Effects of Ustekinumab Induction Therapy on Endoscopic and Histologic Improvement in the UNIFI Phase 3 Study in Ulcerative Colitis

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Background

- Healing of the colonic mucosa was traditionally determined by its endoscopic appearance without histologic assessment
- Ustekinumab (UST) is an effective therapy for moderate-to-severe ulcerative colitis (UC)
- UST effects on histologic improvement, endoscopic improvement, and the combination of the two (histo-endoscopic mucosal healing), are unknown

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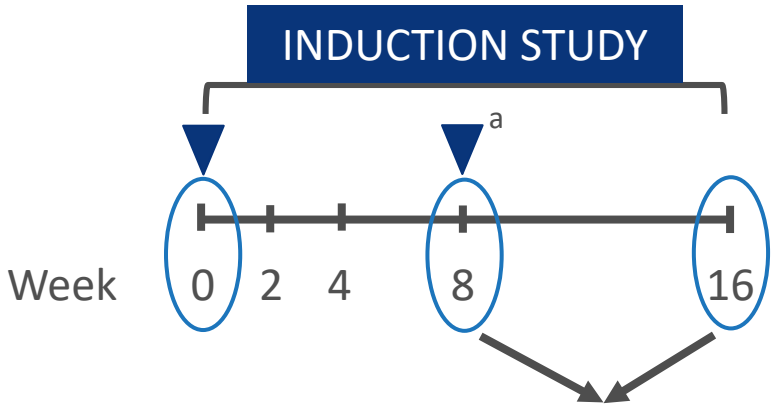
Methods

- Colonic biopsies were obtained during endoscopy in the UNIFI Phase 3 induction study of UST in moderate-to-severe UC (n=961)



Patients in clinical response at Week 8 or Week 16 of Induction entered Maintenance Study

▼ = Study agent administration
0 = Endoscopy

Histo-endoscopic Mucosal Healing[e]:
Achieving both histologic improvement *and* endoscopic improvement

Histologic Improvement:
Derived from features in Geboes scores[b] that are correlated with endoscopic mucosal response[c]:
- <5% of crypts with epithelial neutrophil infiltration
- Absence of crypt destruction
- Absence of erosion or ulceration or granulation tissue

Endoscopic Improvement[d]:
- Mayo endoscopy score 0 or 1

[a]Patients not in clinical response at Week 8. [b]Geboes K, et al. *Gut* (2000). [c]Li K, et al. *JCC* (2019). [d]Defined as Endoscopic Healing per protocol. [e]Defined as Mucosal Healing per protocol.

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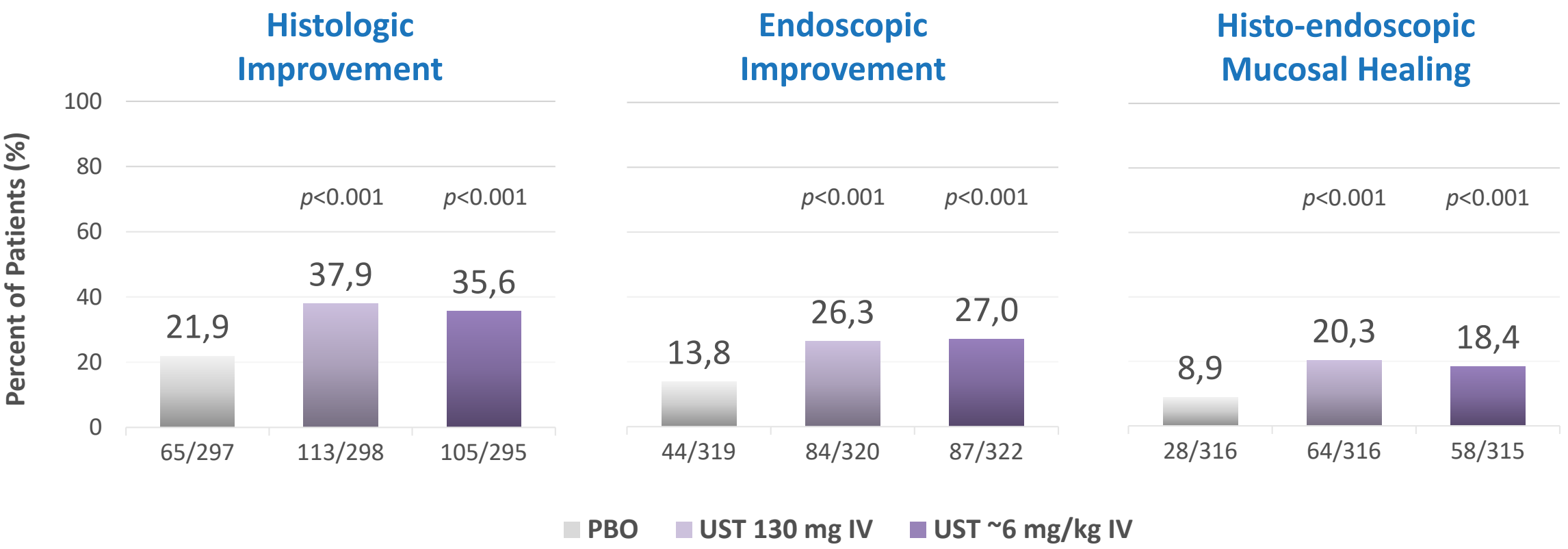
Histologic Improvement, Endoscopic Improvement, and Histo-endoscopic Mucosal Healing at Induction Week 8



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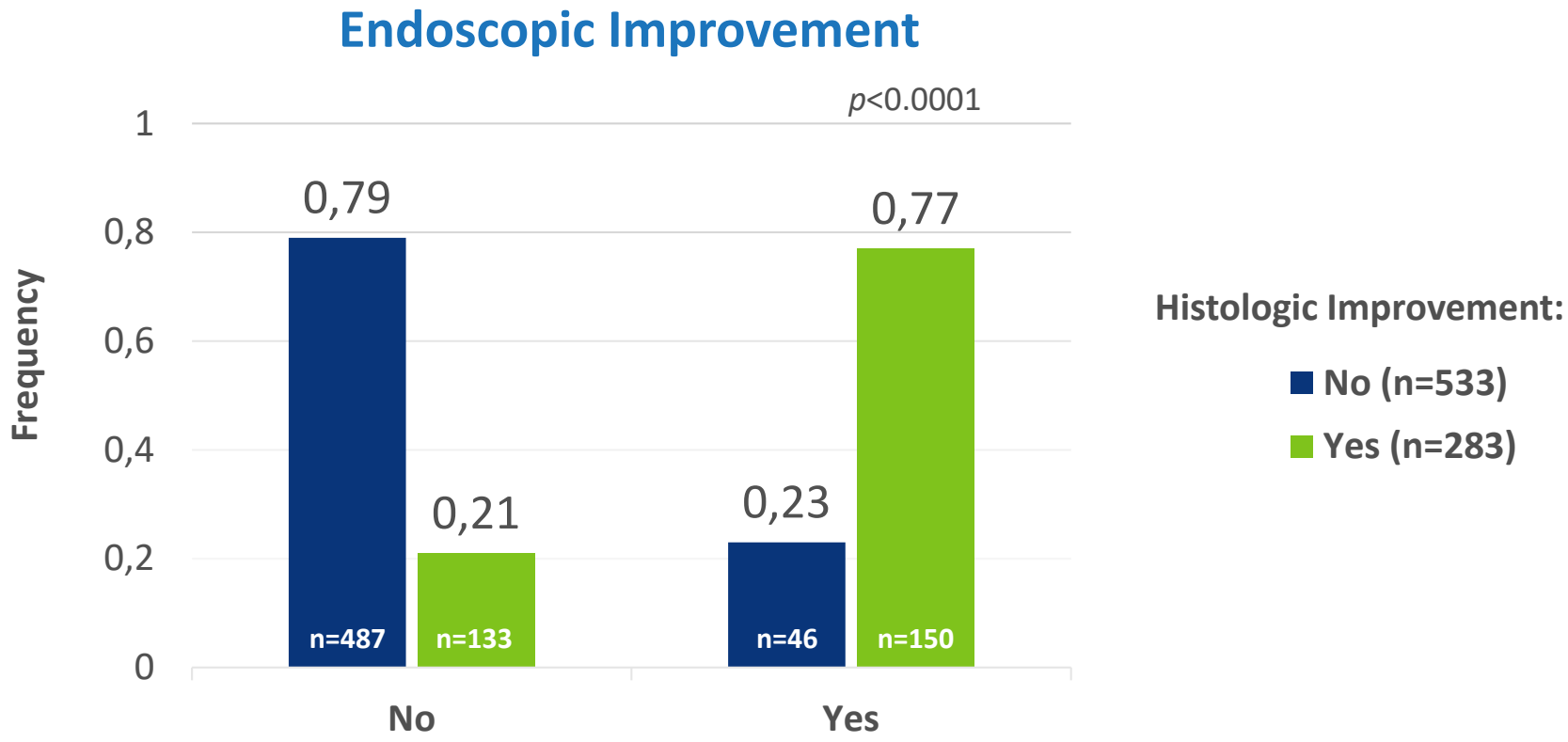
Histologic Improvement Is Significantly Associated With Endoscopic Improvement at Induction Week 8



Similar association was observed between histologic and endoscopic improvement at induction Week 16

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Histologic Improvement Is Associated With Lower Disease Activity and Greater Clinical Improvement at Induction Week 8

Clinical Outcomes at Week 8	With Histologic Improvement[a] (n=283)	Without Histologic Improvement[a] (n=533)	*P*-value[b]
Mayo Score	3.95 ± 2.57	6.89 ± 2.53	<0.0001
Partial Mayo Score	2.45 ± 1.84	4.39 ± 2.21	<0.0001
Stool Frequency	1.09 ± 0.95	1.81 ± 1.03	<0.0001
Rectal Bleeding	0.30 ± 0.56	0.86 ± 0.89	<0.0001
Change in Mayo Score	-4.53 ± 2.65	-2.15 ± 2.39	<0.0001
Change in Partial Mayo Score	-3.46 ± 2.14	-1.89 ± 2.12	<0.0001
Change in Stool Frequency	-1.08 ± 1.01	-0.63 ± 0.90	<0.0001
Change in Rectal Bleeding	-1.18 ± 0.91	-0.69 ± 0.96	<0.0001

Similar association was observed histologic improvement and clinical improvement at induction Week 16

[a]Values are reported as mean ± SD. [b]*P*-values based on t-test.

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Conclusions

- IV UST induced significantly higher rates of histologic improvement, endoscopic improvement, and histo-endoscopic mucosal healing compared to PBO in patients with moderately-to-severely active UC
- Histologic improvement is associated with reductions in clinical and endoscopic disease activity and patient-reported symptoms

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