Cost-Effectiveness of Sequencing Vedolizumab as First-Line Biologic in Ulcerative Colitis and Crohn's Disease in Canada

Fischer A[1], Mac S[1], Freiman E[1], Marshall J[2], Rand K[3], Ramos-Goni JM[3]

[1]Takeda Canada Inc., Toronto, ON, Canada, [2]McMaster University, Hamilton, ON, Canada, [3]Maths in Health B.V., Amsterdam, Netherlands

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Background

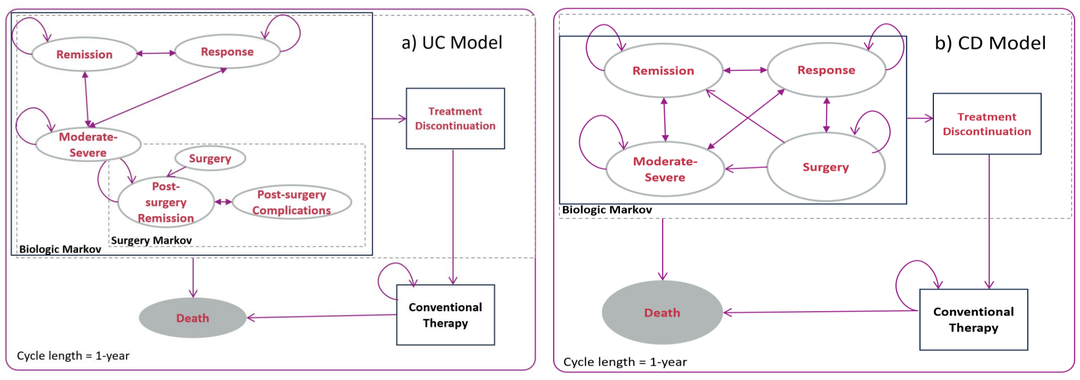
- Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn´s disease (CD), are lifelong progressive disorders characterized by chronic and unpredictable relapsing-remitting inflammation in the gastrointestinal tract.
- Vedolizumab is a gut-selective anti-lymphocyte trafficking biologic indicated for the treatment of adult patients with moderately to severely active UC and CD in Canada.
- Current treatment alternatives include immunomodulators (thiopurines and methotrexate), and biologic agents such as tumour necrosis factor inhibitors (anti-TNFα), monoclonal antibodies (vedolizumab), or small molecules (tofacitinib).
- Recently, the EVOLVE study[1], aimed to compare real world evidence (RWE) on clinical effectiveness and safety of first-line vedolizumab, with other anti-TNFα agents in biologic-naive UC and CD patients.

Aim

- This economic evaluation assesses the potential role and economic value of vedolizumab as first-line biologic for IBD patients, by means of a treatment sequencing analysis supported with recent RWE.

Methods

Figure 1. Markov Model Schematics for UC (Figure 1a – left) and CD (Figure 1b – right)



Model inputs and data sources

- EVOLVE was a multi-country (US, Canada and Greece) retrospective chart review of UC and CD patients treated with vedolizumab or anti-TNFα treatment. It was a multi-centre study (27 centres) including adult patients (≥18 years) diagnosed with UC or CD, who were biologic naïve and initiated first-line biologic "index treatment" with either vedolizumab or an anti-TNFα[1].
- Since EVOLVE results were grouped anti-TNFα, we used the market shares for combining the multiple anti-TNFα treatments into a single arm (anti-TNFα) for UC (28% adalimumab, 10% golimumab and 62% infliximab) and CD (54% adalimumab and 46% infliximab).
- Response and remission data were provided in the form of Kaplan Meier (KM) data. For CD, KM data from the EVOLVE study was used, and for UC we used a recent literature review and meta-analysis.
- Relative risks were calculated for any time point by taking the quotient of the probability of the event in question (response or remission) in the two arms at the chosen point of time. The average of these was used in the model (Table 1).
- Using the same methods as with efficacy parameters we calculated adverse events, dose escalation and regain of response, and surgery rates.

Table 1. EVOLVE/NMA/TLR-based one-year probabilities and relative risks.

UC Remission	1st. line			2nd. line		
	Prob.	95% LB	95%UB	Prob.	95% LB	95%UB
Vedolizumab	27.5%	26.1%	29.0%	17.3%	17.2%	17.4%
Anti-TNFα	21.0%	20.3%	21.8%	15.6%	15.5%	15.7%
Relative risk	RR	95% LB	95%UB	RR	95% LB	95%UB
Vedolizumab / Anti-TNFα	1.250	1.003	1.449	1.133	1.001	1.282
UC Response	**1st. Line**			**2nd. Line**		
	Prob.	95% LB	95%UB	Prob.	95% LB	95%UB
Vedolizumab	45.4%	43.1%	47.9%	60.0%	59.7%	60.4%
Anti-TNFα	34.7%	33.6%	36.0%	54.1%	53.8%	54.5%
Relative risk	RR	95% LB	95%UB	RR	95% LB	95%UB
Vedolizumab / Anti-TNFα	1.250	1.003	1.449	1.133	1.001	1.282
CD Remission	**1st. Line**			**2nd. line**		
	Prob.	95% LB	95%UB	Prob.	95% LB	95%UB
Vedolizumab	59.3%	49.9%	69.1%	55.69%	47.41%	62.84%
Anti-TNFα	51.8%	43.9%	60.3%	60.34%	51.92%	67.39%
Relative risk	RR	95% LB	95%UB	RR	95% LB	95%UB
Vedolizumab / Anti-TNFα	1.131	0.973	1.222	0.923	0.704	1.210
CD Response	**1st. Line**			**2nd. Line**		
	Prob.	95% LB	95%UB	Prob.	95% LB	95%UB
Vedolizumab	62.8%	53.2%	72.3%	65.9%	57.4%	72.7%
Anti-TNFα	54.2%	46.4%	62.5%	68.3%	60.0%	74.9%
Relative risk	RR	95% LB	95%UB	RR	95% LB	95%UB
Vedolizumab / Anti-TNFα	1.135	0.923	1.326	0.965	0.766	1.212

Markov structure and analysis

- Both economic models were developed separately (Figure 1) in Microsoft Excel® to conduct a cost-utility analysis of vedolizumab for the treatment of patients with moderate-to-severe UC or CD versus existing anti-TNFα treatment.
- We have focused our analysis in 2 specific treatment sequences: "Anti-TNFα followed by vedolizumab followed by conventional treatment" (sequence 1) vs. "Vedolizumab followed by anti-TNFα followed by conventional treatment" (sequence 2).
- In general, both models are similar in term of structure and assumptions,[2] except in the UC model, the surgery was modelled in multiple states. Patient can achieve treatment response (response only or remission) and may continue receiving their current treatment (moving to Remission or Response health states) or discontinue biologic therapy due to treatment-related AEs. Patients who do not achieve response or discontinue treatment move to the following treatment line.
- We varied the time horizon in our analysis using 5, 10 and 15 years. All analysis were discounting both cost and benefits at 1.5%[3].
- We ran probabilistic simulations (n=1,000) taking a conservative approach for anti-TNFα by using biosimilar costs from the Ontario Ministry of Health[4].
- Utilities were taken from a systematic literature review.

Results

Base case results

- For UC , vedolizumab in 1st line resulted in 2.66 QALYs at a cost of 124,216 CAD, compared to 2.57 QALYs at a cost of 137,291 CAD with anti-TNFα as 1st line. In other words, vedolizumab in 1st line, followed by anti-TNFα dominated the sequence 1 (anti-TNFα as 1st line, followed by vedolizumab); it was more effective and less costly (Table 2).
- For CD, vedolizumab in 1st line resulted in 3.47 QALYs at a cost of 137,827 CAD, compared to 3.43 QALYs at a cost of 104,666 CAD with anti-TNFα as 1st line. Vedolizumab in 1st line (Sequence 2) was more effective but also more costly

Scenario analysis and PSA

- The probabilistic sensitivity analysis (PSA) of the UC model using 5-years as time horizon (Figure 2a) showed stable results across all simulations (i.e., the sequence starting with vedolizumab is dominant for all simulation given the existing uncertainty surrounding the model parameters).
- The PSA for the CD model using 5-years as time horizon (Figure 2b) showed in most of the simulations more health benefit for the sequence starting with vedolizumab compared with the sequence starting with anti-TNFα. However, the sequence starting with vedolizumab is more costly in almost all simulations.
- With time horizons of 10 or 15 years, results were robust with sequence 2 remaining dominant for UC and being more effective but more costly for CD (Table 3).

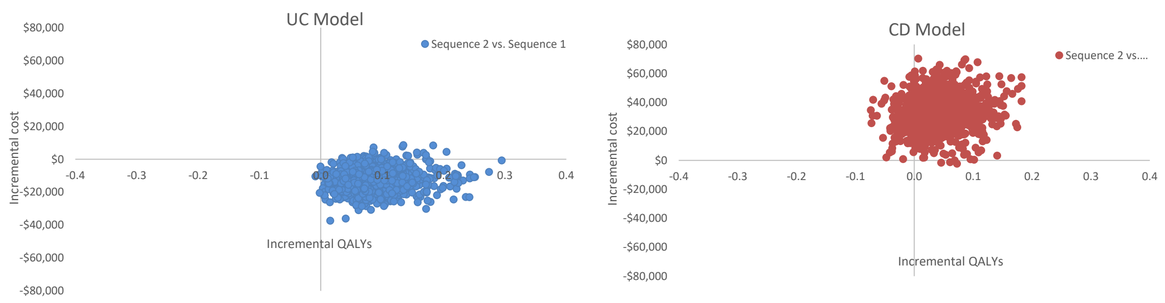
Table 2. Probabilistic base case results (Time horizon= 5 years)

	Ulcerative Colitis (UC)								Crohn's disease (CD)							
Clinical Outcomes (per 1000 Patients)																
	Sequence 1				Sequence 2				Sequence 1				Sequence 2			
	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total
Adverse events experienced, n	105	12	0	117	39	32	0	71	112	4	1	117	75	5	1	81
Surgeries, n	0	0	0	5	0	0	0	5	0	0	0	1	0	0	0	1
Life-years (Discounted per patient)																
	Sequence 1				Sequence 2				Sequence 1				Sequence 2			
	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total
Years on biologic treatment	2.92	1.55	0.00	4.47	3.09	1.42	0.00	4.51	4.26	0.46	0.00	4.72	4.34	0.39	0.00	4.73
Years in response (response + remission; while on treatment)	1.40	0.00	0.01	1.41	1.61	0.00	0.00	1.61	2.28	0.00	0.00	2.28	2.45	0.00	0.00	2.46
Years in remission (while on treatment)	1.23	0.00	0.01	1.24	1.36	0.00	0.00	1.37	0.92	0.00	0.00	0.92	0.88	0.00	0.00	0.88
Years in severe UC/CD	1.52	1.55	0.28	3.35	1.48	1.42	0.24	3.14	1.06	0.46	0.04	1.56	1.00	0.39	0.03	1.42
Years spent in surgery	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Life-years				4.76				4.76				4.76				4.76
Quality-adjusted Life Years (QALYs) (Discounted per patient)																
	Sequence 1				Sequence 2				Sequence 1				Sequence 2			
	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total
QALYs on biologic treatment	1.82	0.63	0.00	2.45	1.97	0.58	0.00	2.56	3.15	0.26	0.00	3.40	3.23	0.22	0.00	3.45
QALYs in response	1.20	0.00	0.01	1.20	1.37	0.00	0.00	1.37	1.88	0.00	0.00	1.88	2.04	0.00	0.00	2.04
QALYs in remission	1.07	0.00	0.00	1.08	1.18	0.00	0.00	1.19	0.67	0.00	0.00	0.67	0.62	0.00	0.00	0.62
QALYs in severe UC/CD	0.62	0.63	0.11	1.37	0.61	0.58	0.10	1.28	0.60	0.26	0.02	0.89	0.57	0.22	0.02	0.81
QALYs in surgery	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Disutilities	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total quality-adjusted life-years (QALYs)				2.58				2.66				3.43				3.47
Cost Outcomes (Discounted per Patient)																
DIRECT COSTS	Sequence 1				Sequence 2				Sequence 1				Sequence 2			
	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total	Anti-TNFα	Vedolizumab	Conventional therapy	Total	Vedolizumab	Anti-TNFα	Conventional therapy	Total
Treatment Costs - Biologic therapy	$70,078	$30,520	$0	$100,598	$71,994	$16,931	$0	$88,926	$73,343	$7,315	$0	$80,658	$111,125	$3,792	$0	$114,917
Non-treatment costs																
Disease management costs (on treatment)	$24,115	$11,533	$644	$36,291	$24,092	$10,382	$545	$35,020	$20,639	$2,920	$105	$23,664	$19,975	$2,451	$90	$22,509
Surgery (procedure)				$109				$107				$185				$174
Adverse event costs	$268	$25	$0	$293	$85	$79	$0	$164	$150	$11	$1	$162	$222	$6	$1	$229
TOTAL COSTS				$137,291				$124,216				$104,666				$137,827
Sequence 2 vs. Sequence 1 Conclusion	Vedolizumab as first line-therapy is more effective, less costly (Dominant)								Vedolizumab as first-line therapy is more effective but more costly							

Table 3. Scenario probabilistic analysis (Time horizon = 10 years and 15 years)

		Ulcerative Colitis (UC)		Crohn's disease (CD)	
Time horizon 10 years	**QALYs (Discounted per patient)**				
		Sequence 1	Sequence 2	Sequence 1	Sequence 2
		Total	Total	Total	Total
	Disutilities	-0.01	0.00	-0.01	0.00
	Total QALYs	5.09	5.14	6.43	6.50
	Cost Outcomes (Discounted per Patient)				
	DIRECT COSTS	Sequence 1	Sequence 2	Sequence 1	Sequence 2
		Total	Total	Total	Total
	Treatment Costs - Biologic therapy	$110,395	$98,253	$130,210	$176,184
	TOTAL COSTS	$183,320	$169,869	$180,702	$224,333
Time horizon 15 years	**QALYs (Discounted per patient)**				
		Sequence 1	Sequence 2	Sequence 1	Sequence 2
	Disutilities	Total	Total	Total	Total
	Total QALYs	0.00	0.00	-0.01	0.00
		6.86	6.91	9.09	9.19
	DIRECT COSTS	**Cost Outcomes (Discounted per Patient)**			
		Sequence 1	Sequence 2	Sequence 1	Sequence 2
	Treatment Costs - Biologic therapy	Total	Total	Total	Total
	TOTAL COSTS	$110,308	$98,221	$146,045	$198,878
		$239,871	$226,296	$234,327	$282,912

Figure 2. Cost-Effectiveness Plane for UC (left) and CD (right) using a time horizon of 5 years



Conclusions

- In Canada, sequencing vedolizumab as a first-line biologic prior to anti-TNFα in UC provides additional clinical benefits and is cost-savings.
- In CD, sequencing vedolizumab as a first-line biologic also resulted in additional clinical benefits, at an incremental cost.

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Abbreviations

CD: Crohn's Disease; IBD: Inflammatory bowel diseases; KM: Kaplan Meier; LB: Lower bound; PSA: Probabilistic sensitivity analysis; QALY: Quality-adjusted life year; RWE: Real world evidence; TNFα: Tumour Necrosis Factor alpha; UB: Upper bound; UC: Ulcerative colitis