Cost-effectiveness of Vedolizumab Compared With Ustekinumab for Treatment of Moderately-to-Severely Active Crohn's Disease in the United Kingdom

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BACKGROUND

- Crohn's disease (CD) treatment can place a substantial economic burden on the health care system.
- Vedolizumab (VDZ), a biological therapy (an anti-α4β7 monoclonal antibody) is approved in the United Kingdom (UK) for adult patients with moderately-to-severely active CD who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or who had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

OBJECTIVE

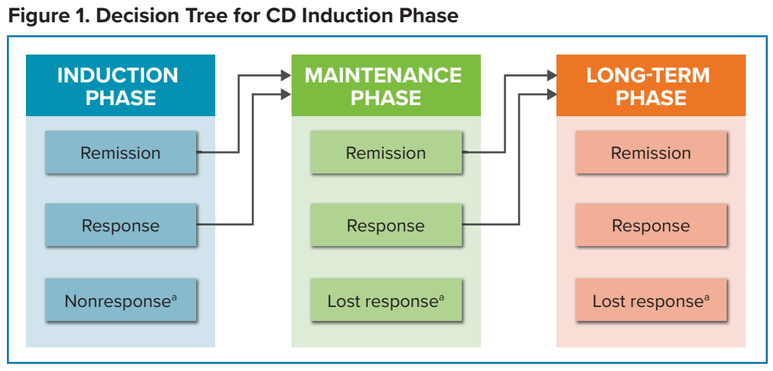
- To examine the clinical and economic impact of VDZ compared with ustekinumab (UST) in the treatment of moderately-to-severely active CD from a UK perspective.

METHODS

Model Structure

- Figure 1 illustrates the decision tree framework for the model's induction phase.

Figure 1. Decision Tree for CD Induction Phase



CDAI = Crohn's Disease Activity Index.

Note: Response is defined as a drop in CDAI score of 100 points or more. This includes patients who also achieve remission, as remission is a subset of response. Remission is defined as a CDAI score lower than 150. For simplicity, we assume patients with response but not remission have a CDAI score of 150 – < 220.

[a]Patients who fail induction treatment, or those who respond in induction but lose response thereafter, are assumed to discontinue biologics and begin conventional therapy induction therapy. Patients in nonresponse or lost response are assumed to be in moderately-to-severely active disease (CDAI ≥ 220). These patients also incur a risk of surgery due to being in moderate/severe disease.[1]

- Within this model structure, health states are defined according to Mayo scores: "Remission" (CDAI < 150), "Response" (CDAI = 150-220), "Nonresponse/Lost Response" (CDAI > 220), "Surgery," and "Death."
- Patients in "Response" or "Remission" continue biologic treatment. Patients who lose response or who fail to respond discontinue to conventional therapy.
- The model estimates the proportion of patients in each health state at the end of induction, the end of maintenance, and annually thereafter. Health-state–specific costs and utilities are estimated over each time period assuming the average of the proportion of patients at the beginning and end of the time period.
- Costs and outcomes (National Health Service and Personal Social Services perspective) were discounted at 3.5% per annum.

Population Characteristics

- Patient characteristics (age, gender, and weight) were based on pooled patient population of all clinical trials used in a network meta-analysis of UC trials.

Clinical Inputs

- Efficacy estimates (Table 1) were obtained from published literature for each treatment[2-5] and were placebo adjusted using the Bucher method.[6]
- Maintenance phase efficacy estimates (Table 1) were also adjusted to control for differences in maintenance trial designs (re-randomization, response criteria for study inclusion, etc).[2,5]
- After 1 year, long-term efficacy estimates (Table 1) were derived from published literature.[7]
- Due to the low rate of adverse events for each treatment, adverse events were not considered.

Table 1. Probability of Response and Remission for Each Treatment

	VZD	UST	Conventional Therapy
Induction			
Response	33.1%	35.6%	22.5%
Remission	13.3%	17.6%	9.7%
Maintenance			
Response	48.0%	35.0%	32.5%
Remission	42.4%	30.1%	19.5%
Long-term			
Response	73.4%	73.4%	59.1%
Remission	71.4%	59.4%	45.1%

Response was defined as a reduction of 100 points or more in CDAI score from baseline, and remission was defined as a CDAI score lower than 150.

Costs

- Drug costs were assumed to be £2,358 per 300 mg vial and infusion of VDZ and £2,147 per 100 mg vial of UST.[8] We assumed no vial sharing.
- Health state costs were obtained from ustekinumab's NICE submission (Table 2).

Utility Weights

- Health state utility weights were obtained from a previous utility study in CD (Table 2).

Mortality

- Age- and gender-specific mortality was obtained from the Office of National Statistics.[10]

Table 2. Health State Costs and Utility Weight

Health State	Cost	Source	Utility Weight	Source
Remission	£464.58	NICE, 2017[4]	0.827	Buxton et al., 2007[9]
Mildly active disease	£1,310.85		0.695	
Moderately-to-severely active disease	£14,073.84		0.425	
Surgery	£22,728.04		0.425	Assumed similar to moderately-to-severely active disease

Response was defined as a reduction of 100 points or more in CDAI score from baseline, and remission was defined as a CDAI score lower than 150.

Sensitivity Analysis

- One-way and probabilistic sensitivity analysis (Monte Carlo simulation) based on varying parameter estimates (costs, treatment efficacy, transition probabilities, utility weights, etc.) was performed to test the impact on the incremental cost-effectiveness ratio (ICER) for VDZ compared with conventional therapy.

RESULTS

Base-Case Results

- VDZ was more effective and less costly than UST over 5-year, 10-year, and 30-year time horizons (Table 3).

Sensitivity Analysis Results

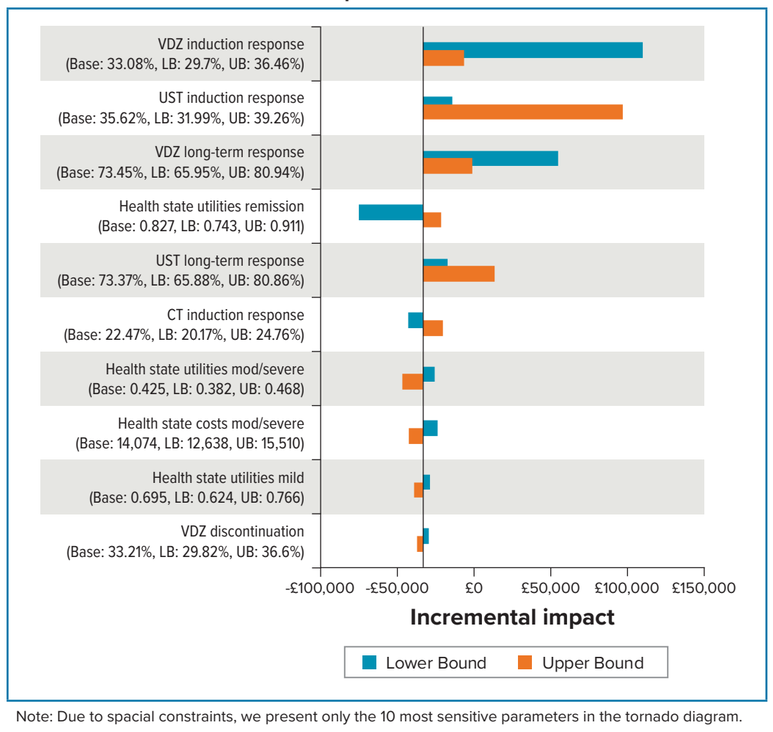
- In one-way sensitivity analyses, VDZ was cost-effective in all cases except the lower bound of VDZ induction efficacy and upper bound of UST induction efficacy (Figure 2).
- In the probabilistic sensitivity analysis, VDZ was cost-effective in 62.3% of cases compared with UST (Figure 3).

Table 3. Incremental Cost-effectiveness of VDZ Compared With UST Over Lifetime Horizons

Results	5 Years		10 Years		30 Years	
	VDZ	UST	VDZ	UST	VDZ	UST
Costs	£76,351	£77,604	£131,298	£132,047	£271,756	£272,400
Drug	£14,002	£13,681	£15,620	£14,448	£15,971	£14,613
Other medical	£62,349	£63,923	£115,678	£117,599	£255,786	£257,787
QALY	2.348	2.341	3.997	3.980	8.111	8.091
Surgeries	0.206	0.210	0.461	0.467	1.483	1.490
Remission years	0.545	0.449	0.659	0.528	0.689	0.548
Incremental cost per QALY gained	VDZ dominant		VDZ dominant		VDZ dominant	

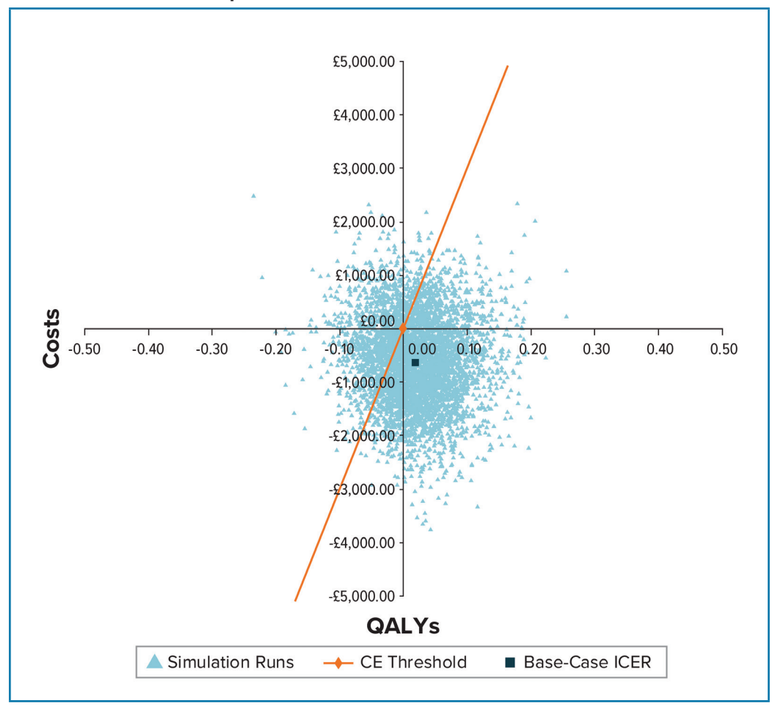
Note: The term dominant refers to a treatment that is both more effective and less costly. QALY = quality-adjusted life-year.

Figure 2. One-Way Sensitivity Analysis Tornado Diagram of VDZ Compared With UST in an Anti-TNF Failure Population



Note: Due to spacial constraints, we present only the 10 most sensitive parameters in the tornado diagram.

Figure 3. Probabilistic Sensitivity Analysis Cost-effectiveness Acceptability Threshold of VDZ Compared With UST



LIMITATIONS

- Lack of head-to-head trial data between biologics requires an indirect comparison methodology in order to assess cost-effectiveness.
- Clinical data are limited for UST in an anti-TNF failure population.
- Differences in trial designs make comparisons challenging.
- The short duration of clinical trials requires extrapolation beyond 1 year to capture the full benefit of treatment for this chronic condition.

CONCLUSIONS

- Treatment with VDZ improves clinical outcomes for patients with anti-TNF failure and moderately-to-severely active CD:
  - Greater QALY
  - More time spent in remission
  - Fewer surgeries
- VDZ is a cost-effective treatment option for patients with anti-TNF failure and moderately-to-severely active CD.

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