P1077 - Impact of baseline body mass index (BMI) on efficacy of obefazimod in patients with moderately to severely active ulcerative colitis: results from the Phase 3 ABTECT induction trials

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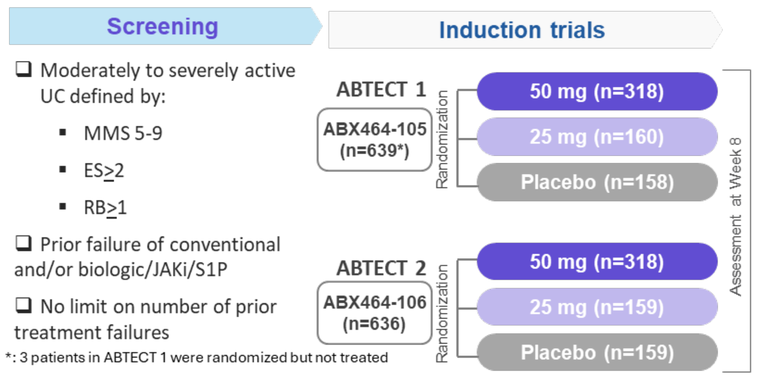
Background

- Obefazimod (Obe) is an oral, once-daily (QD), small molecule that enhances expression of microRNA-124, which restores mucosal immune balance through regulation of Th17 cells and macrophages. Obe has shown efficacy in patients (pts) with moderately to severely active ulcerative colitis (UC) [1-3]. In Phase 3 ABTECT-1 [NCT05507203] and ABTECT-2 [NCT05507216] 8-week induction trials, Obe achieved clinically meaningful improvements in clinical, endoscopic and histologic endpoints.
- Elevated BMI has been associated with a higher risk of treatment failure and suboptimal response to biologic therapy in pts with UC [4]. Here, we report the impact of baseline BMI on efficacy of Obe in pts with UC enrolled in Phase 3 ABTECT trials.

Methods

- The two multicenter, randomized, double-blind, placebo-controlled ABTECT trials enrolled pts with moderate-to-severe UC who had inadequate response, loss of response, or intolerance to at least one prior therapy (no upper limit), including corticosteroids, immunosuppressants, biologics, S1P receptor modulators and/or JAK inhibitors (Fig. 1).
- Pts were randomized 2:1:1 to Obe 50 mg QD (Obe-50), Obe 25 mg QD (Obe-25) or placebo (PBO) for 8 weeks.

Fig. 1: Design of ABTECT induction trials

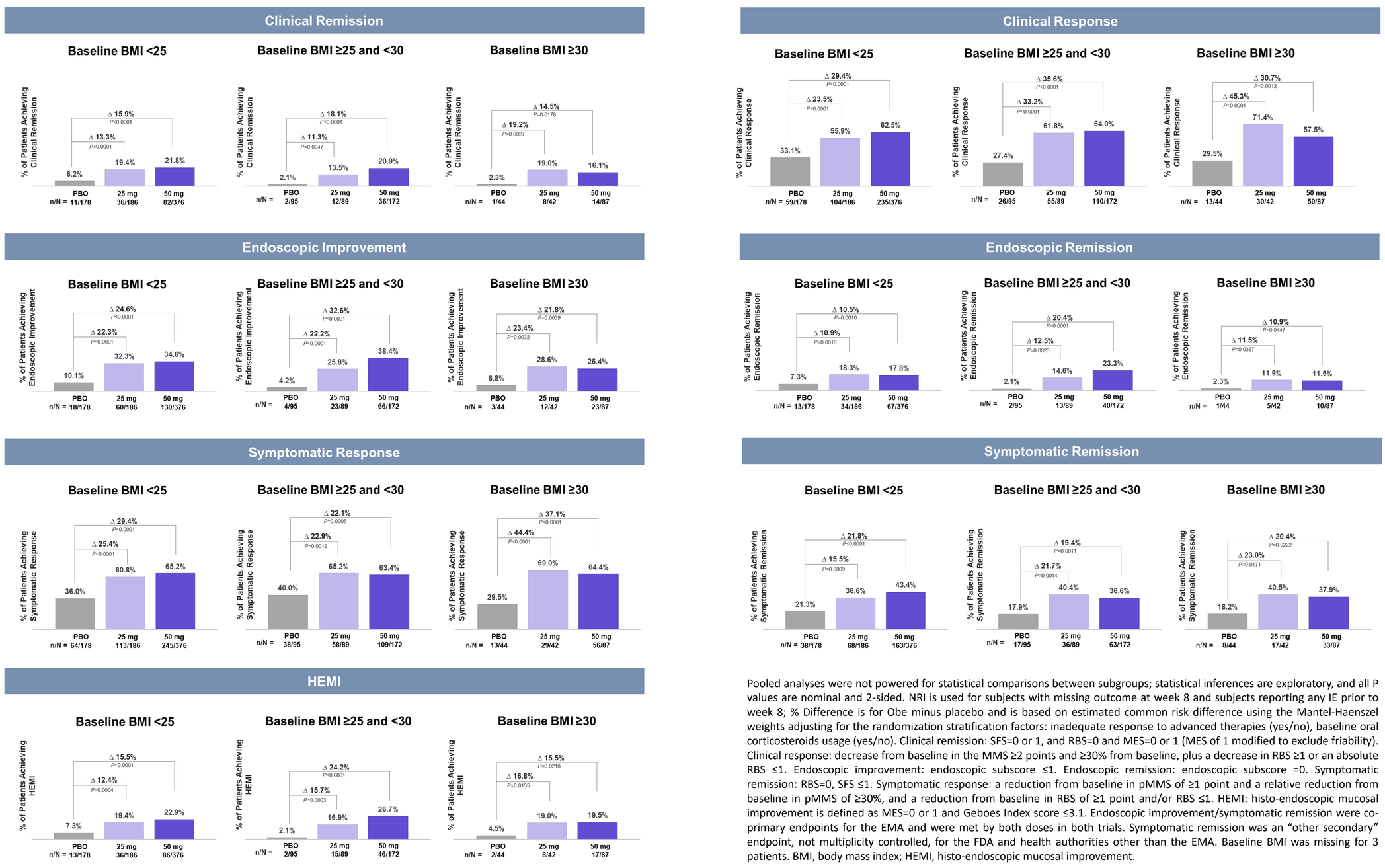


- In this post-hoc analysis, pts were categorized based on BMI at baseline (<25, 25≥ to <30, and ≥30 kg/m2). Efficacy endpoints evaluated included clinical remission (per MMS), clinical response, endoscopic improvement/remission, symptomatic response/remission, and histo-endoscopic mucosal improvement (HEMI). All p-values are nominal.

Results

- Among the 1272 randomized and treated pts in the ABTECT trials, 740 had a BMI<25, 356 had a BMI≥25 to <30, and 173 had a BMI≥30 at baseline. In both trials, baseline demographics and disease characteristics were overall comparable across treatment groups, irrespective of baseline BMI.
- In a pooled analysis, greater proportions of pts receiving Obe-25 or Obe-50 vs PBO achieved clinical remission with similar effect sizes regardless of baseline BMI (Obe-50-PBO difference: pts with BMI<25: 15.9%, p<0.0001; pts with 25≥ BMI <30: 18.1%, p<0.0001; pts with BMI≥30: 14.5%, p=0.0178; Obe-25-PBO difference: pts with BMI<25: 13.3%, p=0.0001; pts with 25≤ BMI <30: 11.3%, p=0.0047; pts with BMI≥30: 19.2%, p=0.0027). Similar results were observed with all other efficacy endpoints evaluated (Fig.2).

Fig. 2: Efficacy in the Pooled ABTECT 1 and ABTECT 2 Population by Baseline BMI



Pooled analyses were not powered for statistical comparisons between subgroups; statistical inferences are exploratory, and all P values are nominal and 2-sided. NRI is used for subjects with missing outcome at week 8 and subjects reporting any IE prior to week 8; % Difference is for Obe minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), baseline oral corticosteroids usage (yes/no). Clinical remission: SFS=0 or 1, and RBS=0 and MES=0 or 1 (MES of 1 modified to exclude friability). Clinical response: decrease from baseline in the MMS ≥2 points and ≥30% from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1. Endoscopic improvement: endoscopic subscore ≤1. Endoscopic remission: endoscopic subscore =0. Symptomatic remission: RBS=0, SFS ≤1. Symptomatic response: a reduction from baseline in pMMS of ≥1 point and a relative reduction from baseline in pMMS of ≥30%, and a reduction from baseline in RBS of ≥1 point and/or RBS ≤1. HEMI: histo-endoscopic mucosal improvement is defined as MES=0 or 1 and Geboes Index score ≤3.1. Endoscopic improvement/symptomatic remission were co-primary endpoints for the EMA and were met by both doses in both trials. Symptomatic remission was an "other secondary" endpoint, not multiplicity controlled, for the FDA and health authorities other than the EMA. Baseline BMI was missing for 3 patients. BMI, body mass index; HEMI, histo-endoscopic mucosal improvement.

Conclusions

In both ABTECT induction trials in moderately to severely active UC, Obe-25 and Obe-50 demonstrated clinically meaningful improvements in clinical, endoscopic, symptomatic, and combined endoscopic-histologic endpoints at week 8, with similar effect sizes, irrespective of baseline BMI.

References 1: Vermeire S et al. *J Crohns Colitis*. 17: 1689-97, 2023 - 2: Vermeire S et al. *Gastroenterology*. 160: 2595-98, 2021 - 3: Vermeire S et al. *The Lancet Gastroenterology & Hepatology*. 7: 1024-35, 2022 - 4: Kurnool S, et al. Aliment Pharmacol Ther. 2018;47:1472–1479.

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