P0952 - Impact of baseline Mayo endoscopic subscore on the efficacy of once-daily oral obefazimod in moderately to severely active ulcerative colitis: week 8 results from the two Phase 3 ABTECT induction trials

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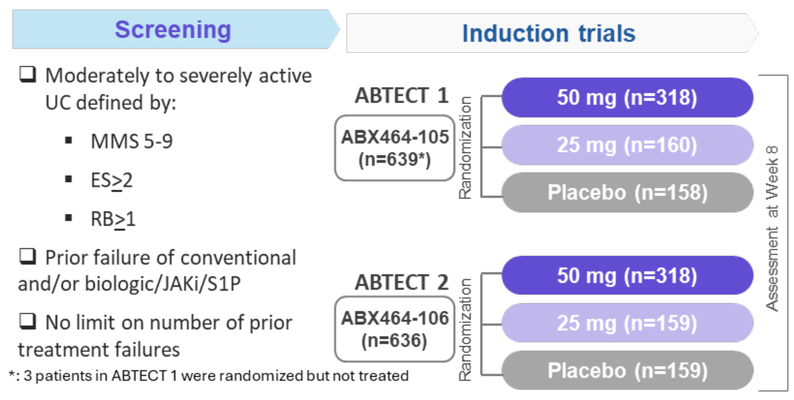
Background

- 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.
- Baseline disease characteristics can influence clinical outcomes and are important to consider when optimizing UC treatment. We report the efficacy of Obe in pts stratified by baseline Mayo endoscopic subscore (MES) from the ABTECT induction 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



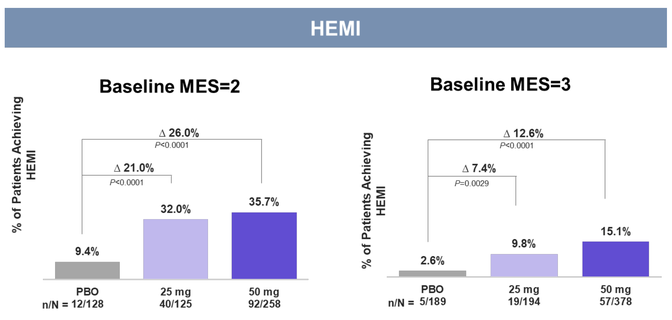
- This post-hoc analysis categorized pts by baseline MES = 2 (MES2) or MES = 3 (MES3). Efficacy endpoints evaluated clinical remission/response, endoscopic improvement/remission, symptomatic response/remission, and histo-endoscopic mucosal improvement (HEMI). All p-values are nominal.

Results

- Among the 1272 randomized and treated pts in ABTECT trials, 40.2% (511) were MES2 and 59.8% (761) were MES3. In both trials, baseline demographics and disease characteristics were similar between treatment groups, regardless of baseline MES.
- In the pooled analysis, higher proportion of pts receiving Obe-25 or Obe-50 versus PBO achieved clinical remission in both the MES2 (Obe-25-PBO difference: 20.2%, p<0.0001; Obe-50-PBO difference: 21.7%, p<0.0001) and MES3 (Obe-25-PBO difference: 8.7%, p=0.0001; Obe-50-PBO difference: 12.5%, p<0.0001) subgroups, and similar trends were observed across all other endpoints (Fig.2).
- Overall, the proportions of pts achieving efficacy endpoints were generally numerically lower in the MES3 subgroup compared with the MES2 subgroup at week 8.

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

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.



Conclusions

- In both ABTECT induction trials in pts with moderately to severely active UC, obefazimod demonstrated clinical meaningful improvements irrespective of baseline MES.
- Efficacy was similar across both subgroups with numerically greater efficacy rates in pts with baseline MES2 vs MES3 in most endpoints.

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

Disclosures : *LPB (consultant or speaker's fees) Abbvie, Abivax, Adacyte, Alimentiv, Amgen, Applied Molecular Transport, Arena, Banook, Biogen, BMS, Celltrion, Connect Biopharm, Cytoki Pharma, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, Gossamer Bio, GSK, IAC Image Analysis, Index Pharmaceuticals, Inotrem, Janssen, Lilly, Medac, Mopac, Morphic, MSD, Nordic Pharma, Novartis, Oncodesign Precision Medicine, ONO Pharma, OSE Immunotherapeuthics, Pandion Therapeuthics, Par' Immune, Pfizer, Prometheus, Protagonist, Roche, Samsung, Sandoz, Sanofi, Satisfay, Takeda, Telavant, Theravance, Thermo Fischer, Tigenix, Tillots, Viatris, Vectivbio, Ventyx, Ysopia (Grant) Celltrion, Fresenius Kabi, Medac, MSD, Takeda; 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, J&J, 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, (stock options) Ventyx Biosciences; AA (consultant or speaker's fees) AbbVie, Abivax, Alfa Sigma, Astra Zeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Eli-Lilly, Enthera, Ferring, Galapagos, Gilead, Giuliani, Janssen, Lionhealth, MSD, Nestlé, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sanofi, Sandoz, Takeda, Teva Pharmaceuticals, Tillots Pharma; speaker's fees from AbbVie, Abivax, AG Pharma, Biogen, Bristol-Myers Squibb, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, Lionhealth, MSD, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda, Teva Pharmaceuticals; and research support from Biogen, MSD, Takeda, Pfizer; HT (consultant or speaker's fees) AbbVie, Calypso Biotech, Celtrion, Immunic, Pharmacosmos, Takeda Pharma, Biogen, BMS, Falk Foundation, Galapagos, J&J, Pfizer, Pharmacosmos; SN (consultant or speaker's fees) Abbvie, Alfasigma, Amgen, Celltrion, Ferring, Fresenius-Kabi, J&J, Lilly, Medac, MSD, Pfizer, Sandoz, Takeda; GDA (consultant or speaker's fees) Abbvie, Abivax, Agomab, Alimentiv, Anaptys Bio, AstraZeneca, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom Biosciences, Galapagos, Glaxo Smith Kline, Dr Falk Pharma, Pfizer, J&J, Merck, Mirador, Polpharma, Procise Diagnostics, Prometheus Biosciences, Sorriso Pharma, Spyre, Takeda, Ventyx (Grant) Pfizer, BMS, J&J, Abbvie, Alimentiv BV, Eli Lilly, Takeda, Prometheus Laboratories; DL (consultant or speaker's fees) Abbvie, Alfasigma, Amgen, Biocon, Celltrion, Ferring, Fresenius-Kabi, Johnson & Johnson, Lilly, Medac, MSD, Pfizer, Sandoz, Takeda; MD (consultant or speaker's fees) Abbvie, Abivax, Arena Pharmaceuticals, Astra Zeneca, Boehringer Ingelheim International GmbH, Bristol-Meyer Squibb, Eli Lilly and Company, F. Hoffmann-La Roche Ltd, Genentech Inc, Gilead, Janssen Pharmaceuticals, Merck, Pfizer Inc, Prometheus Biosciences, Takeda Pharmaceuticals*

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