologies.* 2023;3(2). 3. Furie R, et al. *N Engl J Med.* 2020;383:1117–1128. 4. Petrou P. *Value in Health Reg Issues.* 2022.27:32–40. 5. Mandrik O, et al. *Clin J Am Soc Nephrol. 2022;*17(3):385–394.

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