EPH29

The cost of managing safety events: ozanimod versus tofacitinib – a UK perspective

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Introduction

- Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by mucosal inflammation. Clinical and humanistic burden depends on disease severity and symptoms experienced
- Incidence of UC in the United Kingdom is approximately 10 per 100,000[1]; prevalence is approximately 240 per 100,000; and approximately 146,000 persons in the United Kingdom have a UC diagnosis[2]
- Ozanimod is an oral agonist of sphingosine 1-phosphate receptor subtypes 1 and 5,[3] that received US and EU approval in 2021 for the treatment of moderately to severely active UC
- Ozanimod functions by causing proinflammatory lymphocytes to remain in the lymph nodes, preventing their migration to sites of inflammation including the gastrointestinal tract[3]
- This analysis modeled the cost-effectiveness of ozanimod compared with currently approved therapy as treatment for adult patients with moderate to severe UC in the United Kingdom

Objectives

- A cost comparison of adverse event (AE) and malignancy management costs for moderate to severe UC was conducted
- Tofacitinib, the only appropriate oral agent, was the comparator

Methods

- The cost comparison was based on published pooled safety data in patients with moderate to severe UC
- Serious infections and malignancies were investigated as the AEs with the most publicly available data for both tofacitinib and ozanimod. Furthermore, these AEs have been included in NICE TA456 (ustekinumab) and TA342 (vedolizumab) appraisals[4,5]
- Safety data were pooled from phase 2 (NCT01647516), phase 3 (NCT02435992), and open-label extension (NCT02531126) trials for ozanimod, and from two phase 3 induction trials (NCT01465763, NCT01458951), a maintenance study (NCT01458574), and an open-label, long-term extension study for tofacitinib (NCT01470612)
- The malignancy analyses excluded non-melanoma skin cancers (NMSC) to follow the precedent of inflammatory bowel disease safety analysis
- Incidence rates of serious infection and malignancy were measured as the number of unique patients with events per 100 patient-years (PY) of exposure in the active treatment arms for ozanimod and tofacitinib and their respective placebo arms
- Serious infections and malignancies were classified by International Classification of Diseases-10 (ICD) codes, and their assigned Healthcare Resource Group (HRG) codes were used to obtain costs from NHS National Cost Collection data[6,7]
- Costs were calculated for any serious infection with an incidence of ≥ 2 in the clinical trials

Results

Malignancies

Table 1. Incidence rate of malignancies

	Total exposure, PY		
	Intervention	Placebo	Reference
Ozanimod	1922.50	249.20	D'Haens[8]
Tofacitinib	2656.37	148.77	Lichtenstein[9]

Figure 1. Incidence rate of malignancies excluding NMSC across follow-up (events per 100 PY; ozanimod/tofacitinib vs placebo)

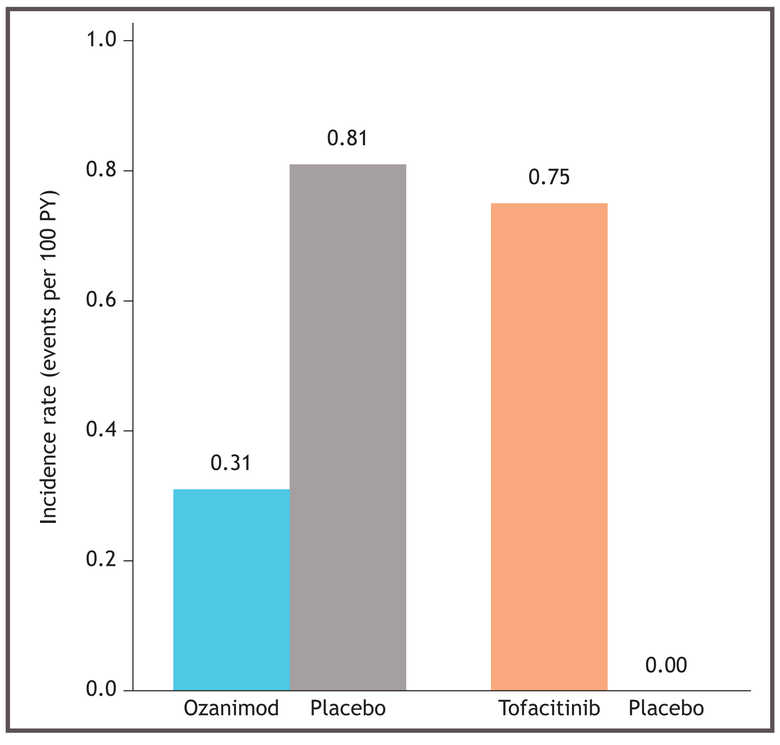


Table 2. Ozanimod-associated malignancy costs

Malignancy	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Adenocarcinoma	C34.90	DZ17	1869.78	1	97.26
Breast cancer	C50	JA12	715.00	1	37.19
Lung neoplasm malignant	C34.90	DZ17	1869.78	1	97.26
Prostate cancer	C61	LB06	1777.85	1	92.48
Rectal adenocarcinoma	C20	FD11	1911.64	1	99.44
Rectal cancer stage 2	C18.9	FD11	1911.64	1	99.44
Total					**523.05**

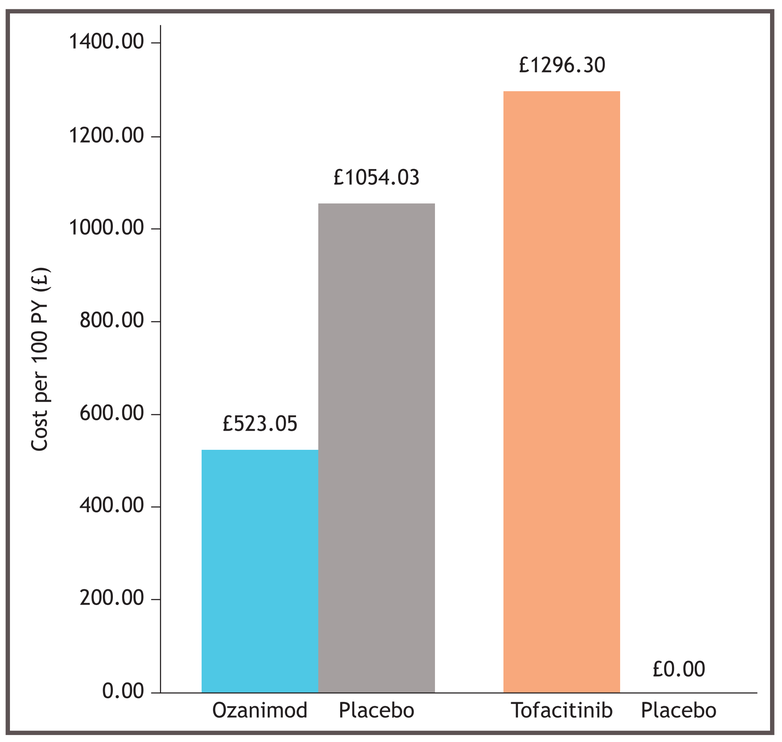
Table 3. Placebo-associated malignancy costs (ozanimod trials)

Malignancy	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Adenocarcinoma of the colon	C18.9	FD11	1911.64	1	767.11
Breast cancer	C50	JA12	715.00	1	286.92
Total					**1054.03**

Table 4. Tofacitinib-associated malignancy costs

Malignancy	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Breast cancer	C50	JA12	715.00	3	80.75
Cervical cancer	C53.9	MB05	2299.63	1	86.57
Cholangiocarcinoma	C22.1	GC12	1931.15	1	72.70
Leukemia	C95.91	SA25	3991.78	1	150.27
Lung cancer	C34.9	DZ17	1869.78	1	70.39
Melanoma	C43.9	JD07	1479.28	2	111.38
Non-Hodgkin lymphoma	C85.90	SA31	2626.53	1	98.88
Essential thrombocythemia	D47.3	SA07	357.96	1	13.48
Renal cancer	C64.9	LB06	1777.85	1	66.93
Colorectal cancer	C18.8	FD11	1911.64	2	143.93
Cutaneous leiomyosarcoma	C49.21	HD40	1370.11	1	51.58
Hepatic angiosarcoma	C22.3	GC12	1913.15	1	72.02
Cervical dysplasia	N87.9	MB09	1269.54	1	47.79
Esophageal adenocarcinoma	C15.9	FD11	1911.64	1	71.96
Cancer of the penis	C60.9	LB58	1561.94	1	58.80
B-cell lymphoma	C85.12	SA31	2626.53	1	98.88
Total					**1296.30**

Figure 2. Cost comparison: malignancy events per 100 PY (ozanimod/tofacitinib vs placebo)



Serious infections

Table 5. Incidence rate of any serious infections

	Any serious infection				Total exposure, PY		
	Induction, intervention	Maintenance, intervention	Across follow-up, intervention	Across follow-up, placebo	Intervention	Placebo	Reference
Ozanimod	3.96	-	1.32	2.84	1922.50	249.20	D'Haens[8]
Tofacitinib	4.83	1.35	1.70	1.38	2581.3	145.2	Winthrop[10]

Figure 3. Incidence rate of any serious infection across follow-up (events per 100 PY; ozanimod/tofacitinib vs placebo)

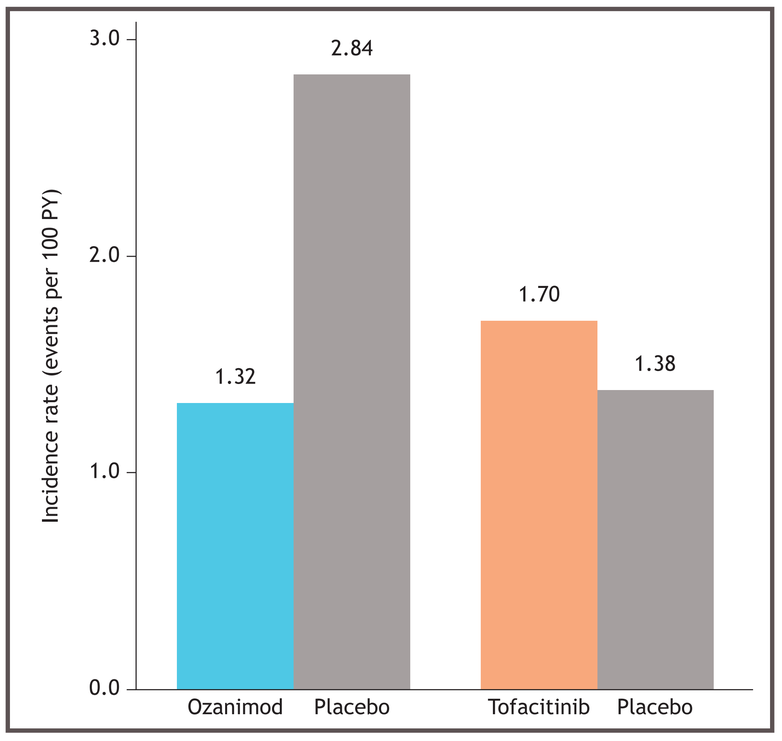


Table 6. Ozanimod-associated any serious infection (n ≥ 2) costs

Serious infection	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Appendicitis	K37	FD10	1446.00	6	451.29
Pneumonia influenza	J09.X1	WJ03	1246.00	4	259.25
Clostridium difficile infection	A047	FD01	1366.10	2	142.12
Gastroenteritis	K52.9	FD02	685.00	2	71.26
Urinary tract infection	N39.0	LA04	1725.00	2	179.45
Total					**1103.37**

Table 7. Placebo-associated any serious infection (n ≥ 2) costs (ozanimod trials)

Serious infection	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Appendicitis	K37	FD10	1446.00	3	1740.77
Total					**1740.77**

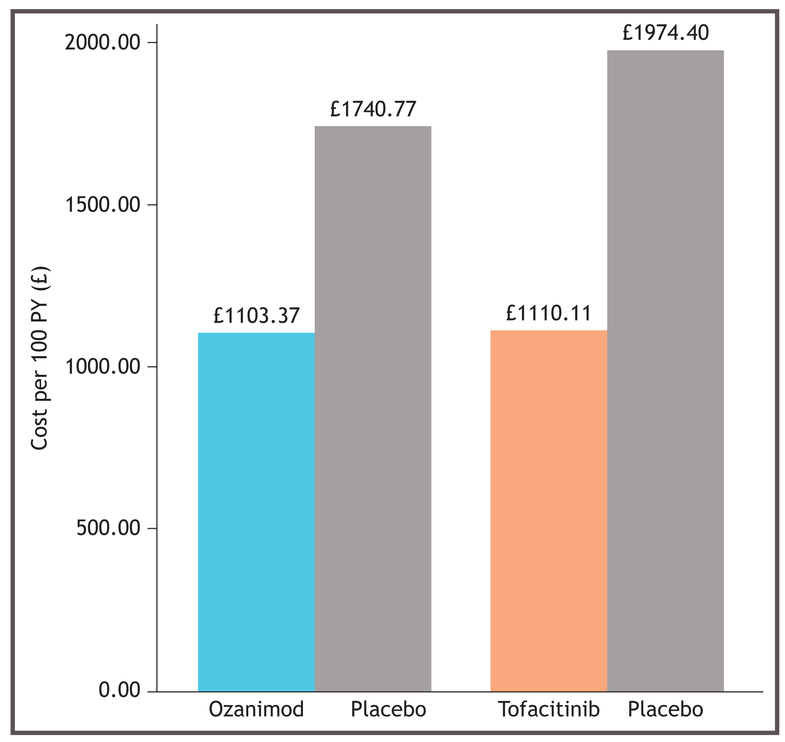
Table 8. Tofacitinib-associated any serious infection (n ≥ 2) costs

Serious infection	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Anal abscess	K610	FD10	1446.16	4	224.10
Appendicitis	K37	FD10	1446.00	3	168.05
Herpes zoster	B02	WJ01	2372.00	5	459.46
Ophthalmic herpes zoster	B023	BZ24	1012.24	2	78.43
Clostridium difficile infection	A047	FD01	1366.10	2	105.85
Sinusitis	J01	CB02	958.00	2	74.23
Total					**1110.11**

Table 9. Placebo-associated any serious infection (n ≥ 2) costs (tofacitinib trials)

Serious infection	ICD code	HRG code	Cost per event, £	Incidence	Cost per 100 PY, £
Unspecified	-	-	1433.42	2	1974.40
Total					**1974.40**

Figure 4. Cost comparison: any serious infection (n ≥ 2) events per 100 PY (ozanimod/tofacitinib vs placebo)



Cost comparison

Table 10. Cost comparison: all AEs per 100 PY (ozanimod vs tofacitinib)

Cost per 100 PY, £	Ozanimod vs placebo	Tofacitinib vs placebo	Delta, ozanimod vs tofacitinib
Malignancy	−530.98	1296.30	−1827.27
Any serious infection	−637.40	−864.29	226.89
All AEs	−1168.38	432.01	−1600.39

Limitations

- Data for ozanimod serious infections of n = 1 and for serious infections in the tofacitinib placebo arm were lacking, resulting in less accurate analyses
- Because of a lack of available data for tofacitinib in the reporting of overall malignancies, this analysis focuses only on patients with malignancies excluding NMSC
- Means of NHS HRG data were used to cost individual AEs. A distribution of costs would more accurately reflect reality

Conclusions

- The results of this analysis show that the incidence rate and costs of managing any serious infections and malignancies are potentially greater for tofacitinib than ozanimod versus placebo
- Per 100 PY, the estimated cost saving of the investigated AEs for ozanimod versus tofacitinib is £1600.39 (−£1168.38 vs £432.01, respectively)
- Future work to explore the AE management costs of ozanimod versus its comparators can address the limitations and uncertainty in the analysis presented here
- With respect to data availability, aligning future safety reporting of ozanimod data with publicly available tofacitinib reports may increase homogeneity across the analyzed AE data sets
- The inclusion of an indirect treatment comparison would decrease the uncertainty between the study populations and result in a more accurate treatment comparison
- The estimation of costs per AE currently lies as a point estimate from aggregated data. Use of a cost distribution will better characterize the uncertainty of the estimates produced and provide more meaningful conclusions for budget holders

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