

Treatment of patients with moderate-to-severe Crohn's disease with subcutaneous infliximab leads to an endoscopic response across all segments of the colon and terminal ileum: A *post hoc* analysis of the LIBERTY-CD study

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BACKGROUND

- Mucosal healing (MH) has been associated with positive long-term clinical and surgical outcomes in patients with Crohn's disease (CD).¹
- Patterns of MH vary by therapeutic agent, with limited efficacy typically observed in the terminal ileum.^{2–4}
- The Phase 3 LIBERTY-CD study demonstrated superior efficacy of SC CT-P13 120 mg Q2W versus placebo following IV IFX induction, in terms of clinical remission and endoscopic response at Week 54.⁵
- This *post hoc* analysis aimed to investigate the pattern of endoscopic MH across ileocolonic segments following SC IFX maintenance treatment in the LIBERTY-CD study.

METHODS

- LIBERTY-CD (NCT03945019) was a randomised, placebo-controlled, double-blind trial conducted in patients with moderate-to-severely active CD.⁵
 - Patients received open-label CT-P13 IV 5 mg/kg at W0, 2 and 6 as induction therapy; at W10, clinical responders were randomised to receive CT-P13 SC 120 mg or placebo Q2W up to W54.

RESULTS

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Baseline characteristics

- Endoscopic characteristics at baseline were generally comparable between arms (**Table 1**).
 - Baseline ileal involvement was reported in 45.5% of patients across both arms.
 - Segmental SES-CD scores were comparable between arms for each segment.

Table 1. Baseline characteristics

Parameter	CT-P13 SC (n=231)	Placebo (n=112)
Disease classification, n (%)		
Colonic CD	118 (51.1)	55 (49.1)
Ileal CD	33 (14.3)	18 (16.1)
lleocolonic CD	72 (31.2)	33 (29.5)
Not applicable	8 (3.5)	6 (5.4)
Disease duration (year), n (%)		
0-1	67 (29.0)	37 (33.0)
1-5	88 (38.1)	39 (34.8)
5+	76 (32.9)	36 (32.1)

- This post hoc analysis evaluated centrally read and batch-analysed SES-CD values obtained at screening, W22 and W54 for five ileocolonic segments (rectum; left, transverse and right colon; and terminal ileum).
- Endoscopic complete MH (CMH; defined as SES-CD=0) or partial MH (PMH; defined as ≥50% decrease in the SES-CD from screening) were evaluated for segments with endoscopic abnormalities (segmental SES-CD \geq 1) at screening, in patients with available SES-CD data at each timepoint.
- Absolute SES-CD scores were compared between CT-13 SC and placebo at Weeks 0, 22, and 54 in patients with available SES-CD data at each timepoint.
- Patients who underwent dose escalation to SC IFX 240 mg Q2W upon loss of response from W22 were imputed as non-responders in the W54 analysis.
- In the ileum, a time-series assessment of multi-category outcomes was presented in a Sankey plot (R-package, ggsankey by David Sjoberg⁶).
- Results were analysed descriptively.

Affected intestinal segments, n (%) Terminal ileum Right colon Transverse colon Left colon Rectum	105 (45.5) 124 (53.7) 90 (39.0) 121 (52.4) 113 (48.9)	51 (45.5) 61 (54.5) 44 (39.3) 66 (58.9) 50 (44.6)
SES-CD score, mean (95% CI)	11.46 (10.56 – 12.36)	11.74 (10.57 – 12.91)
Segmental SES-CD score, mean (95% Cl) Terminal ileum Right colon Transverse colon Left colon Rectum	2.41 (2.02 - 2.81) 2.58 (2.22 - 2.93) 1.78 (1.45 - 2.11) 2.61 (2.23 - 2.99) 2.08 (1.73 - 2.43)	2.58 (2.00 – 3.16) 2.69 (2.15 – 3.23) 1.74 (1.28 – 2.20) 2.86 (2.32 – 3.40) 1.87 (1.40 – 2.34)

Data are reported as n patients (%) or mean (95% CI). CD, Crohn's disease; CI, confidence intervals; SC, subcutaneous; SES-CD, Simple Endoscopic Score in Crohn's Disease.

RESULTS

Endoscopic CMH and PMH rates across segments

- Across ileocolonic segments, endoscopic CMH and PMH rates were higher with CT-P13 SC compared with placebo at both Week 22 and Week 54 (Figure 1).
- In the CT-P13 SC arm, endoscopic MH was achieved across ileocolonic segments as early as Week 22 in ≥69% of patients and was well-maintained in ≥62% of patients at Week 54.

Figure 1. Endoscopic CMH and PMH rates at Weeks 22 and 54



CMH, complete mucosal healing: IFX, infliximab: IV, intravenous: PMH, partial mucosal healing: SC, subcutaneous

Absolute SES-CD scores

- Across ileocolonic segments, segmental SES-CD scores were consistently lower in patients who received CT-P13 SC maintenance treatment versus placebo (Figure 2).
- In the CT-P13 SC arm, total and segmental SES-CD scores remained below 4 and 1, respectively, from Week 22 to Week 54, highlighting the potency of SC IFX treatment in both the early and sustained phase.



Q2W upon loss of response from W22 were excluded from the analysis at W54. IFX, infliximab; SC, subcutaneous; Q2W, every 2 weeks; SES-CD, Simple Endoscopic Score in Crohn's Disease; W, Week.

Figure 3. Patterns of MH in terminal ileum in patients receiving CT-P13 SC

MH in the terminal ileum in patients receiving CT-P13 SC

• A terminal ileum SES-CD score of 0 was detected in 74.0% (n=171/231) of patients at Week 22 and 71.9% (n=166/231) of patients at Week 54 (Figure 3). This included: Patients with no terminal ileum disease activity at Week 0 who maintained their inactive state in the terminal ileum Patients with terminal ileum disease activity at Week 0 who achieved PMH or CMH In patients with active terminal ileum disease at Week 0, MH rates were higher at W54 in patients who achieved CMH at W22 (n=41/56; 73.2%) than in patients who had remaining active disease at W22 (n=12/36; 33.3%), indicating an association between early MH and long-term outcomes (p=0.0002).



Active, segmental SES-CD score ≥1. Inactive, segmental SES-CD score=0 at screening or SES-CD score=0 at W22 or W54 in segments which were inactive at screening. CMH, SES-CD score=0 at W22 or W54 in segments which were inactive at screening. CD=0 at W22 or W54 in segments which were active at screening. PMH, ≥50% reduction in SES-CD score at W22 or W54 from screening in segments which were active at screening. Missing, segments with missing data at any time point. DE, segments in patients who experienced dose escalation from W22 due to loss of response. CMH, complete mucosal healing; DE, dose escalation; MH, mucosal healing; PMH, partial mucosal healing; SC, subcutaneous, SES-CD, Simple Endoscopic Score for Crohn's Disease; W, Week.

CONCLUSIONS

- With a stringent definition of endoscopic MH, SC IFX 120 mg Q2W led to high and consistent rates of endoscopic MH across all ileocolonic segments.
- Early observation of endoscopic MH at W22 and its maintenance until W54 underscores the potency of SC IFX treatment across all segments.
- IFX SC maintenance therapy was effective for inducing and maintaining MH/inactive status in the terminal ileum.
- Time series analysis of mucosal healing shows linear progress with early healing signals being associated with better W54 outcomes.

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Abbreviations: CD, Crohn's disease; CI, confidence interval; CMH, complete mucosal healing; IFX, infliximab; IV, intravenous; PMH, partial mucosal healing; Q2W, every 2 weeks; SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's Disease; W, Week. Acknowledgements: This analysis was supported by Celltrion Inc. (Incheon, Republic of Korea). Medical writing support was provided by Samantha Booth, PhD (Aspire Scientific, Bollington, UK), and was funded by Celltrion Inc.

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