P0894 - Impact of prior advanced therapy inadequate response by drug class on symptomatic improvement with obefazimod in patients with moderately to severely active ulcerative colitis: pooled analysis of ABTECT Phase 3 induction trials

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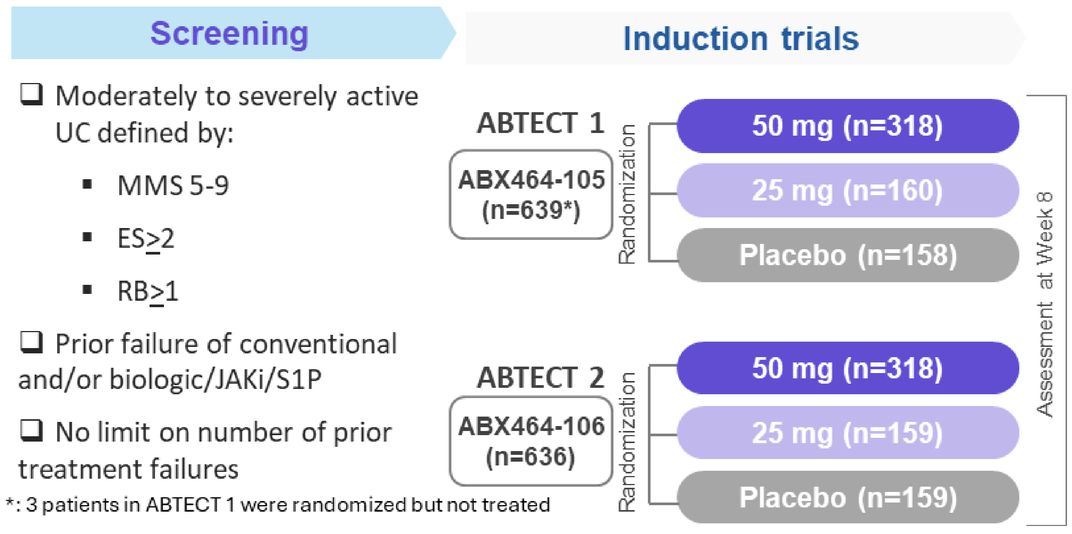
Background

- 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 the two 8-week ABTECT induction trials (NCT05507203, NCT05507216), Obe achieved clinically meaningful improvements in all clinical, endoscopic and histologic endpoints regardless of prior advanced therapy inadequate response (ATIR), including highly refractory pts with ≥4 prior treatment failures.
- Here, a pooled analysis evaluates the impact of specific classes of ATIR on the efficacy of Obe in the two Phase 3 ABTECT trials.

Methods

- The multicenter, randomized, double-blind, placebo-controlled ABTECT trials enrolled pts with moderate-to-severe UC (MMS≥ 5, with rectal bleeding sub-score (RBS) ≥ 1 and centrally read endoscopic score (ES) ≥2) 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.
- Rates of symptomatic remission and symptomatic response were evaluated across 6 subgroups of ATIR pts having received:
  - 1 TNF inhibitor only (TNFi-IR)
  - Vedolizumab only (Vedo-IR)
  - 1 TNFi+Vedo (TNFi/Vedo-IR) only
  - 1 TNFi+Vedo+ustekinumab (TNFi/Vedo/Uste-IR) only
  - Ustekinumab (Uste-IR) or a JAK inhibitor (JAK-IR) in any line of therapy.

Fig. 1: Design of ABTECT induction trials

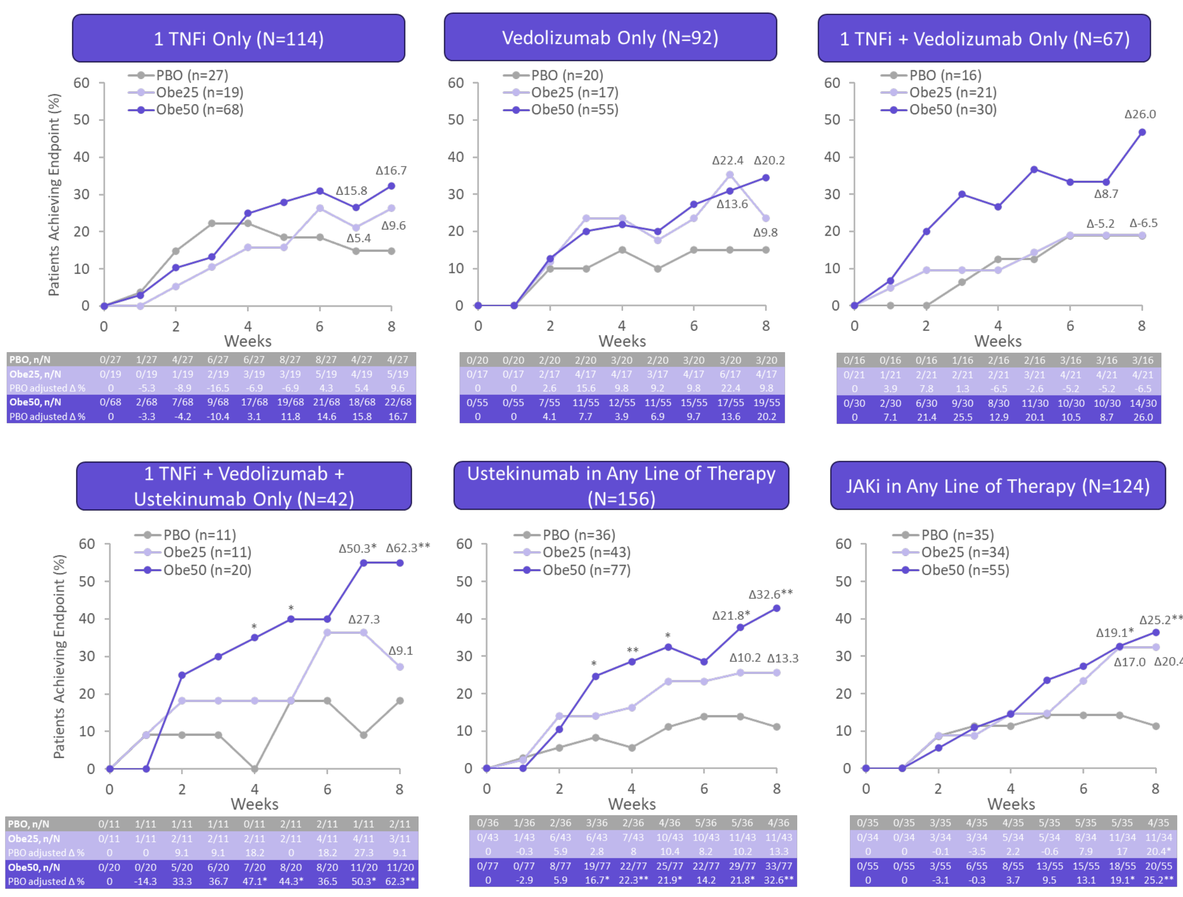


Results

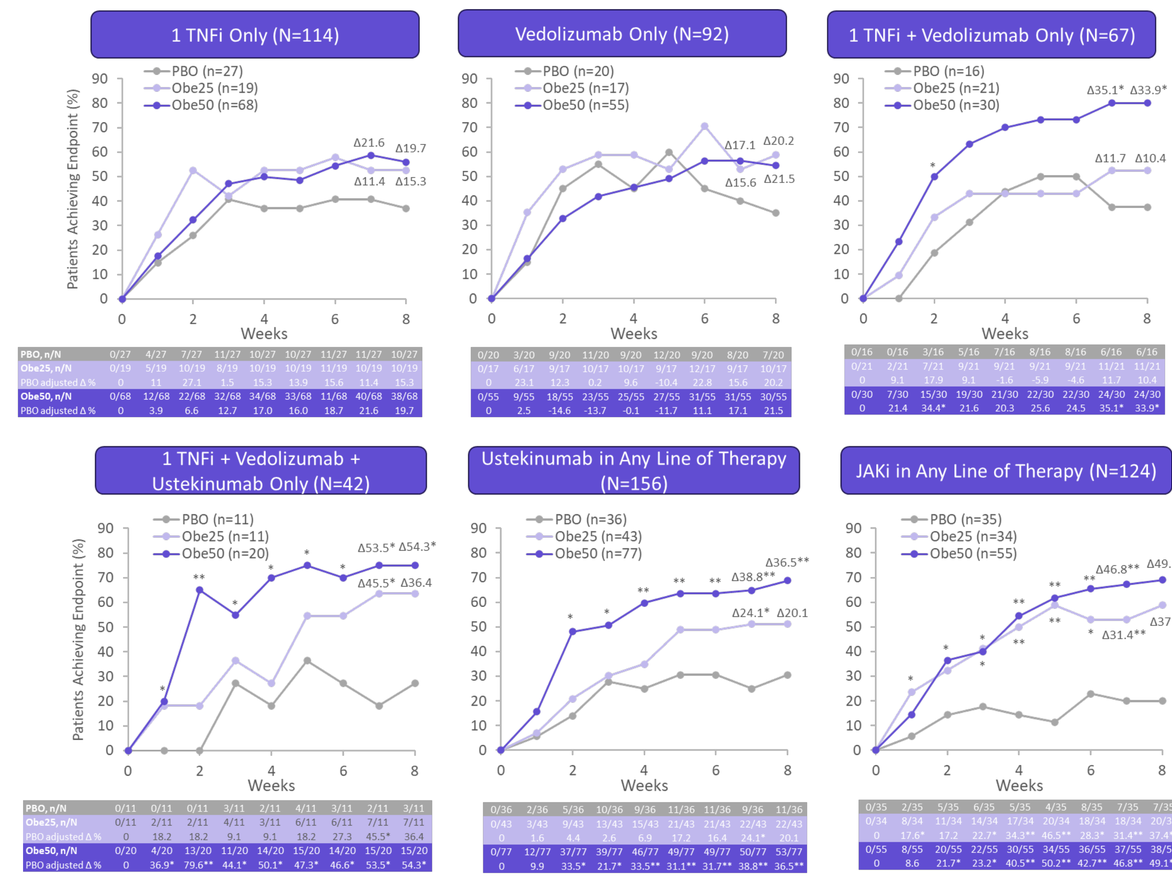
- Among pts enrolled in the ABTECT trials, 114 were TNFi-IR, 92 were Vedo-IR, 67 were TNFi/Vedo-IR, 42 were TNFi/Vedo/Uste-IR, 156 were Uste-IR, and 124 were JAK-IR.
- Higher proportion of pts receiving Obe versus PBO achieved symptomatic remission and symptomatic response from the first weeks of treatment (Fig. 2).
- In pts receiving Obe-50, proportions of patients achieving symptomatic remission and symptomatic response increased over time across all of ATIR subgroup drug classes.
- For pts receiving Obe-50, symptomatic remission continued to improve through W8, without evidence of a plateau.

Fig. 2: Rates of symptomatic remission and symptomatic response across subgroups of ATIR pts

A. Symptomatic remission



B. Symptomatic response



Analyses not powered for statistical significance in small subgroups; results are exploratory and directional. Nominal *P* values are provided for descriptive purposes only. NRI is used for subjects with missing outcome at W8 and subjects reporting any IE prior to W8; % Difference is for Obe minus OBO and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: ATIR (yes/no), baseline oral corticosteroids usage (yes/no). *P* values are 2-sided. Symptomatic remission: RBS=0, SFS <1. Symptomatic response: 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. **P*<0.05; ***P*<0.01.

Conclusions

- In this pooled analysis of ABTECT trials in pts with moderately to severely active UC, obefazimod demonstrated symptomatic improvements as early as the first weeks of treatment, irrespective of prior inadequate response to any specific class of AT.
- Symptomatic remission continued to increase through week 8 across all ATIR subgroup drug classes without plateau, indicating potential for additional gains beyond week 8.

Disclosures : *SD (consultant or speaker's fees): AbbVie, Ferring, Hospira, Johnson & Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, Boehringer Ingelheim. BES (consultant or speaker's fees) AbbVie, Abivax, Adiso Therapeutics, AgomAb, Alimentiv, Amgen, Arena Pharmaceuticals, Artizan Biosciences, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Connect Biopharm, Cytoki Pharma, Eli Lilly and Company, Enthera, Evommune, Ferring, Fresenius Kabi, Galapagos, Gilead Sciences, Genentech, Glaxo SmithKline, Gossamer Bio, HMP Acquisition, Imhotex, Immunic, InDex Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Kalyope, Merck, MiroBio, Morphic Therapeutic, MRM Health, OSE Immunotherapeutics, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma Global, Surrozen, Synlogic Operating Company, Takeda, Target RWE, Theravance Biopharma R&D, TLL Pharmaceutical, USWM Enterprises, Ventyx Biosciences, Viela Bio, and stock options from Ventyx Biosciences. MG (grants, consultant or speaker's fees) Eli Lilly Slovakia, AbbVie, Celltrion, Takeda, Roche, Janssen, Pfizer, Zentiva. MS (grants, consultant or speaker's fees) Gilead, Celltrion, Janssen, Abbvie, Ferring, Takeda, Pfizer, Eli Lilly, Dr. Falk Pharma,Celgene, MSD, Emerge Health, BMS, Alimentiv*

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

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