

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.
- 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 $\geq 50\%$ decrease in the SES-CD from screening) were evaluated for segments with endoscopic abnormalities (segmental SES-CD ≥ 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 Sjöberg⁶).
- Results were analysed descriptively.

RESULTS

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)
Ileocolonic 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)
Affected intestinal segments, n (%)		
Terminal ileum	105 (45.5)	51 (45.5)
Right colon	124 (53.7)	61 (54.5)
Transverse colon	90 (39.0)	44 (39.3)
Left colon	121 (52.4)	66 (58.9)
Rectum	113 (48.9)	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% CI)		
Terminal ileum	2.41 (2.02 – 2.81)	2.58 (2.00 – 3.16)
Right colon	2.58 (2.22 – 2.93)	2.69 (2.15 – 3.23)
Transverse colon	1.78 (1.45 – 2.11)	1.74 (1.28 – 2.20)
Left colon	2.61 (2.23 – 2.99)	2.86 (2.32 – 3.40)
Rectum	2.08 (1.73 – 2.43)	1.87 (1.40 – 2.34)

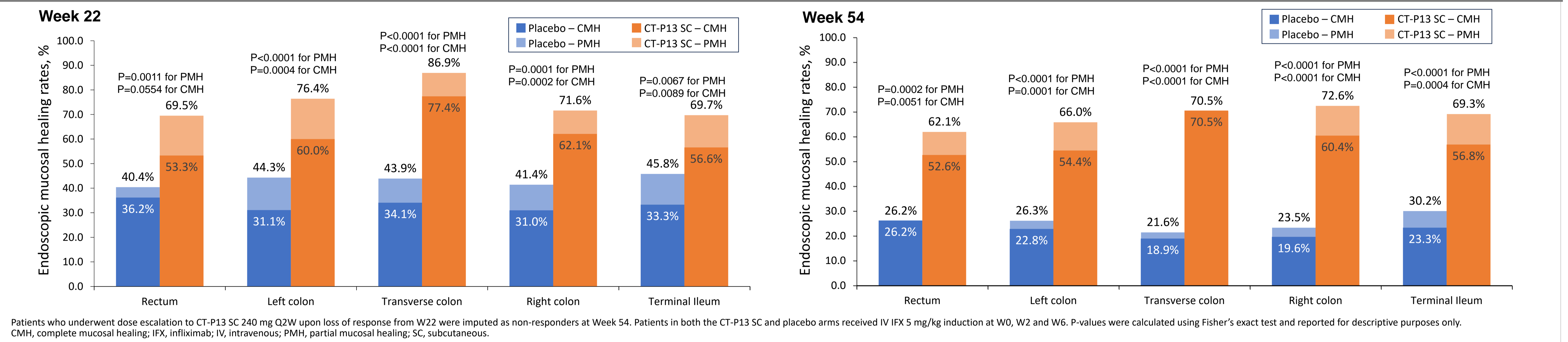
Data are reported as n patients (%) or mean (95% CI). CD, Crohn's disease; CI, confidence intervals; SC, subcutaneous; SES-CD, Simple Endoscopic Score in Crohn's Disease.

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 $\geq 69\%$ of patients and was well-maintained in $\geq 62\%$ of patients at Week 54.

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



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.

Figure 2. Total and segmental SES-CD scores at Weeks 22 and 54

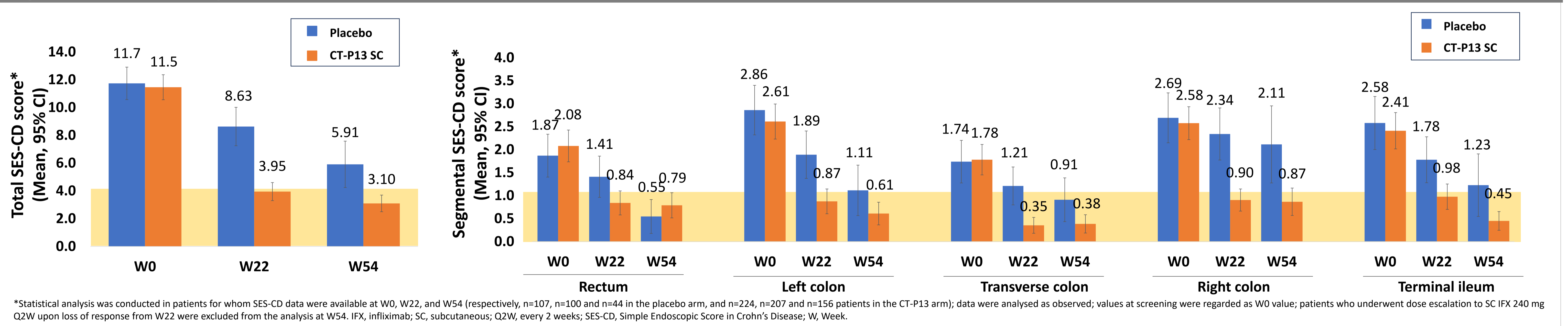
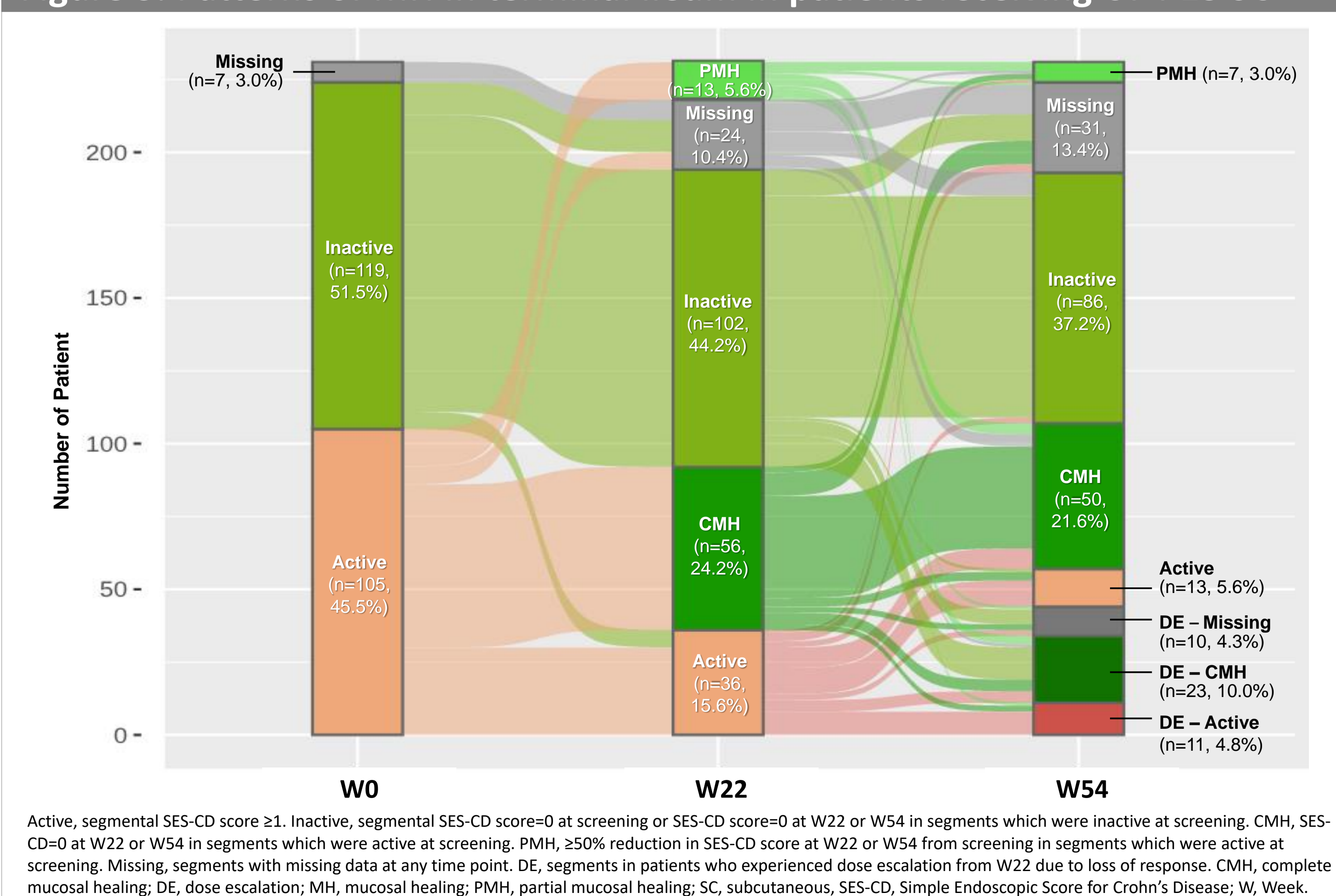


Figure 3. Patterns of MH in terminal ileum in patients receiving CT-P13 SC



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).

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.