An economic evaluation of tofacitinib in the treatment of moderately to severely active ulcerative colitis in the United Kingdom

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Objectives

The objective of this analysis was to evaluate the cost-effectiveness of tofacitinib and other approved biologic therapies for the treatment of moderately to severe active ulcerative colitis in the UK.

Background

Ulcerative colitis is a chronic inflammatory disorder of the colon that has a large, negative impact on quality of life and daily functioning. Current biologic agents are limited and only induce remission in a minority of patients. Tofacitinib is a novel therapy indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent. This economic model compares tofacitinib to licensed biological therapies for ulcerative colitis.

Methods

A Markov model was used to compare lifetime costs and consequences of treatment with tofacitinib, biologics and conventional therapy. Benefits were measured using quality-adjusted life years (QALYs) under a UK NHS perspective; future costs and benefits were discounted at 3.5% annually.¹

The model contained nine health states relating to treatment type and disease control (Figure 1). All patients in the model received induction therapy for 8 weeks (TNFi, vedolizumab or tofacitinib). Responders were separated into remission and response-without-remission groups and non-responders were assumed to still have active ulcerative colitis and transitioned to conventional therapy.

Responders and remitters in the induction phase entered the model maintenance phase and continued to receive the same treatment until loss of response, acute exacerbation event requiring emergency colectomy, or death. Those losing response transitioned to conventional therapy.

During conventional therapy, non-responders were assumed to remain in the active ulcerative colitis state, and some were offered elective colectomy.

The analysis also considered perioperative and long-term complications from emergency and elective colectomy.

The treatment effect for each model comparator was informed by the results of a network meta-analysis (NMA) and considered TNFi-naïve and TNFi-exposed patients separately in the base-case analysis.² ³

Health state utility values were sourced from a UK study⁴ and were adjusted over time to account for a decline in physical and mental functions due to age and comorbidities.⁵

Drug acquisition costs were derived from the Monthly Index of Medical Specialties (MIMS).⁶ Total drug costs were estimated for 8-week cycles. The drug cost of infliximab was calculated based on the weight and patient characteristics in the OCTAVE trials. Resource use for outpatient visits, treatment monitoring, and hospitalisation was based on a UK cost-effectiveness model.⁷ Unit costs were taken from the 2016–2017 NHS England reference costs.⁸

Deterministic and one-way sensitivity analysis were performed for key model parameters. Scenario analyses explored the effect of different model assumptions on the results.
Base-case analysis
For TNF- naïve patients, the ICER for tofacitinib compared with conventional treatment was £21,338 per QALY; tofacitinib was predicted to provide an additional 0.544 QALYs compared with conventional treatment, at an additional lifetime cost of £11,615.

In the TNF-exposed subgroup, the ICER for tofacitinib compared with conventional treatment was £22,816 per QALY; tofacitinib was predicted to provide an additional 0.337 QALYs at an additional lifetime cost of £7,687 compared with conventional treatment.

For both TNF-naïve and TNF-exposed subgroups, tofacitinib dominated infliximab and vedolizumab. Additionally, both adalimumab and golimumab were extendedly dominated by tofacitinib (Table 1).

Sensitivity analysis
Deterministic sensitivity analysis results for tofacitinib versus conventional therapy showed that the model results were robust. The ICER exceeded £30,000 per QALY in two cases: when the rates of response and remission for tofacitinib were set to their lower 95% credible interval limit from the NMA for induction in TNF-exposed patients and in maintenance for TNF-naive patients (Table 2).

Probabilistic sensitivity analysis showed that tofacitinib was more likely than the biological therapies to be the most cost-effective therapy at a willingness-to-pay threshold of £30,000 per QALY (54% probability in TNF-naive patients, 46% in TNF-exposed patients; Figure 2).

Scenario analysis
In the scenario analyses, the ICER per QALY ranged between £20,319 to £33,115 for the TNF-naive subgroup and £21,706 to £33,471 for the TNF-exposed subgroup. The only scenarios to generate an ICER above £30,000 per QALY was when 50% of patients were assumed to need a higher dose of maintenance therapy (both subgroups) and when alternative health state utility values were used (TNF-exposed subgroup only).

When the ITT population values were used instead of modelling by TNF-exposure subgroup, tofacitinib dominated vedolizumab and had an ICER of £20,038 per QALY gained versus conventional therapy (Table 2).

<table>
<thead>
<tr>
<th>Strategy</th>
<th>ICER, strategy vs conventional therapy, £/QALY</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>TNF-naive</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>£21,338</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>£30,982</td>
</tr>
<tr>
<td>Golimumab</td>
<td>£30,602</td>
</tr>
<tr>
<td>Infliximab</td>
<td>£37,495</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>£43,205</td>
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</tbody>
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Yellow cells denote extended dominance and orange cells absolute dominance of tofacitinib. Grey cells denote missing values.

Table 2. Deterministic sensitivity and scenario analysis for tofacitinib versus conventional therapy

<table>
<thead>
<tr>
<th>Base case</th>
<th>ICER, tofacitinib vs conventional therapy, £/QALY</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>lower 95% CrI limit—upper 95% CrI limit</td>
</tr>
<tr>
<td>TNF-naive</td>
<td>£21,338</td>
</tr>
<tr>
<td>TNF-exposed</td>
<td>£22,816</td>
</tr>
</tbody>
</table>

Sensitivity analysis
- Induction phase treatment phase treatment effects (response/remission): £19,745—£23,962
- Maintenance phase treatment effects (response/remission): £13,220—£69,500
- Serious infection costs: £20,308—£26,400
- Conventional treatment costs: £18,933—£22,239
- Colectomy risk: £13,652—£25,066
- Annual HS-related HCRU: £21,140—£23,790
- Pre-surgery HSUV: £20,196—£23,661
- Serious infection risk: £19,903—£20,343

Scenario analysis
- Exacerbations: Can happen from any health state (50% of patients), Only happen from active UC state (25% of patients)
- Alternative health state utility values*: £29,753 (50% of patients), £32,825 (25% of patients)
- Centrally read endoscopic subscores (OCTAVIA): £22,755

Clinical response and remission data from ITT NMA £20,038

Higher dose of maintenance therapy needed for:
- 25% of patients: £27,582
- 50% of patients: £33,115

Time horizon:
- 5 years: £21,388
- 10 years: £20,319

Abbreviations:
CrI, credible interval; HCRU, healthcare resource utilisation; HS, health state; HSUV, health state utility value; TNFi, tumour necrosis factor inhibitor
Base case results shown in yellow. Results shown in bold when ICER exceeds £30,000 per QALY.
The economic model followed best-practice research guidelines. All assumptions regarding model structure and inputs were reviewed by UK clinicians and independent health economists.

This cost-effectiveness model expanded on work conducted in previous economic evaluations, updating assumptions based on contemporary evidence where necessary. This model generated lower QALYs than previous economic models, likely due to the addition of age-dependent and gender-dependent adjustments.

Several assumptions were necessary due to data reporting limitations. It was assumed that there was a direct relationship between maintenance phase response levels and treatment duration to help derive transition probabilities for maintaining response or remission, conditional on induction response levels. Other inputs requiring assumptions included the conventional treatment drug mix, complication costs and event types caused by serious infections. Assumptions were tested using scenario and one-way sensitivity analysis. None of the above assumptions were found to be major drivers of the cost-effectiveness results.

This cost-effectiveness model found tofacitinib to be an efficacious treatment for moderately to severely active ulcerative colitis and is likely to be a cost-effective use of NHS resources.

References


Discussion

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Conclusion

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