Multivariable analysis of baseline variables associated with efficacy outcomes in the ELEVATE UC clinical programme

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Background

- Baseline variables that are associated with response to advanced therapies have the potential to improve the management of UC in patients[1]
- Etrasimod is an oral, once-daily, selective $S1P_{1,4,5}$ receptor modulator for the treatment of moderately to severely active UC

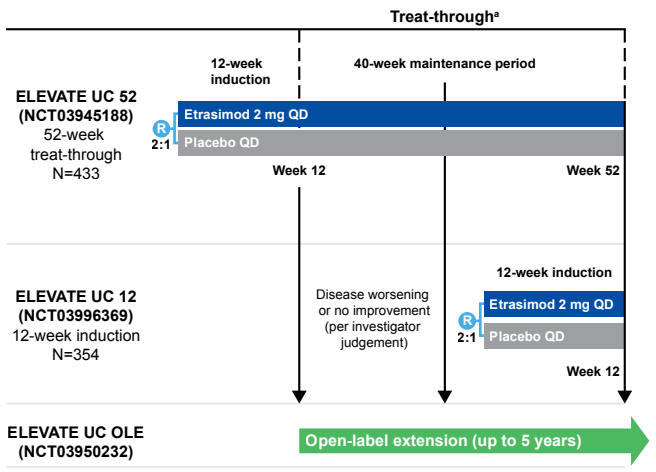
Objective

- This post hoc analysis aimed to identify baseline demographic and disease activity characteristics associated with response in the ELEVATE UC clinical programme

Methods

- Details of the ELEVATE UC programme design are shown in **Figure 1**
- Efficacy endpoints of clinical remission and endoscopic improvement, and change from baseline in MMS and ES, were analysed using logistic or linear regression models, respectively, at Week 12 (pooled data) and Week 52 (ELEVATE UC 52 only)
- Baseline variables assessed in this analysis were based on clinical input (**Table 1**). Those associated with efficacy outcomes were pre-selected by simple regression analyses (⩾1 comparison $p<0.1$) and were further assessed using multivariable logistic/linear regression using backward selection (stay criterion $p<0.05$)

Figure 1. ELEVATE UC programme trial design[2]



Patients with an inadequate or loss of response or intolerance to ⩾1 approved UC therapy were randomised (2:1) to etrasimod 2 mg QD or placebo.

At study entry, patients could receive concomitant treatment with a CS (prednisone [⩽20 mg/day], budesonide [⩽9 mg/day] or equivalent), provided they were on a stable dose 4 weeks prior to the screening endoscopy. Investigators were directed to taper CS after Week 12.

[a]Beginning at Week 12, all patients could continue their randomised treatment into a 40-week maintenance period; those whose disease had not improved or worsened vs baseline (based on investigator judgement) could continue and, if objective disease worsening criteria were met (having either or both RBS ⩾2 or RBS + SFS ⩾4 at two time points ⩾7 to ⩽14 days apart), enrol in an OLE study (NCT03950232).

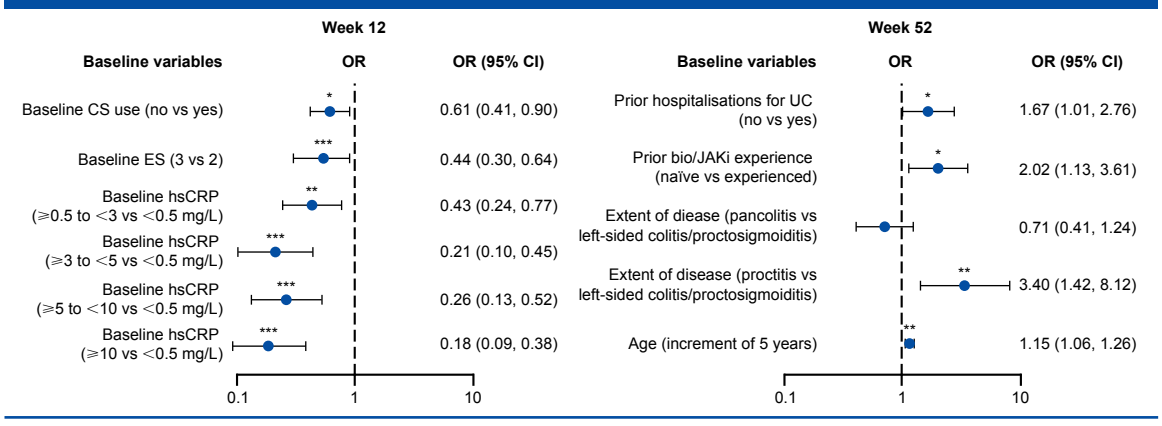
Table 1. Baseline variables assessed

Baseline variables	Reference group
Age	5-year increment
Sex (female vs male)	Male
Geographic region (North America, Europe, Others)	Others
BMI group (<25, 25–29, ⩾30 kg/m²)	⩾30 kg/m²
Baseline MMS (4–6 vs 7–9)	MMS 7–9
Baseline ES (3 vs 2)	2
Robarts Histopathology Index	1-score unit increment
Duration of UC disease since diagnosis	2-year increment
Age at UC diagnosis	2-year increment
Prior hospitalisations for UC (no vs yes)	Yes
Extent of disease (proctitis, pancolitis, left-sided colitis/proctosigmoiditis)	Left-sided colitis/ proctosigmoiditis
Prior bio/JAKi experience (naïve vs experienced)	Experienced
Baseline CS use (no vs yes)	Yes
Baseline hsCRP (<0.5, ⩾0.5 to <3, ⩾3 to <5, ⩾5 to <10 and ⩾10 mg/L)	<0.5 mg/L
Baseline FCP (greater vs less than median FCP at baseline)	Pooled Week 12: ⩽993.7 mg/kg Week 52: ⩽1125.4 mg/kg

Backward selection included baseline variables with ⩾1 comparison $p<0.1$ from simple (univariate) analyses. Treatment group, baseline value (linear regression only) and study stratification (Week 12 only) were mandatorily included and not subject to backward selection.

Results

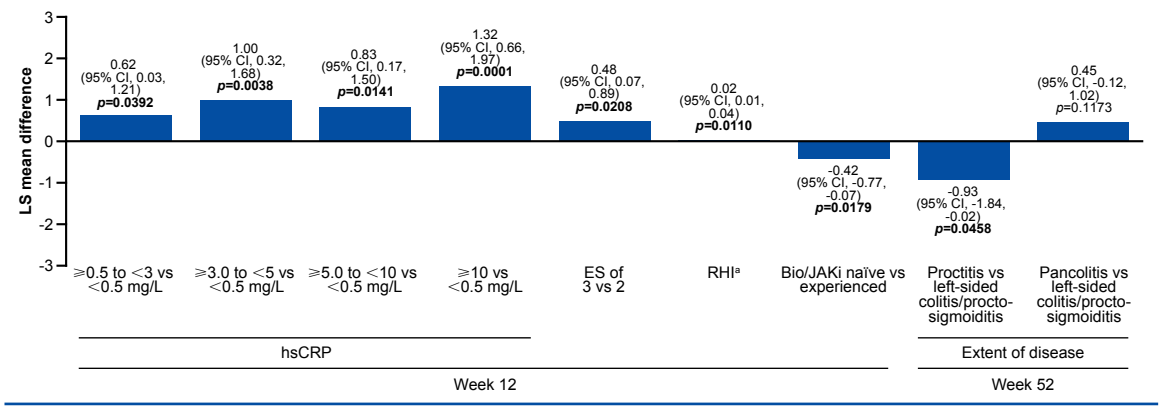
Figure 2. Multivariable logistic regression analysis of baseline variables for clinical remission at Week 12 and Week 52 (MMS 4–9)



*$p<0.05$, **$p<0.01$, ***$p<0.001$.

Sex was also included in this multivariable logistic regression analysis (Week 12: OR 1.53 [95% CI, 1.06, 2.21]).
Clinical remission was defined as an SFS of 0 (or 1 with a ⩾1-point decrease from baseline), an RBS of 0 and an ES of ⩽1 (excluding friability).

Figure 3. Multivariable linear regression analysis of baseline variables for change in baseline from MMS at Week 12 and Week 52 (MMS 4–9)



[a]Increment of 1 score unit.

$p<0.05$ values are highlighted in bold.

Multivariable linear regression data for geographic region at Week 12 (not plotted): Europe vs Others: -0.73 (95% CI, -1.14, -0.32), $p=0.0005$; North America vs Others: -0.22 (95% CI, -0.81, 0.38), $p=0.4756$.

Summary of multivariable logistic/linear regression analyses following backward selection

- At Week 12, lower baseline ES and lower hsCRP were associated with achieving all outcomes assessed ($p<0.05$) (**Figure 4**)
  - A higher baseline RHI, no prior bio/JAKi experience and baseline CS use were associated with achieving select outcomes assessed ($p<0.05$) at Week 12 (**Figure 4**)
- At Week 52, other than etrasimod vs placebo, no variable showed consistent significant comparisons ($p<0.05$) across the assessed outcomes (**Figure 4**)
  - Extent of disease was associated with achieving select outcomes assessed at Week 52; baseline MMS was associated with achieving endoscopic improvement only (**Figure 4**)

Multivariable logistic regression analysis for clinical remission

- At Week 12, lower odds of achieving clinical remission were independently associated with no baseline CS use, higher ES and higher hsCRP (**Figure 2**)
- No prior bio/JAKi experience was associated with higher odds of achieving clinical remission at Week 52 (**Figure 2**)

Multivariable linear regression analysis for changes in baseline MMS

- At Week 12, higher hsCRP and a baseline ES of 3 were associated with an increase in MMS from baseline, while no prior bio/JAKi experience was associated with a decrease in MMS from baseline (**Figure 3**)
- At Week 52, only extent of disease for proctitis vs left-sided colitis/proctosigmoiditis was significantly associated with change from baseline in MMS (**Figure 3**)

Figure 4. Summary of multivariable logistic/linear regression analyses of baseline variables at Week 12 and Week 52

✓ Significant comparison ($p<0.05$) ☐ Nonsignificant comparison ($p⩾0.05$) or not included in multivariable analysis[a]

	Clinical Remission		Endoscopic Improvement		Change from baseline in MMS		Change from baseline in ES	
	Week 12	Week 52	Week 12	Week 52	Week 12	Week 52	Week 12	Week 52
Etrasimod 2 mg QD vs placebo QD[b]	✓	✓	✓	✓	✓	✓	✓	✓
Age (increment of 5 years)		✓		✓				
Sex (female vs male)	✓						✓	
Geographic region (North America vs Others)								
Geographic region (Europe vs Others)					✓			
Baseline BMI group[c]								
Baseline MMS (4–6 vs 7–9)				✓			✓	
Baseline ES (3 vs 2)	✓		✓		✓		✓	✓
RHI (increment of 1)				✓	✓		✓	
Duration of UC disease since diagnosis (increment of 2 years)								
Age at UC diagnosis (increment of 2 years)								
Prior hospitalisations for UC (no vs yes)		✓						
Extent of disease (proctitis vs left-sided colitis/proctosigmoiditis)		✓				✓		
Extent of disease (pancolitis vs left-sided colitis/proctosigmoiditis)				✓				
Prior biologics/JAKi use (naïve vs experienced)		✓	✓		✓			
Baseline corticosteroid use (no vs yes)	✓		✓					
Baseline hsCRP[d]	✓		✓		✓		✓	
Baseline FCP (⩽ vs > median FCP at baseline)								

[a]Variables not included in the multivariable analysis were not pre-selected by the simple regression analysis, having not met the criteria of ⩾1 comparison $p<0.1$.

[b]Etrasimod vs placebo was not subject to variable selection.

[c]Baseline BMI group data were consistent for all comparisons (<25 vs ⩾30kg/m², 25–29 vs ⩾30kg/m²).

[d]Baseline hsCRP had consistent significance across all comparisons (⩾0.5 to <3 vs <0.5, ⩾3 to <5 vs <0.5, ⩾5 to <10 vs <0.5 and ⩾10 vs <0.5 mg/L).

Clinical remission was defined as an SFS of 0 (or 1 with a ⩾1-point decrease from baseline), an RBS of 0 and an ES of ⩽1 (excluding friability). Endoscopic improvement was defined as an ES ⩽1.

Limitations

- This analysis was post hoc and contains subgroups with relatively small sample sizes
- The ELEVATE UC clinical programme was not designed nor powered to identify variables related to response
- The selection of variables associated with efficacy responses was model dependent

Conclusions

- **In this analysis, certain baseline variables related to higher disease activity (ES of 3, high baseline hsCRP) were associated with lower odds of achieving efficacy endpoints at Week 12**
- **These associations were not retained at Week 52, which may be due to a lack of statistical power or suggests that some patients with moderately to severely active UC could benefit from longer exposure to etrasimod to achieve these clinical outcomes**
  - **This is consistent with previous findings that assessed etrasimod response by baseline ES[3]**
- **This analysis may provide important information to help healthcare professionals choose appropriate patients for therapy with etrasimod**

Electronic poster

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Abbreviations

BMI, body mass index; **CI**, confidence interval; **CS**, corticosteroid; **ES**, endoscopic subscore; **FCP**, faecal calprotectin; **hsCRP**, high-sensitivity C-reactive protein; **bio/JAKi**, biologic/Janus kinase inhibitor; **LS**, least squares; **MMS**, modified Mayo score; **N**, number of patients; **OLE**, open-label extension; **OR**, odds ratio; **QD**, once daily; **R**, randomisation; **RBS**, rectal bleeding subscore; **RHI**, Robarts Histopathology Index; **S1P**, sphingosine 1-phosphate; **SFS**, stool frequency subscore; **UC**, ulcerative colitis.

References

1. Lee HS, Cleynen I. Cells 2019; 8: 535.
2. Sandborn WJ et al. Lancet 2023; 401: 1159–1171.
3. Yarur AJ et al. Am J Gastroenterol 2024; 119: S1025–S1026.
4. DeTora LM et al. Ann Intern Med 2022; 175: 1298–1304.

Disclosure of interests

BGF is a consultant/advisory board member for Pfizer Inc. **MK** has received lecture/speaker and consultant/advisory fees from Pfizer Inc. **MTA** is a consultant for Pfizer Inc. **SS** has received lecture/speaker and consultant/advisory board fees from Pfizer Inc. **RB** is an advisory board member of, has received grants from and is a speaker for, Pfizer Inc. **MF** and **MG** are employees of Pfizer AG and shareholders of Pfizer Inc. **AMA**, **JCW**, **JW** and **MK** are employees and shareholders of Pfizer Inc. **DTR** is a consultant/advisor for Pfizer Inc.

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