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# Etrolizumab Induction in Moderate/Severe Anti-TNF Intolerant/Refractory (IR) Ulcerative Colitis (UC): The HICKORY Open-Label Induction (OLI) Trial

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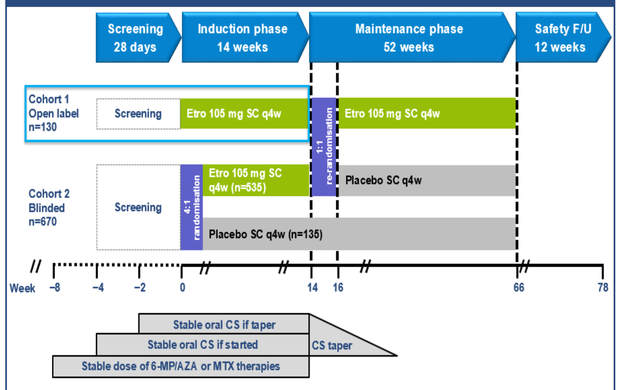
## BACKGROUND

- In the Phase 2 EUCALYPTUS trial, etrolizumab was well tolerated and efficacious in patients with moderate to severe UC[1]
- HICKORY (NCT02100696) is an ongoing phase 3 clinical trial examining the safety and efficacy of etrolizumab in patients with moderately to severely active UC and prior TNF antagonist (aTNF) failure
- At ECCO 2017, the HICKORY open-label induction (OLI) cohort demonstrated remission of rectal bleeding (RB) in 50% of etrolizumab-treated patients at week 8, which was observed consistently through Week 14[2]
- Endoscopic assessments of disease activity and treatment response in UC clinical trials now rely on assessments by blinded central readers and were used in this analysis
- A complete efficacy analysis for the difficult-to-treat patients enrolled in the HICKORY OLI cohort includes endoscopic outcomes, as well as patient-reported assessments of symptoms and inflammatory biomarkers

## METHODS AND OBJECTIVES

- To assess improvements in disease activity UC after 14 weeks of etrolizumab in patients intolerant or refractory to aTNF with moderately to severely active UC (MCS 6–12 with an endoscopy subscore (ES) of ≥ 2, a RB subscore ≥ 1, and a stool frequency (SF) subscore of ≥ 1)
- Efficacy assessments included:
  - Endoscopic assessment of changes in disease activity using the ES of the Mayo Clinic Score at Week 14
  - Patient-reported changes in SF and RB throughout the 14-week induction period
  - Changes in inflammatory biomarkers between baseline and Week 14

**Figure 1**. Study design




6-MP, mercaptopurine; AZA, azathioprine; CS, corticosteroid; F/U, follow-up; MTX, methotrexate; q4w, every 4 weeks; SC, subcutaneous

## RESULTS

### *Baseline demographics and disease characteristics*

- The baseline characteristics highlight a population with significant disease burden (Table 1)

**Table 1.** Baseline demographics and disease characteristics

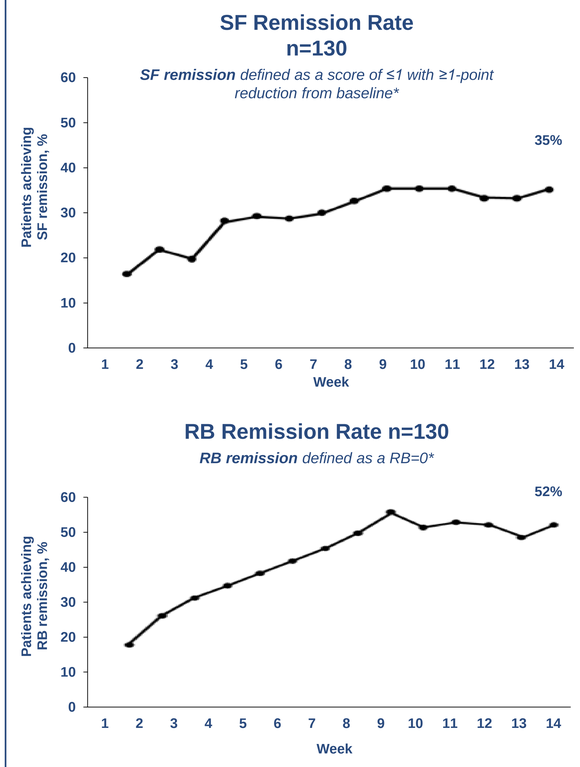
| Characteristic | HICKORY Cohort 1 n=130 |
|---|---|
| Age, mean ± SD, years | 39.4 ± 13.5 |
| Sex, male, % | 61 |
| Race, white, % | 84 |
| Body weight, mean ± SD, kg | 74.8 ± 16.8 |
| UC duration, mean ± SD (median), years | 8.7 ± 7.8 (5.9) |
| Previous aTNF use, % | |
| 1 aTNF | 55 |
| >1 aTNFs | 45 |
| Disease extent, % | |
| Left-sided colitis | 49 |
| Pancolitis/extensive colitis | 51 |
| MCS, mean ± SD | 9.4 ±1.3 |
| Faecal calprotectin, median (Q1–Q3), mg/kg | 1778 (898–3452) |
| C-reactive protein, median (Q1–Q3), mg/L | 6.6 (2.9–14.5) |
| CS use during induction*, % | 49 |
| IS use during induction*, % | 35 |

*Doses of IS and CS remained unchanged in screening and during induction treatment except if needed to manage treatment-related toxicity
IS, immunosuppressant; MCS, Mayo Clinic Score; SD, standard deviation

### *Stool frequency and rectal bleeding remission*

- Patients in SF remission and RB remission increased through Week 14 (Figure 2)

**Figure 2.** Stool frequency and rectal bleeding remission rates

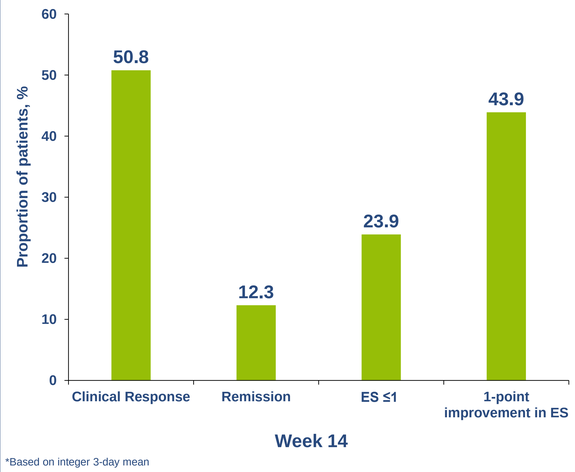



*Based on integer 3-day mean

### *Clinical and endoscopy results*

- At week 14, etrolizumab treatment was associated with clinical response in 50.8% of patients (remission in 12.3%) and an ES ≤1 in 23.9% (43.9% with a 1-point improvement in ES) (Figure 3)

**Figure 3.** Clinical improvement in aTNF-failed patients at Week 14




*Based on integer 3-day mean

- Endoscopic improvement at Week 14 was associated with a lower SF score (Figure 4) and a greater RB remission rate (Figure 5)

**Figure 4**. Endoscopic score improvement and stool frequency

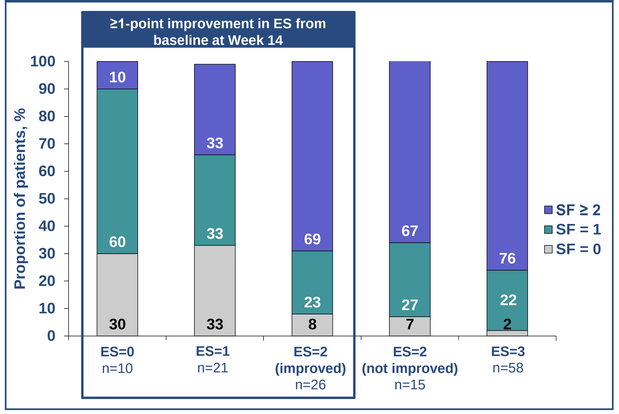
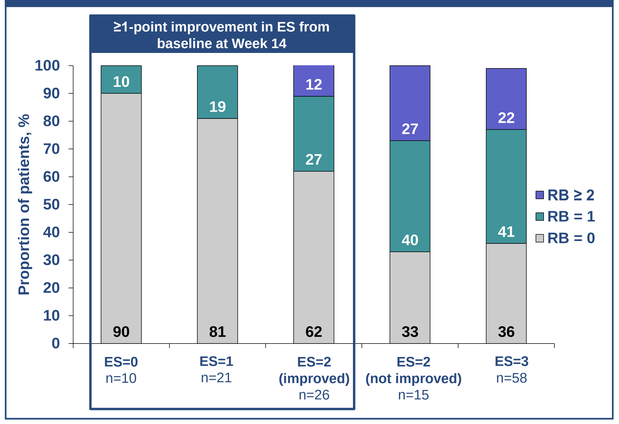



**Figure 5**. Endoscopic score improvement and rectal bleeding remission rate




### *Inflammatory biomarkers*

- Patients who achieved either SF or RB remission or ES ≤1 also demonstrated a >70% geometric mean reduction in faecal calprotectin (FC) (Figure 6) and a >50% geometric mean reduction in C-reactive protein CRP (BL ≥ 2.87 mg/L) (Figure 7)

**Figure 6.** Reductions in inflammatory biomarkers (FC)

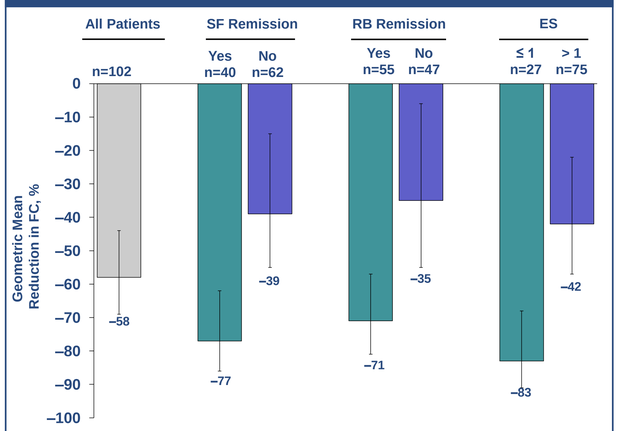
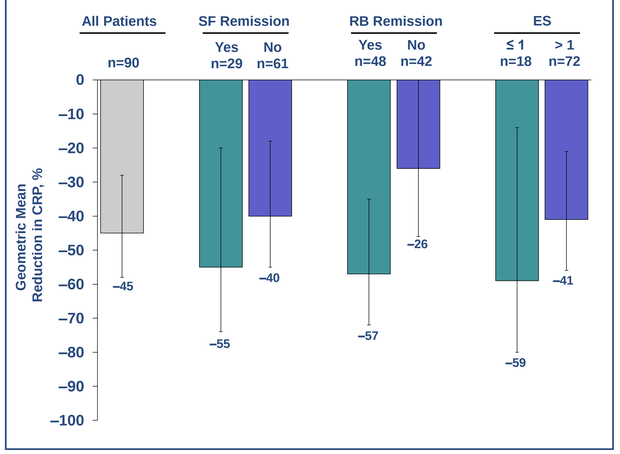



**Figure 7.** Reductions in inflammatory biomarkers (CRP)




### *Safety and tolerability*

- Etrolizumab treatment was well tolerated in patients with moderate to severe UC who have experienced aTNF failure
- The most common adverse events (AEs) reported were:
  - Ulcerative colitis (11%)
  - Nasopharyngitis (10%)
  - Headache (8%)
  - Fatigue (6%)
- Serious AEs (SAE) were reported by 11 (8%) patients; 6 patients (5%) reported a SAE for UC
- Two (2%) patients experienced worsening UC leading to discontinuation of study drug; no deaths, anaphylaxis, or progressive multifocal leukoencephalopathy events were reported

## CONCLUSIONS

- In a difficult-to-treat population of patients with prior aTNF failure, etrolizumab treatment resulted in:
  - Clinically meaningful rates of endoscopic improvement
  - Symptomatic remission
  - Improvements in inflammatory biomarkers
- Improvement in endoscopic score was associated with:
  - RB remission
  - Lower SF scores
  - Greater reductions in inflammatory biomarkers
- Etrolizumab treatment is well tolerated in patients with moderate to severe UC who have experienced aTNF failure[2]
- Evaluation of the efficacy and safety of etrolizumab in patients who experienced aTNF failure continues in the randomised, controlled maintenance phase of the HICKORY study
- Recruitment is ongoing for the pivotal randomised, placebo-controlled HICKORY induction cohort

## ACKNOWLEDGMENTS

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These data were previously presented at UEGW 2017.

## REFERENCES

1. Vermeire S et al. Lancet. 2014;384(9940):309–318
2. Peyrin-Biroulet L et al. 12th Congress of ECCO, February 2017; Barcelona, Spain