Ozanimod for treating moderately to severely active ulcerative colitis [ID3841]

Part 1: Slides for PUBLIC

Contains no ACIC information

Technology appraisal committee A [12 July 2022]

Chair: Jane Adam

Lead team: Steve Edwards

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NICE National Institute for Health and Care Excellence

Clinical issues

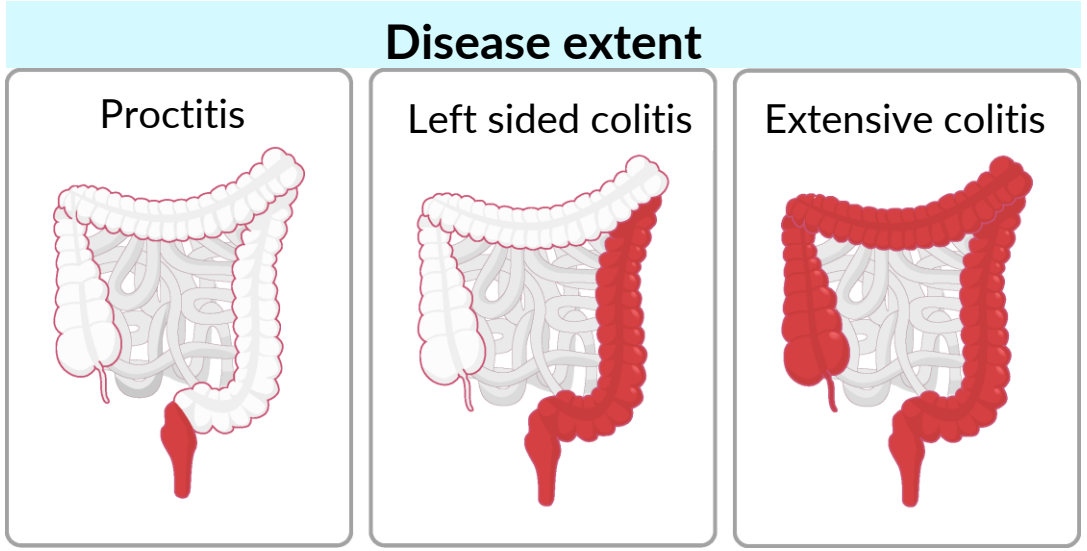
- Are the pre- and post-biologic subgroups rather than the whole population the most relevant for decision-making?
- The company proposes that ozanimod could be used before any other treatment, when standard care is not working.
    - Is this likely in clinical practice?
    - Are TNF-alpha inhibitors usually used first after standard care, and is this generally adalimumab or infliximab?
    - How often would another treatment be offered instead?
- After a TNFi, what would be the next treatment offered? Is there wide use of a second TNFi or would an alternative treatment be offered such as vedolizumab, ustekinumab or tofacitinib?
- Like ozanimod, tofacitinib is an oral treatment. How much is tofacitinib used in clinical practice?
- Are the results of the NMAs acceptable for decision making? How reliable are the calculated differences between treatments as shown by the NMAs?

 Abbreviations: NMA, network meta-analysis; TNFi, tumour necrosis factor inhibitor

Background on ulcerative colitis

Chronic inflammatory condition affecting the colon and rectum

- Lifelong condition, relapsing and remitting with periods of diffuse inflammation of rectal and colonic mucosa
- **Causes:** unknown; possible factors include genetic, environmental, dysregulated immune response, defects in protective lining of colon
- **Epidemiology (England in 2020):** ~4,400 to 6,000 adults diagnosed each year (peak incidence 15 to 35 years and 55 to 65 years); ~104,405 adults affected; 52% have moderately to severely active UC
- **Symptoms:** rectal bleeding, faecal urgency, diarrhoea, lower abdominal pain. Other areas such as joints, eyes, skin and liver may be affected
- **Aim of treatment:** remission to avoid complications such as bowel cancer, haemorrhage, perforation, strictures, abscesses, liver disease, osteoporosis and emergency toxic megacolon
- **Diagnosis and classification:** disease extent (colonoscopy) and severity (Mayo scoring system)



Abbreviations: UC, ulcerative colitis

Ozanimod

Marketing authorisation	Adults with moderately to severely active ulcerative colitis who had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent (MHRA: March 2022)
Mechanism of action	sphingosine 1-phosphate (S1P) receptor modulator : interacts with S1P receptors 1 and 5 to decrease circulating lymphocytes to reduce inflammation
Administration	Oral **Induction** • Dose escalation (1 week): 0.25 to 0.5 mg OD • 1 mg OD starting on Day 8 **Maintenance** • 1 mg OD
Price (list)	• Initiation pack (4 x 0.25 mg & 3 x 0.5 mg): £343 • Maintenance pack (28 x 1 mg): £1,373 • Maintenance pack (98 x 1 mg): £4,805 • Annual cost – induction (Year 1) and maintenance (Year 2 onwards): £17,910 • Patient access scheme is applicable

NICE Abbreviations: MHRA, Medicines and Healthcare products Regulatory Agency; OD, once daily

Treatment pathway

Treatment highly individualised and clinical practice variable across UK

Conventional therapy
corticosteroids, mesalazine, azathioprine, mercaptopurine

Vedolizumab? NICE guidance does not specify only after conventional therapy

Inadequate/loss response or intolerance

- **Biologic therapy** [TNFi (adalimumab, golimumab, infliximab)* (TA329), vedolizumab (TA342)]
- **Non-biologic therapy** [tofacitinib (TA547)**]

Inadequate/loss response or intolerance

- **Biologic therapy** [TNFi (adalimumab, golimumab, infliximab)* (TA329), vedolizumab (TA342), ustekinumab (TA633)]
- **Non-biologic therapy** [tofacitinib (TA547)**]

Surgery / Best supportive care

Company proposed position: ozanimod
"…who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent"
- **TNFi-naïve**
- **TNFi-experienced**

Is there a clinical need for a different type of treatment either before or after administration of a biologic?
How important is route of administration?
Is the treatment pathway representative of NHS practice?
Is the company stratification based on TNFi experience only appropriate?

TNFα inhibitor integrin inhibitor IL-12/IL-23 inhibitor JAK inhibitor

*Includes biosimilars; **filgotinib (TA792) published June 2022

Comparators

Subgroups	Company comments	ERG comments
TNFi-naïve	• TNFis, vedolizumab • Tofacitinib not used; used in later lines of treatment because of safety issues • ERG's tofacitinib usage is over-estimated (feedback from tertiary referral centre)	Tofacitinib: feedback from 1 specialist referral centre suggests increasing use (oral, fast acting). Included in TA633 (ustekinumab) for completeness but committee considered not relevant
TNFi-experienced	• vedolizumab, ustekinumab • Tofacitinib not used because of safety concerns ***MHRA guidance on tofacitinib*** • *Increased risk of cardiovascular events and malignancies* • *Only use if no suitable alternative treatment is available for people more than 65 years, who smoke (current or past), have a history of diabetes, coronary artery disease*	• 2nd TNFi: can be used if 1st stopped because of immunogenicity (uncommon); TA633 included adalimumab • Tofacitinib: use increasing despite safety concerns

Would a TNFi be used first after conventional therapy?
Would an alternative TNFi be used if the first TNFi is not tolerated or ineffective?
Is tofacitinib used in NHS practice? If so, at which point in the treatment pathway?
What are the relevant comparators for TNFi-naïve and TNFi-experienced subgroups?

 Abbreviations: TNFi, tumour necrosis factor inhibitor

Patient perspectives

Ulcerative colitis can have a devastating impact on all aspects of life

Submission from Crohn's & Colitis UK

- Condition is unpredictable
- Acute severe colitis has 1% mortality risk and 29% chance of needing emergency surgery to remove inflamed bowel (colectomy)
- Symptoms and side effects of medicines can have a profound and devastating impact on all aspects of a person's life:
    - ability to work, study, socialise, take part in leisure activities, have intimate relationships
    - emotional wellbeing, difficulty coping, feelings of anger, embarrassment, frustration, sadness and fears of needing surgery or developing cancer
    - stigma and lack of wider understanding of condition can exacerbate impact

… the constant anaemia make everyday life feel like wading through treacle … The very real concern of faecal incontinence gives me physical symptoms of stress as well as affecting me emotionally and mentally.

… I was off sick from work for 8 months. There was no fun time …, I was always in bed, in pain or on the toilet. This period of illness really affected my confidence. My friends gave up coming around as I was so poorly. My quality of work really dropped. I continuously made mistakes because of the side effects from all the drugs.

Clinical perspectives

TNFis have high failure rates

Submissions from British Society of Gastroenterology (Inflammatory Bowel Disease Committee) and UK Clinical Pharmacy Association

- High failure rates for current treatments
  - 19-58% of people in clinical trials: condition does not respond to TNFi induction therapy
  - 17-22% of people whose condition responds to TNFis stop because of secondary loss of response
  - about 40% need dose escalation to maintain TNFi effectiveness
  - higher rates in people having second line TNFis (68-77% at 12 months and 82-90% by end of year 2)
- Ozanimod is an oral medication with a novel mechanism of action that would provide an alternative to existing therapies
- Ozanimod is likely to be used exclusively in secondary and tertiary care by gastroenterologists experienced in ulcerative colitis
- Ozanimod has potentially serious side effects that need additional monitoring and is contraindicated in people at risk of symptomatic bradycardia

Abbreviations: TNFi, tumour necrosis factor inhibitor

Clinical effectiveness

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Key clinical trial: TRUENORTH

	TRUENORTH (NCT02435992)
Design	Phase 3, double-blind, randomised, placebo-controlled, multi-centre trial
Population	1,012 adults: moderately to severely active UC • Disease extending ≥15cm from anal verge • Active UC, 4-component Mayo score 6–12, endoscopic subscore ≥2, rectal bleeding subscore ≥1, stool frequency score ≥1
Intervention	1 mg/day of ozanimod administered orally during induction and maintenance
Comparator	Placebo (oral)
Duration	52 weeks (10-week induction including 1 week dose escalation, 42-week maintenance)
Primary outcome	Proportion of people in clinical remission at Week 10 and Week 52, overall and subscores of 3- and 4-component Mayo scoring system
Key secondary outcomes	• Proportion of people with clinical response, endoscopic improvement mucosal healing, sustained clinical remission, corticosteroid-free remission and durable clinical remission • EQ-5D-5L
Locations	285 study sites in North America, Europe, Asia Pacific, South America, South Africa

TOUCHSTONE, a phase 2 dose-finding trial provided supporting data; not used in economic model

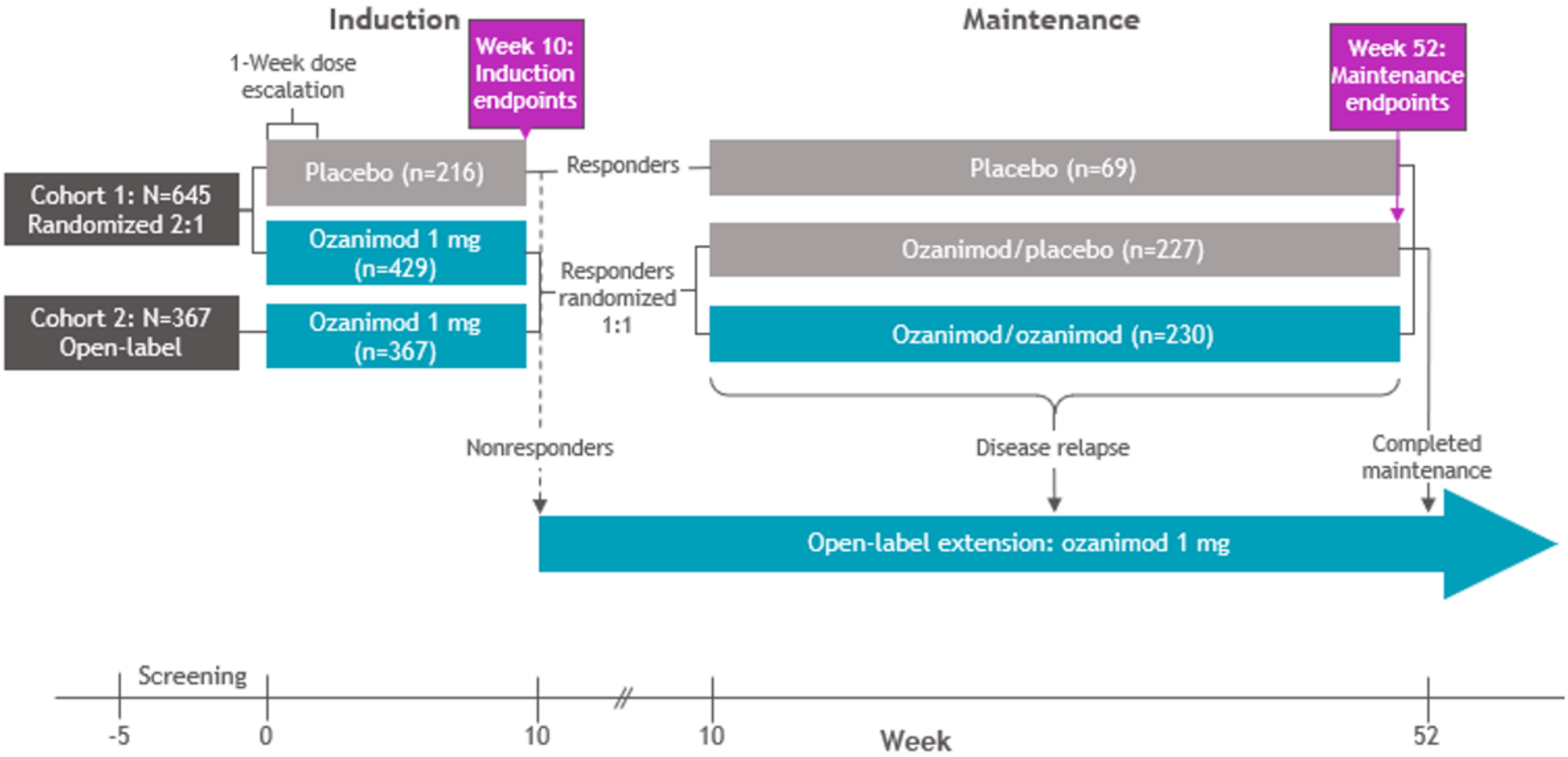
 Abbreviations: EQ-5D-5L, Euro-Qol 5 dimension; UC, ulcerative colitis

Cohort 1 and 2: induction

TRUENORTH: re-randomised design	Cohort 1 (n=645)	Cohort 2 (n=367)
Method	Randomised to placebo or ozanimod	Open-label group received ozanimod only
Proportion who had TNFi previously	Limited to [redacted]	Once limit of 30% is reached in Cohort 1, Cohort 2 recruited people with TNFi experience, up to [redacted]
Inclusion criteria	Had stable doses of oral aminosalicylates and/or steroids for ≥2 weeks before screening endoscopy; continued on same dose for induction; steroid dose tapered on entering maintenance	
Exclusion criteria	• biologic agent within 8 weeks or 5 elimination half-lives before randomisation • investigational agent within 5 elimination half-lives before randomisation • topical rectal 5-aminosalicylic acid or topical rectal corticosteroids within 2 weeks of screening endoscopy or anti-motility medications during screening • Natalizumab, fingolimod or etrasimod • Immunosuppressive agents (azathioprine, mercaptopurine, or methotrexate) at screening must be stopped before randomisation • Oral cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil or tofacitinib	
Analysis	Efficacy induction endpoints	Excluded from efficacy induction endpoints. Safety data only

 Abbreviations: TNFi, tumour necrosis factor inhibitor

TRUENORTH study design



TRUENORTH baseline characteristics: induction

People is broadly generalisable to UK population, but may be 10 years younger

	TNFi-naïve		TNFi-experienced	
	Cohort 1		Cohort 1	
	Ozanimod (n=[redacted])	Placebo (n=[redacted])	Ozanimod (n=[redacted])	Placebo (n=[redacted])
Male, %	[redacted]	[redacted]	[redacted]	[redacted]
Age (years), mean (SD)	[redacted]	[redacted]	[redacted]	[redacted]
Extensive colitis, %	[redacted]	[redacted]	[redacted]	[redacted]
Prior treatment				
TNFi, %	NR	NR	NR	NR
Non-TNFi biologics, %	[redacted]	[redacted]	[redacted]	[redacted]
Primary non-responder, %	[redacted]	[redacted]	[redacted]	[redacted]
Secondary non-responder, %	[redacted]	[redacted]	[redacted]	[redacted]
Intolerant, %	[redacted]	[redacted]	[redacted]	[redacted]
Vedolizumab, %	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab, %	[redacted]	[redacted]	[redacted]	[redacted]
Tofacitinib, %	[redacted]	[redacted]	[redacted]	[redacted]

Are these baseline characteristics, particularly prior treatments generalisable to NHS clinical practice?

Abbreviations: NR, not reported; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

TRUENORTH results: Week 10 induction

Ozanimod statistically significantly improves clinical outcomes compared to placebo, except for some in the TNFi-experienced subgroup

	TNFi-naïve		TNFi-experienced		
	Ozanimod (n=[redacted])	Placebo (n=[redacted])	Ozanimod (n=[redacted])	Placebo (n=[redacted])	p value
Clinical remission, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Clinical response, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Endoscopic improvement, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Mucosal healing (combined endoscopic and histological healing, Geboes score <2.0), %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Differences between ozanimod and placebo are all statistically significant ($p<0.05$) in the TNFi-naïve population

Is ozanimod likely to be less effective after an initial TNFi than before?

Abbreviations: TNFi, tumour necrosis factor inhibitor

TRUENORTH baseline characteristics: maintenance

	TNFi-naïve			TNFi-experienced		
		Re-randomised			Re-randomised	
	Placebo (n=[redacted])	Placebo (n=[redacted])	Ozanimod (n=[redacted])	Placebo (n=[redacted])	Placebo (n=[redacted])	Ozanimod (n=[redacted])
Male, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Age, years, mean (SD)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Extensive colitis, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Prior treatment						
TNFi, %	NR	NR	NR	NR	NR	NR
Non-TNFi biologics, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Primary non-responder, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Secondary non-responder, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Intolerant, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Vedolizumab, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Tofacitinib, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Are these baseline characteristics generalisable to NHS clinical practice?

NICE Abbreviations: NR, not reported; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

TRUENORTH results: Week 52 maintenance

Ozanimod statistically significantly improves clinical outcomes compared to placebo, except for some in the TNFi-experienced subgroup

	TNFi-naive		TNFi-experienced		
	Ozanimod (n=[redacted])	Placebo (n=[redacted])	Ozanimod (n=[redacted])	Placebo (n=[redacted])	p value
Clinical remission, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Clinical response, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Endoscopic improvement, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Mucosal healing (combined endoscopic and histological healing, Geboes score <2.0), %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Maintenance of remission, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Corticosteroid-free remission, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Durable remission, %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Differences between ozanimod and placebo are all statistically significant ($p<0.05$) in the TNFi-naïve population

 Abbreviations: TNFi, tumour necrosis factor inhibitor

Network meta-analysis: ozanimod vs comparators

Company

- NMA efficacy estimates used in economic model
- NMAs of 25 RCTs based on TNFi experience (TNFi-naïve vs TNFi-experienced) and treatment phase (induction 6 to 14 weeks vs maintenance 52 to 60 weeks)
- Comparators: TNFis (adalimumab, infliximab, golimumab), vedolizumab, ustekinumab and tofacitinib
- Common comparator: placebo
- Base case: different doses of same treatment with same method of administration pooled
- Sources of heterogeneity: trial design (treat-through, re-randomised), treatment periods (induction, maintenance), eligibility criteria, subgroup definitions (TNFi vs biologic; TNFi experience vs failure), baseline characteristics, outcome definitions
- Random effects ordinal model with a probit link used to assess clinical response and clinical remission
- In line with ERG's approach, assessed baseline risk in placebo arm of NMAs using single trials from NMAs considered representative of UK clinical practice

Abbreviations: NMA, network meta-analysis; RCT, randomised controlled trial; TNFi, tumour necrosis factor inhibitor

ERG comments on company revised NMAs

- Overall, company's NMAs are in line with recommended practice and have accounted for some potential effect modifiers (mainly prior TNFi treatment and differences in trial design)
- While company used ERG's approach to estimate baseline risk in placebo arms and ERG considers approach to be broadly appropriate, ERG notes that the most suitable trial per setting may not have been identified
    - If there is a subset of trials suitable for baseline estimation, ERG believes that pooling this data would provide a more robust estimation of baseline placebo risk
- Compared to company's original submission, company's updated random effects model with informative priors and approach to estimating baseline risk in placebo arms, modelled probabilities of:
    - non-response are increased
    - clinical response or clinical remission are decreased
- ERG considers company's updated approach is preferable to its original, but is still suboptimal

Is the company's updated approach to calculating baseline risks acceptable for decision making?

Abbreviations: NMA, network meta-analysis, TNFi, tumour necrosis factor inhibitor

NMA results used in economic model: TNFi-naïve

NMA outcomes for treatments during induction

Treatments	Dose	Clinical remission (%)		Clinical response (%)		No response (%)	
		Company	ERG	Company	ERG	Company	ERG
Placebo	Oral	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ozanimod	**1 mg QD**						
Adalimumab	160/80/40 mg Q2W						
Golimumab	200/100 mg SC						
Infliximab	Pooled						
Tofacitinib	10 mg BID						
Ustekinumab	Pooled						
Vedolizumab	300 mg IV						

NMA outcomes for treatments during maintenance

Treatments	Dose	Clinical remission (%)		Clinical response (%)		No response (%)	
		Company	ERG	Company	ERG	Company	ERG
Placebo	Oral	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ozanimod	**1 mg QD**						
Adalimumab	160/80/40 mg Q2W						
Golimumab	200/100 mg SC						
Infliximab	Pooled						
Tofacitinib	10 mg BID						
Ustekinumab	Pooled						
Vedolizumab	300 mg IV						
VEDO 108	108 mg IV						

NICE Categories may not add up to 100% because of rounding error. Company and ERG results differ slightly because of random sampling error

NMA results used in economic model: TNFi-experienced

NMA outcomes for treatments during induction

Treatments	Dose	Clinical remission (%)		Clinical response (%)		No response (%)	
		Company	ERG	Company	ERG	Company	ERG
Placebo	Oral	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ozanimod	**1 mg QD**	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adalimumab	160/80/40 mg Q2W	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Tofacitinib	10 mg BID	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab	Pooled	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Vedolizumab	300 mg IV	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

NMA outcomes for treatments during maintenance

Treatments	Dose	Clinical remission (%)		Clinical response (%)		No response (%)	
		Company	ERG	Company	ERG	Company	ERG
Placebo	Oral	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ozanimod	**1 mg QD**	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adalimumab	160/80/40 mg Q2W	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Tofacitinib	10 mg BID	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab	Pooled	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Vedolizumab	300 mg IV	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
VEDO 108	108 mg IV	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Categories may not add up to 100% because of rounding error. Company and ERG results differ slightly because of random sampling error and because of an error in the trial used by ERG to estimate baseline risk

Clinical issues

- Are the pre- and post-biologic subgroups rather than the whole population the most relevant for decision-making?
- The company proposes that ozanimod could be used before any other treatment, when standard care is not working.
    - Is this likely in clinical practice?
    - Are TNF-alpha inhibitors usually used first after standard care, and is this generally adalimumab or infliximab?
    - How often would another treatment be offered instead?
- After a TNFi, what would be the next treatment offered? Is there wide use of a second TNFi or would an alternative treatment be offered such as vedolizumab, ustekinumab or tofacitinib?
- Like ozanimod, tofacitinib is an oral treatment. How much is tofacitinib used in clinical practice?
- Are the results of the NMAs acceptable for decision making? How reliable are the calculated differences between treatments as shown by the NMAs?

 Abbreviations: NMA, network meta-analysis; TNFi, tumour necrosis factor inhibitor

Cost effectiveness

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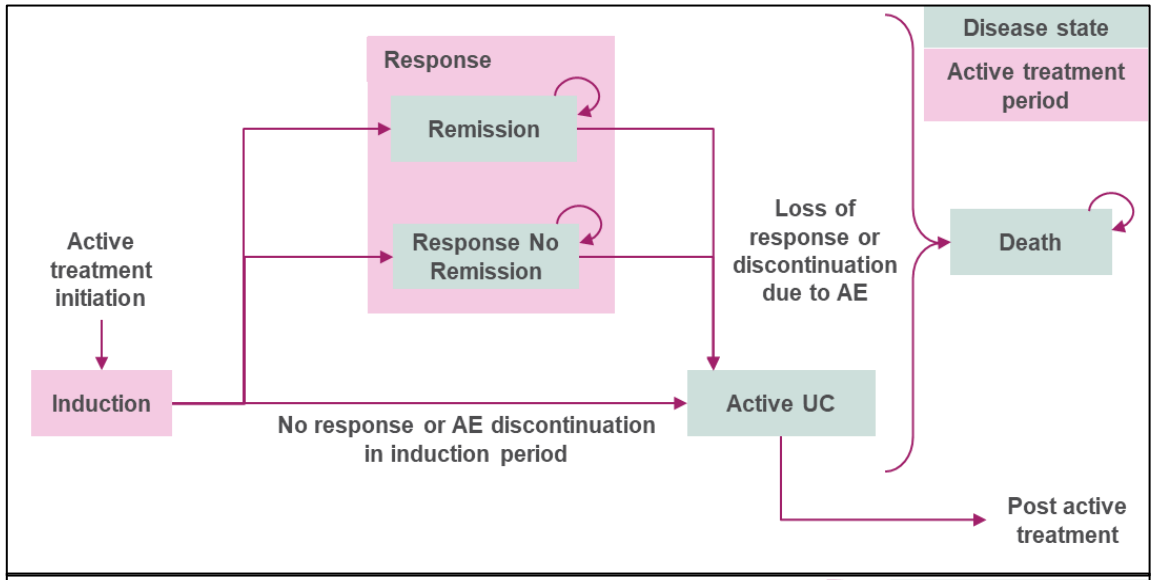
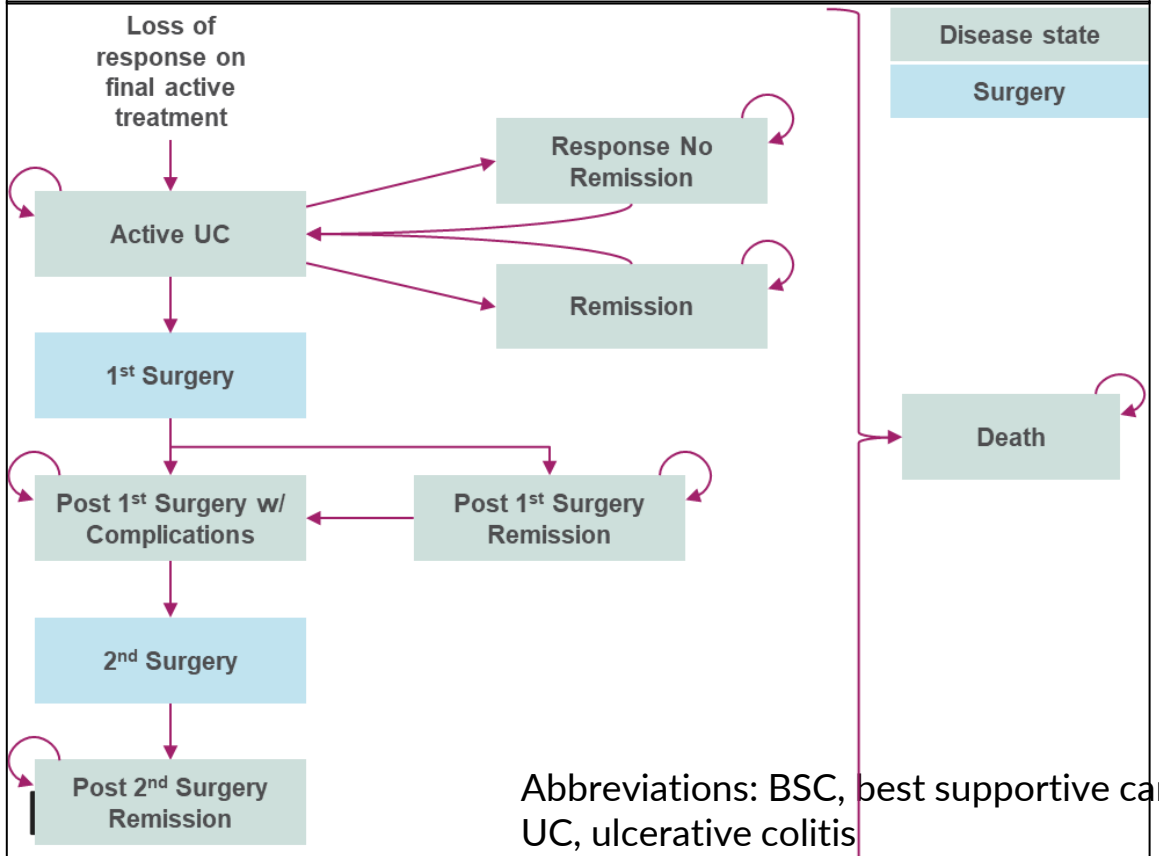
Cost-effectiveness issues

- What treatments are the most appropriate comparators for ozanimod?
- How should best supportive care be accounted for in the post-active treatment phase? (only "unresolved" issue for cost-effectiveness with the ERG)





Company's model overview

- Markov cohort model in line with previous NICE technology appraisals
- Lifetime time horizon, 2-week cycle length, no half-cycle correction (little impact on ICERs)
- Discount 3.5% for costs and benefits
- No treatment waning in base case (scenario 25% waning after 2 years)
- Technology affects **costs** by: lower administration and drug acquisition costs; ozanimod needs an electrocardiogram during induction
- Technology affects **QALYs** by: more people in no remission health states have loss of response to treatment; stopping treatments due to adverse events have BSC and enter 'Active' UC health state accruing costs and QALYs associated with this health state

Abbreviations: BSC, best supportive care; ICER, incremental-cost effectiveness ratio; QALY, quality-adjusted life year; UC, ulcerative colitis

How company incorporated evidence into model

Input	Assumption and evidence source
Baseline characteristics	2 subgroups: TNFi-naïve and TNFi-experienced patients; characteristics from TRUENORTH
Treatments efficacy	Random effects NMA
Stopping because of adverse events	Derived from trials used in the NMA. People who stopped treatment due to AEs moved to 'Active UC' health state at end of induction
Loss of response	In line with TA633, a constant loss of response beyond trial duration. Estimates calculated from NMA results for sustained remission/response
Subsequent treatment	Surgery in each cycle possible in post-active treatment 'Active UC' state. In line with TA633, probability of 2nd surgery from 'Post 1st Surgery Complications' state same as for 1st surgery. Surgery same for TNFi-naïve and TNFi-experienced
Utilities	In line with TA633, published literature used. TRUENORTH utility values not used because not consistent with literature, no utility data for surgery model health states and inconsistency between treatment continuation in 'Active UC' health state in trial and model
Costs	Treatments, managing AEs, surgery, health state, monitoring for treatments
Resource use	In line with TA633, used UK-based literature to estimate annual resource use for each state. Assumed resource use for 1st surgery and 2nd surgery same in active UC health state

Abbreviations: AE, adverse event; NMA, network meta-analysis; TNFi, tumour necrosis factor inhibitor; UC, ulcerative colitis

Modelled efficacy estimates for best supportive care in post-active treatment phase

Background

- Company used TNFi-experienced data to inform transition probabilities for TNFI-naïve subgroup in BSC arm and used overall response data (including remission) to inform remission transition probabilities for BSC in post-active treatment phase

Company

- Maintains data from **TNFi-experienced** subgroup were more appropriate to inform BSC transition probabilities for **TNFi-naïve** subgroup because people in active treatment phase have already failed at least 1 treatment
  - Provides scenario analysis using ERG's preferred approach for BSC transitions, i.e. using TNFi-specific subgroup data

ERG comments

- In line with TA633, ERG maintains subgroup-specific data should inform transition probabilities in BSC arm, i.e. loss of response and loss of response (no remission) calculated based on TNFi-naïve and TNFi-experienced estimates. Inappropriate to ignore TNFi-naïve specific data

How should transition probabilities in BSC arm be modelled? ERG preferred approach of using subgroup-specific data or company preferred approach of using TNFi-experienced data only?

Abbreviations: BSC, best supportive care; TNFi, tumour necrosis factor inhibitor

Summary of company and ERG base case assumptions

Persisting area of disagreement on BSC transition probabilities has only a small effect on ICER, and only in TNFi-naïve; otherwise company and ERG ICERs are same

Assumption	Company revised base case	ERG base case
Tofacitinib as a comparator	Included (maintains it is not relevant)	Same
Baseline risk for placebo anchors	Included baseline placebo risk from 1 UK generalisable trial per NMA setting, as per ERG scenario	Same Comments: approach suboptimal; would prefer comprehensive assessment of baseline placebo risk
Model type used for maintenance NMA	Random effects with informative prior	Same
Method of estimating remission transition probabilities for BSC	Estimated based on 'loss of remission', calculated directly from sustained remission estimates	Same
BSC transition probabilities for the TNFi-naïve population	Used TNFi-experienced data for both subgroups	Used **TNFi-specific subgroup data,** i.e. TNFi-naïve data for this population

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; NMA, network meta-analysis; TNFi, tumour necrosis factor inhibitor

Other considerations

Equality considerations

- Oral administration of ozanimod may reduce need for travel to hospital and may benefit people with disability, people “in cultures where it may be harder to speak openly about the condition” or people living in remote areas
- For certain religious groups, impact of active disease and effects of surgery may interfere with religious practices and cause distress, which could be reduced by another medical treatment option
- Prescription costs may be a factor related with lower income

Innovation

- Ozanimod has a novel mechanism of action
- Ozanimod addresses an unmet need by providing people with a new therapeutic oral option to treat symptoms and induce remission

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts

Abbreviations: ICER, incremental-cost effectiveness ratio; PAS, patient access scheme

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Thank you