P0862 - Continued efficacy improvement beyond the induction period with once-daily obefazimod: week 8 to week 48 outcomes from the Phase 2b open-label maintenance study in patients with moderately to severely active ulcerative colitis, stratified by prior advanced-therapy exposure

European Crohn's and Colitis Organisation
This poster was presented at the annual ECCO Congress.

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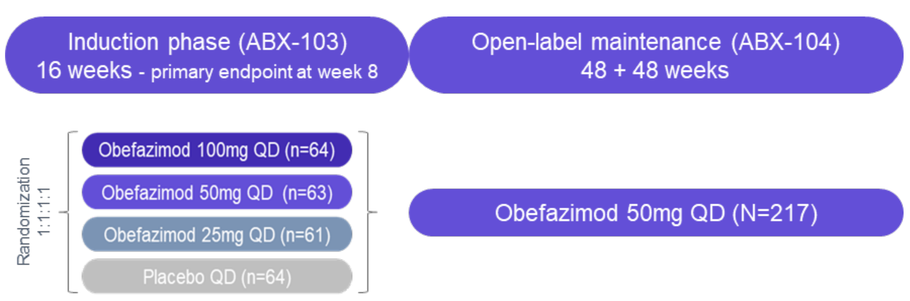
Background

- 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 is currently in Phase 3 clinical trials for the treatment of patients (pts) with moderately to severely active ulcerative colitis (UC) [1]. Obe showed efficacy in pts with UC at week 8 (W8) in a Phase 2b, double-blind, placebo (PBO)-controlled, induction trial and the subsequent open-label maintenance (OLM) study [2].
- Similar to the ongoing Phase 3 ABTECT program, the Phase 2b program enrolled pts with inadequate response, loss of response, or intolerance to conventional treatments and/or advanced therapies [AT] (biologics/JAK inhibitors) with no upper limit AT exposure.
- We report results from the Phase 2b OLM study focusing on patient subgroups aligned with the population enrolled in the ongoing Phase 3 Maintenance trial [NCT05535946], specifically the proportion of W8 obe-treated clinical responders (W8CR) achieving efficacy endpoints by prior AT experience.

Methods

- In the Phase 2b induction trial, pts were randomized to PBO or obe (25mg, 50mg [Obe-50] or 100mg QD) for 16 weeks, and, irrespective of their clinical response, could enter the optional OLM study with Obe-50 (Fig. 1).
- For this post-hoc analysis, endpoints including clinical remission, endoscopic improvement/remission and histo-endoscopic mucosal improvement (HEMI) were assessed at W48 among W8CR, stratified by prior AT experience (AT-experienced vs AT-naïve).

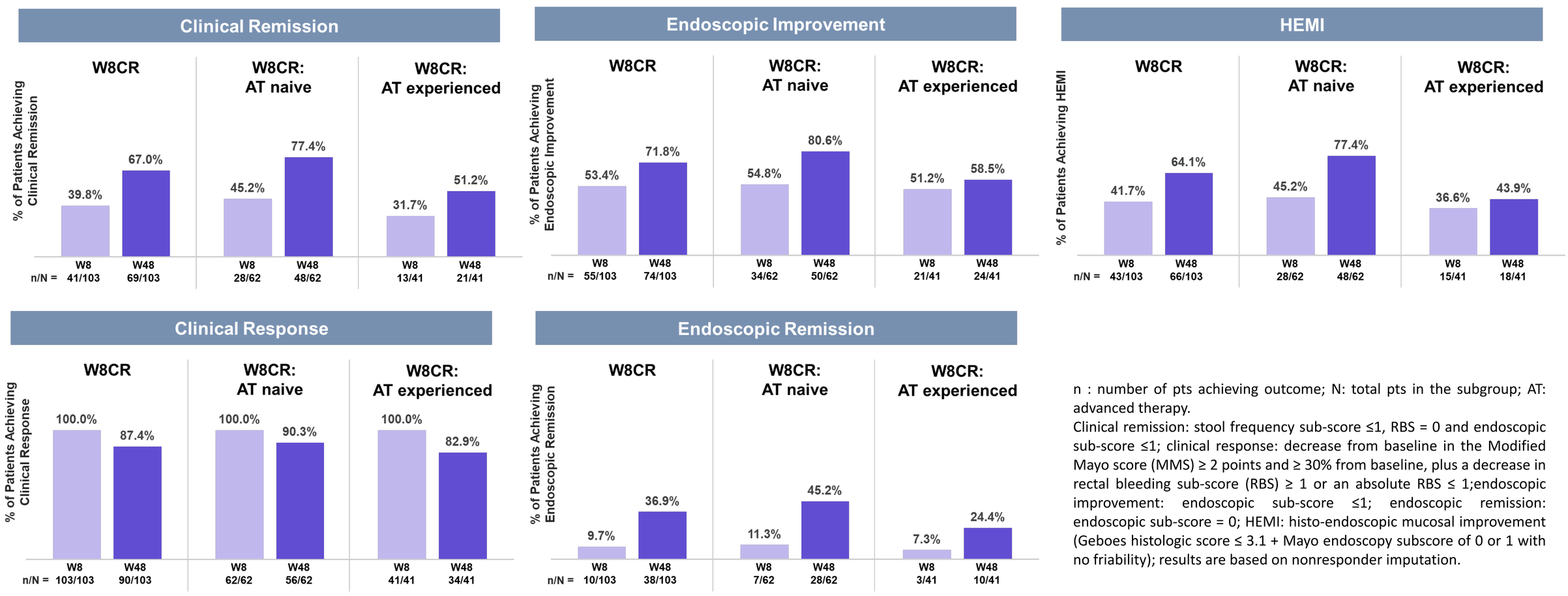
Fig. 1: Phase 2b induction and OLM study design



Results

- Of the 217 pts who participated in the OLM, 74.7% (162/217) received Obe at any dose during induction.
- Among the Obe-treated pts, 63.6% (103/162) were W8CR, of whom 60.2% (62/103) were AT-naïve and 39.8% (41/103) were AT-experienced.
- Among W8CR pts, the proportion achieving clinical remission increased from W8 to W48 irrespective of prior AT experience:
  - Overall, from 39.8% (41/103) at baseline of the OLM to 67.0% (69/103) (net increase of +28 pts)
  - AT-naïve from 45.2% (28/62) to 77.4% (48/62) (net increase of +20 pts)
  - AT-experienced: from 31.7% (13/41) to 51.2% (21/41) (net increase of +8 pts) (Fig.2).
- Most efficacy endpoints showed increased proportions of pts meeting efficacy criteria at W48 vs W8, regardless of prior AT experience.

Fig. 2: Increased proportions achieving efficacy endpoints at W48 vs W8 among obefazimod-treated pts by prior advanced-therapy status



n : number of pts achieving outcome; N: total pts in the subgroup; AT: advanced therapy.
Clinical remission: stool frequency sub-score ≤1, RBS = 0 and endoscopic sub-score ≤1; clinical response: decrease from baseline in the Modified Mayo score (MMS) ≥ 2 points and ≥ 30% from baseline, plus a decrease in rectal bleeding sub-score (RBS) ≥ 1 or an absolute RBS ≤ 1;endoscopic improvement: endoscopic sub-score ≤1; endoscopic remission: endoscopic sub-score = 0; HEMI: histo-endoscopic mucosal improvement (Geboes histologic score ≤ 3.1 + Mayo endoscopy subscore of 0 or 1 with no friability); results are based on nonresponder imputation.

Conclusions

- Pts with moderately to severely active UC treated with Obe who achieved clinical response at W8 demonstrated continued improvement across all efficacy endpoints at W48, including clinical remission, independent of prior AT experience.
- Since both the Phase 2 and 3 studies enrolled similar populations of both AT-naïve and AT-experienced pts (including pts who failed prior AT), these findings provide relevant context for the ongoing Phase 3 maintenance trial.

References 1: Vermeire S et al. *J Crohns Colitis*. 17: 1689-97, 2023 - 2: Vermeire S et al. *The Lancet Gastroenterology & Hepatology*. 7: 1024-35, 2022

Disclosures : *AA (consultant or speaker's fees) 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, AG Pharma, Novartis; (Grant) Biogen, MSD, Takeda, and Pfizer; 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; RA (consultant or speaker's fees) AbbVie, Abivax, AstraZeneca, Bristol-Myers Squibb, Celltrion Healthcare, Galapagos, J&J, Lilly, MSD, Pfizer, and Takeda Pharma; 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; 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, and stock options from Ventyx Biosciences; PSD (consultant) Abbvie, Abivax, Adiso, Alimentiv, Bristol Meyer Squibb, Celltrion, Genentech, Geneoscopy, Janssen, Pfizer, Takeda; DR (consultant or speaker's fees) Abbvie, Abivax SA, Altrubio, Athos Therapeutics, Inc, Bristol-Myers Squibb, Celltrion, Connect BioPharma, Eli Lilly & Co., Genentech Inc., Iterative Health, Janssen Pharmaceuticals, J&J, Merck & Co., Odyssey Therapeutics, Pfizer, Sanofi, Spyre, Takeda Pharmaceuticals, Vedanta Biosciences, Ventyx (Grant) Takeda.*

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