The effectiveness and value of targeted immune modulators for moderate to severe ulcerative colitis

A summary from the Institute for Clinical and Economic Review's California Technology Assessment Forum

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Ulcerative colitis (UC) is a chronic inflammatory bowel condition affecting nearly 1 million individuals in the United States.[1,2] UC causes inflammation in the inner lining of the large intestine, including the colon and the rectum.[3] The course of the disease is characterized by phases of remission and relapsing symptoms such as frequent diarrhea, often with blood or pus; abdominal discomfort; rectal pain; fatigue; and weight loss.[4] The onset of UC usually peaks between the ages of 15 and 35 years.[5]

Treatment options for moderate to severe UC are aimed at inducing clinical response or complete remission in the short-term (induction phase, 6-14 weeks) and maintaining response or remission in the longer term (maintenance phase), often with a lower dose. Treatment options depend largely on the extent of the disease and the severity of symptoms. These may include conventional systemic immune modulators such as aminosalicylates, thiopurines, and budesonide or systemic corticosteroids.

When the disease has not responded adequately to systemic immune modulators, patients are potentially eligible to receive a targeted immune modulator (TIM). TIMs may be used alone or in combination with other systemic agents, such as azathioprine, to induce response.[2] The U.S. Food and Drug Administration (FDA) has approved multiple TIMs, including the tumor necrosis factor (TNF) inhibitors adalimumab (Humira, AbbVie), golimumab (Simponi, Janssen), and infliximab (Remicade, Janssen). Infliximab now has 2 FDA-approved biosimilars available for use in the United States: infliximab-adba (Reneflexis, Merck) and infliximab-dyyb (Inflectra, Pfizer). Other available TIMs include the JAK inhibitor tofacitinib (Xeljanz, Pfizer), the IL-12/23 inhibitor ustekinumab (Stelara, Janssen), and the α4β7 integrin inhibitor vedolizumab (Entyvio, Takeda).

The Institute for Clinical and Economic Review (ICER) conducted a systematic literature review and cost-effectiveness analysis to evaluate the health and economic outcomes of these TIMs for UC. Here, we present a summary of key findings and highlights of the policy discussion with key stakeholders held at a public meeting of the California Technology Assessment Forum (CTAF) on September 24, 2020. Complete details of ICER's systematic literature search and protocol, as well as the methodology and model structure for the economic evaluation, are available in the full report at https://icer.org/assessment/ulcerative-colitis-2020/.

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Summary of Findings

CLINICAL EFFECTIVENESS

We compared the clinical effectiveness of TIMs with the ongoing background conventional therapy (i.e., placebo arms of clinical trials) and to each other.

We identified 19 randomized controlled trials (RCTs) among the adult

population,[4,6-22] with only 1 head-to-head trial (VARSITY) of 2 active treatments, adalimumab and vedolizumab.[16] Primary efficacy endpoints were clinical response and clinical remission assessed at the end of weeks 6-14 (induction phase) and week 52-60s (maintenance phase). The trials were generally comparable, allowing the conduct of Bayesian network meta-analyses (NMAs) to obtain indirect comparative efficacy estimates. Induction and maintenance phase benefits were assessed separately for 2 patient subpopulations: (1) patients without evidence of previous TIM exposure ("biologic-naive") and (2) those with previous exposure to TIMs ("biologic-experienced").

Data for all TIMs were available in the biologic-naive population.[4,6-20] We did not identify any evidence for golimumab or infliximab in the biologic-experienced population. Our assessment of tofacitinib was limited to the biologic-experienced population based on a recent change to its label that now specifies a requirement for previous TNF inhibitor use.[23]

In placebo-controlled trials, TIMs demonstrated superior rates of response, remission, or both at the end of induction and maintenance. Results from the VARSITY head-to-head trial showed that vedolizumab had a higher rate of response than adalimumab during induction in the biologic-naive and biologic-experienced populations and a higher rate of remission during maintenance in the biologic-naive population.[16]

NMA results suggested inferior rates of response and remission for adalimumab compared with several other agents as well. For induction, the NMA showed adalimumab to be inferior to infliximab and vedolizumab in the biologic-naive population and inferior to ustekinimab, tofacitinib, and vedolizumab in the biologic-experienced population. In addition, rates of response and remission were higher with vedolizumab compared with golimumab and adaliumab in the biologic-naive population during maintenance. No other statistical differences among TIMs were observed.

Mortality rates and serious adverse events in available long-term RCT extensions generally showed rates similar to those observed during randomized periods. Of note, 3 TNF inhibitors (adalimumab, golimumab, and infliximab), as well as tofacitinib, carry a black box warning in their FDA labels for an increased risk of serious infections, lymphomas, and other malignancies.[24-27] Data from observational studies demonstrate slightly higher rates of serious infection for certain TIMs versus conventional therapy but no consistent differences among TIMs; long-term data are lacking for the newer TIMs.

LIMITATIONS OF CLINICAL EVIDENCE

Comparative clinical effectiveness among TIMs was largely assessed indirectly through NMAs, the results of which can be susceptible to potential effect modification. The sparsity of data in the biologic-experienced population and adjustment for trial differences added additional uncertainty. Also, the lack of evidence on efficacy for some agents (e.g., infliximab and golimumab) for the biologic-experienced population, as well as limited longer-term safety data for newer therapies, poses a challenge in the interpretation and application of the data.

LONG-TERM COST-EFFECTIVENESS

We evaluated the cost-effectiveness from the U.S. health care sector perspective of the 6 TIMs and 2 biosimilars over a lifetime time horizon. We developed a Markov model with 8-week cycles and the following health states: active UC, clinical response without remission, clinical remission, postcolectomy (with and without complications), and death. Analyses were conducted in the biologic-naive and biologic-experienced populations.

All moderate to severe UC patients entered the model in an active state. At the end of induction, patients with response continued to receive the TIM (or conventional treatment) and those without response or discontinuation shifted to induction with a subsequent treatment. Outcomes and cost for subsequent treatment were represented by a "market basket" of TIMs, with data from treating patients in the biologic-experienced population. Patients without response to subsequent treatment discontinued the treatment and followed transition probabilities of conventional treatment for the remainder of the model time horizon. A proportion of patients with active UC were assumed to opt for colectomy in each cycle.[28]

The model was informed by the ICER NMA of key clinical trials. The average net pricing estimates for TIMs with oral and subcutaneous modes of administration were obtained from SSR Health. For IV-administered TIMs, we used Centers for Medicare & Medicaid Services average sales prices (ASP) plus 6%.[29] Full details of ICER's cost-effectiveness analysis and model are available at https://icer.org/assessment/ulcerative-colitis-2020/.

The cost-effectiveness ratios for TIMs in the biologic-naive and biologic-experienced populations in nearly all scenarios were above commonly cited thresholds when compared with conventional treatment. In the biologic-naive population (Table 1), cost-effectiveness was closest to $150,000 per quality-adjusted life-year (QALY) for infliximab and its biosimilars: infliximab-dyyb and infliximab-adba ($212,000, $186,000 and $195,000 per QALY, respectively).

TABLE 1 Cost-Effectiveness Results for TIMs Versus Conventional Treatment: Biologic Naive

Parameter	Estimated Annual Net Price for Maintenance Year, $	Cost per QALY Gained, $	Cost per evLYG, $
Adalimumab	46,933	1,870,000	1,847,000
Golimumab	42,332	1,455,000	1,432,000
Infliximab	14,614[a]	212,000	209,000
Infliximab-dyyb	13,451[a]	186,000	184,000
Infliximab-abda	13,883[a]	195,000	193,000
Ustekinumab	91,609	1,163,000	1,155,000
Vedolizumab	44,224[a]	887,000	880,000

[a]*Net prices represented by ASP + 6%.*

ASP = average selling price; evLYG = equal value life-year gained; QALY = quality-adjusted life-year; TIM = targeted immune modulator.

TABLE 2 Cost-Effectiveness Results for TIMs Versus Conventional Treatment: Biologic Experienced

Parameter	Estimated Annual Net Price for Maintenance Year, $	Cost per QALY Gained, $	Cost per evLYG, $
Adalimumab	46,933	1,885,000	1,878,000
Tofacitinib	35,506	495,000	489,000
Ustekinumab	91,609	1,252,000	1,239,000
Vedolizumab	44,224[a]	902,000	895,000

[a]*Net prices represented by ASP + 6%.*

ASP = average selling price; evLYG = equal value life-year gained; QALY = quality-adjusted life-year; TIM = targeted immune modulator.

When compared with infliximab, all TIMs produced fewer QALYs except ustekinumab, with a cost-effectiveness ratio of approximately $2.9 million per QALY. In the biologic-experienced population (Table 2), the incremental cost-effectiveness ratio compared with conventional treatment was highest for adalimumab ($1,885,000) and lowest for tofacitinib ($495,000). When compared with adalimumab, tofacitinib resulted in lower costs and higher QALYs. Ustekinumab and vedolizumab also generated higher QALYs but at much higher cost ($996,000 and $464,000 per QALY, respectively). The equal value of life-years gained (evLYG) and cost per evLYG outcomes were similar to those for the QALY, given the relatively minor mortality effects. Full results from the one-way sensitivity analysis, as well as the probabilistic sensitivity analysis are available in the full report (https://icer.org/assessment/ulcerative-colitis-2020/).

LIMITATIONS OF LONG-TERM COST-EFFECTIVENESS

The primary limitations of our cost-effectiveness analysis included restricted data availability, a paucity of information on treatment sequencing or switching, and our need to base outcomes for conventional treatment solely on the results from the placebo arms of the trials. As previously noted, the model is based on treatment benefit inputs obtained from the NMA and, as such, is subject to the limitations previously described.

Policy Discussion

The CTAF is one of the independent appraisal committees convened by ICER to engage in the public deliberation of the evidence on clinical and cost-effectiveness of health care interventions. CTAF is composed of medical evidence experts (e.g., practicing clinicians and methodologists) and leaders in patient engagement and advocacy. Their deliberation includes input from clinical experts and patient representatives specific to the condition under review, as well as formal comments from manufacturers and the public. A policy roundtable concludes each meeting during which representatives from insurers and manufacturers join clinical experts and patient representatives to discuss how best to apply the findings of the evidence to clinical practice, insurance coverage, and pricing negotiations.

After deliberation, the CTAF panel members voted 12-2 that the evidence was adequate to demonstrate that vedolizumab has greater net health benefits compared with adalimumab. However, they voted unanimously that the evidence was inadequate to demonstrate a superior net health benefit for ustekinumab compared with adalimumab, and they voted 14-1 that the evidence was inadequate to distinguish the net health benefit among tofacitinib, ustekinumab, and vedolizumab.

The panel also voted on "other potential benefits" and "contextual considerations" of these treatments as part of a process intended to signal to policymakers whether there are important considerations when making judgments about long-term value for money that are not adequately captured in the analyses of clinical effectiveness and cost-effectiveness. The results of these votes highlight several

TABLE 3 Votes on "Other Benefits" that May Not Be Adequately Captured in the Base-Case Cost-Effectiveness Model

Does treating patients with TIMs offer one or more of the following potential "other benefits" compared with conventional therapy?	
These interventions offer reduced complexity that will significantly improve patient outcomes.	2/15
These interventions will significantly reduce caregiver or broader family burden.	9/15
These interventions offer a novel mechanism of action or approach that will allow successful treatment of many patients for whom other available treatments have failed.	13/15
These interventions will have a significant impact on improving patients' ability to return to work and/or their overall productivity.	12/15
There are other important benefits or disadvantages that should have an important role in judgments of the value of these interventions.	2/15

TIM = targeted immune modulator.

TABLE 4 Votes on "Contextual Considerations" Important in Assessing Long-Term Value for Money

Are any of the following contextual considerations important in assessing the long-term value for money of TIMs?	
These interventions are intended for the care of individuals with a condition of, particularly high severity in terms of impact on length of life and/or quality of life.	12/15
These interventions are intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness.	13/15
These interventions are the first to offer any improvement for patients with this condition.	0/15
Compared with conventional therapy, there is significant uncertainty about the long-term risk of serious side effects of these interventions.	13/15
Compared with conventional therapy, there is significant uncertainty about the magnitude or durability of the long-term benefits of these interventions.	12/15
There are additional contextual considerations that should have an important role in judgments of the value of these interventions.	0/15

TIM = targeted immune modulator.

factors that the panel recognized could be influential when making decisions about the value of these treatments (Table 3 and Table 4).

The culminating vote of the CTAF panel on "long-term value for money" was intended to reflect the members' integration of all elements of value. The panel only voted on infliximab and its 2 biosimilars, infliximab-dyyb and infliximab-adba, because for all the other TIMs the results in the base-case economic analysis and other scenarios greatly exceeded commonly cited cost-effectiveness thresholds. In this final vote, a majority of the panel judged the long-term value for money of infliximab and its biosimilars as "intermediate."

The policy roundtable discussion explored how best to translate the evidence and broader perspectives discussed into clinical practice and into pricing and insurance coverage policies. The full set of policy recommendations can be found in the final evidence report; however, several key policy recommendations are as follows:

- The significantly lower prices seen for infliximab and its biosimilars highlight the important potential for improved value with broader availability and uptake of biosimilar treatment options. All stakeholders should collaborate to ensure that TIM biosimilars have an increasing and comprehensive role in the UC treatment landscape.
- The "bundled rebate" approach to price negotiation and formulary development should be replaced with an indication and value-based pricing approach.
- Patients eligible for TIMs include those with moderate to severe UC whose disease has had an inadequate response to conventional systemic therapy. Patient eligibility criteria should be flexible given that clinical trials used tools (e.g., Mayo Score for disease severity) that are not routinely used in clinical practice. Inadequate response to conventional systemic therapy is the facet of clinical criteria that insurers may choose to define by specifying particular types of systemic therapies, number of attempts, or duration. This approach is reasonable as long as there is a valid citation or reference for the specifications given. Measurement of therapy "failure" in clinical trials is based on the Mayo Score, but as noted, this should not be used as a criterion within insurance coverage.
- Given the lack of biomarkers and other predictors of TIM treatment success in UC, it is not unreasonable to use step therapy in this case to manage the costs of treatment. Step therapy among agents for UC appears to meet criteria for reasonable step therapy.
- Switching: Consideration of required switching policies of TIM therapy for patients who are stable on a current treatment should be limited to switches from an originator to a biosimilar agent.

Conclusions

The clinical evidence shows that TIMs are superior to conventional therapy alone. Results supported by the single head-to-head trial and indirect treatment comparison suggests that vedolizumab had greater rates of clinical response and remission than adalimumab, but distinguishing further between the effectiveness of different agents is not possible. At the current pricing, most TIMs were estimated to have incremental cost-effectiveness ratios far higher than traditional thresholds. Notably, infliximab and infliximab biosimilars have much lower average net prices than other TIMs and therefore had markedly better cost-effectiveness ratios, which points to the significant potential for improved value with biosimilar treatment alternatives. Despite this sign of promise, the overall cost of TIMs for UC is too high, even given their substantial clinical benefits, to align reasonably with those benefits. As a result, given that there are no clinical markers suggesting which patients will benefit most from particular TIMs, it is not unreasonable for payers to use prior authorization and judiciously designed step therapy to help manage utilization and seek equivalent outcomes at lower costs.

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REFERENCES

1. Turner D, Levine A, Escher JC, et al. Management of pediatric ulcerative colitis: joint ECCO and ESPGHAN evidence-based consensus guidelines. *J Pediatr Gastroenterol Nutr.* 2012;55(3):340-61.

2. Rubin DT, Dubinsky MC, Lukas M. Long-term efficacy of tofacitinib in patients who received extended induction therapy: results of the OCTAVE open study for tofacitinib delayed responders. *J Crohns Colitis.* 2019;13(Suppl 1):S050-S052 [Abstract DOP43]. Accessed February 1, 2021. https://academic.oup.com/ecco-jcc/article/13/Supplement_1/S050/5301027

3. American Society of Colon and Rectal Surgeons. Ulcerative colitis. Retrieved September 23, 2019. Accessed February 9, 2021. https://fascrs.org/patients/diseases-and-conditions/a-z/ulcerative-colitis

4. Sandborn WJ, Baert F, Danese S, et al. Efficacy and safety of vedolizumab subcutaneous formulation in a randomized trial of patients with ulcerative colitis. *Gastroenterology.* 2020;158(3):562-72.e512.

5. Crohn's and Colitis Foundation of America. The facts about inflammatory bowl diseases. November 2014. Accessed February 9, 2021. https://www.crohnscolitisfoundation.org/sites/default/files/2019-02/Updated%20IBD%20Factbook.pdf

6. Kobayashi T, Suzuki Y, Motoya S, et al. First trough level of infliximab at week 2 predicts future outcomes of induction therapy in ulcerative colitis-results from a multicenter prospective randomized controlled trial and its post hoc analysis. *J Gastroenterol.* 2016;51(3):241-51.

7. Jiang X-L, Cui H-F, Gao J, Fan H. Low-dose infliximab for induction and maintenance treatment in chinese patients with moderate to severe active ulcerative colitis. *J Clin Gastroenterol.* 2015;49(7):582-88.

8. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. *New Engl J Med.* 2005;353(23):2462-76.

9. ClinicalTrials.gov. A study to evaluate the effectiveness and safety of infliximab in chinese patients with active ulcerative colitis. ClinicalTrials.gov Identifier: NCT01551290. 2014. Accessed February 9, 2021. https://clinicaltrials.gov/ct2/show/NCT01551290

10. Suzuki Y, Motoya S, Hanai H, et al. Efficacy and safety of adalimumab in Japanese patients with moderately to severely active ulcerative colitis. *J Gastroenterol.* 2014;49(2):283-94.

11. Reinisch W, Sandborn WJ, Hommes DW, et al. Adalimumab for induction of clinical remission in moderately to severely active ulcerative colitis: results of a randomised controlled trial. *Gut.* 2011;60(6):780-87.

12. Sandborn WJ, van Assche G, Reinisch W, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. *Gastroenterology.* 2012;142(2):257-65.e1-3.

13. Hibi T, Imai Y, Senoo A, Ohta K, Ukyo Y. Efficacy and safety of golimumab 52-week maintenance therapy in Japanese patients with moderate to severely active ulcerative colitis: a phase 3, double-blind, randomized, placebo-controlled study-(PURSUIT-J study). *J Gastroenterol.* 2017;52(10):1101-11.

14. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis. *Gastroenterology.* 2014;146(1):85-95.

15. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis. *Gastroenterology.* 2014;146(1):96-109.e1.

16. Sands BE, Peyrin-Biroulet L, Loftus EV, et al. Vedolizumab versus adalimumab for moderate-to-severe ulcerative colitis. *New Engl J Med.* 2019;381(13):1215-26.

17. Motoya S, Watanabe K, Ogata H, et al. Vedolizumab in Japanese patients with ulcerative colitis: a phase 3, randomized, double-blind, placebo-controlled study. *PloS One.* 2019;14(2):e0212989-e0212989.

18. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N *Engl J Med.* 2013;369(8):699-710.

19. Sandborn WJ, Su C, Sands BE, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. N *Engl J Med.* 2017;376(18):1723-36.

20. Sands BE, Sandborn WJ, Panaccione R, et al. Ustekinumab as induction and maintenance therapy for ulcerative colitis. N *Engl J Med.* 2019;381(13):1201-14.

21. Dubinsky MC, Peyrin-Biroulet L, Melmed GY, et al. Efficacy of tofacitinib in patients with ulcerative colitis by prior tumor necrosis factor inhibitor treatment status: results from OCTAVE induction and maintenance studies: 640. *Am J Gastroenterol.* 2017;112:S354.

22. Sands BE, Peyrin-Biroulet L, Marano C, et al. P312 Efficacy in biologic failure and non-biologic-failure populations in a Phase 3 study of ustekinumab in moderate–severe ulcerative colitis: UNIFI. *J Crohns Colitis.* 2019;13(Suppl 1):S256-S257.

23. U.S. Food and Drug Administration. FDA approves boxed warning about increased risk of blood clots and death with higher dose of arthritis and ulcerative colitis medicine tofacitinib (Xeljanz, Xeljanz XR). July 26, 2019. Accessed February 2, 2021. https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-boxed-warning-about-increased-risk-blood-clots-and-death-higher-dose-arthritis-and

24. REMICADE (infliximab) lyophilized concentrate for injection, for intravenous use. Janssen. Revised November 2013. Accessed February 2, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/103772s5359lbl.pdf

25. HUMIRA (adalimumab) injection, for subcutaneous use. AbbVie. Revised August 2018 . Accessed February 2, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125057s410lbl.pdf

26. SIMPONI (golimumab) injection, for subcutaneous use. Janssen. Revised December 2011. Accessed February 2, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125289s0064lbl.pdf

27. XELJANZ (tofacitinib) tablets, for oral use. Pfizer. Revised May 2018. Accessed February 2, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/203214s018lbl.pdf

28. Samuel S, Ingle SB, Dhillon S, et al. Cumulative incidence and risk factors for hospitalization and surgery in a population-based cohort of ulcerative colitis. *Inflamm Bowel Dis.* 2013;19(9):1858-66.

29. Centers for Medicare & Medicaid Services. Payment allowance limits for Medicare Part B drugs effective July 1, 2020 through September 30, 2020. 2020. Accessed February 2, 2021. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice