P1159 - Pooled analysis of efficacy and safety of once-daily oral obefazimod in European patients from the ABTECT Phase 3, double-blind, placebo-controlled induction trials

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to access *all* obefazimod publications at ECCO26

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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 two 8-week ABTECT induction trials (NCT05507203, NCT05507216), Obe achieved clinically meaningful improvements in clinical, endoscopic and histologic endpoints.
- This pooled analysis evaluates the efficacy and safety of Obe in the European subgroup of pts enrolled in the 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 (with 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. This analysis focuses on subgroups of pts from Western (WE) and Eastern Europe (EE).
- Efficacy endpoints included clinical remission, clinical response, endoscopic improvement, symptomatic remission, and histo-endoscopic mucosal improvement (HEMI).
- Treatment emergent adverse events (TEAEs), serious TEAEs and dropout rates were evaluated.

Results

- In the ABTECT trials, there were 285 WE pts and 479 EE pts.
- Baseline characteristics were generally balanced between treatment groups and comparable between regions except for a higher proportion of WE pts with prior inadequate response to advanced therapy (81.8-86.9%) vs EE pts (19.1-27.2%).
- A higher proportion of WE pts receiving Obe-50 vs. PBO achieved clinical remission and all other endpoints with nominal significance.
- Among EE pts both Obe-25 and Obe-50 met all efficacy endpoints vs. PBO with nominal significance (Fig.2).
- TEAEs were reported more frequently in WE pts (Obe-50: 78.8%, Obe-25: 67.5%, PBO: 64.8%) than in EE pts (Obe-50: 48.0%, Obe-25: 30.4%, PBO: 43.6%). Headache was the most common TEAE (Table 1). Rates of serious TEAEs were comparable across treatment groups. TEAE leading to study discontinuations was more frequent with Obe-50 vs PBO. No signal was observed for serious/severe and opportunistic infections or malignancies.

Table 1: Summary of adverse events of Obe in the subgroup of European patients

	Obe-50 (n=381)	Obe-25 (n=202)	PBO (n=181)
Any TEAEs, n (%)	225 (59.1)	90 (44.6)	94 (51.9)
TEAE leading to study discontinuation, n (%)	18 (4.7)	4 (2.0)	4 (2.2)
Serious TEAE, n (%)	13 (3.4)	5 (2.5)	4 (2.2)
TEAE leading to death, n (%)	0	0	0
Malignancies	1 (0.3)[a]	0	0
Serious/severe/opportunistic infections	4 (1.0)	1 (0.5)	0
TEAEs occurring in patients (≥3% in Obe groups and greater than PBO), n (%)			
Headache	80 (21.0)	25 (12.4)	10 (5.5)
Nausea	23 (6.0)	8 (4.0)	3 (1.7)
Lipase increased[b]	19 (5.0)	7 (3.5)	5 (2.8)
Abdominal pain upper	13 (3.4)	1 (0.5)	0
Nasopharyngitis	10 (2.6)	9 (4.5)	7 (3.9)

[a]Prostate cancer stage I. [b]To date, no safety signals have been observed related to either elevations in lipase or more specifically to pancreatitis.

Conclusions

In the European population included in the ABTECT induction trials in moderately to severely active UC, obefazimod demonstrated consistent efficacy and safety comparable to the overall study population.

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

Fig. 1: Design of ABTECT induction trials

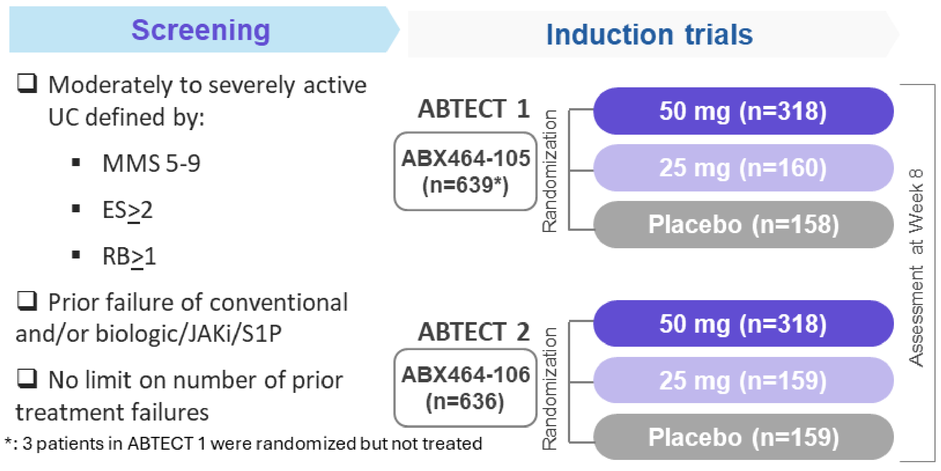
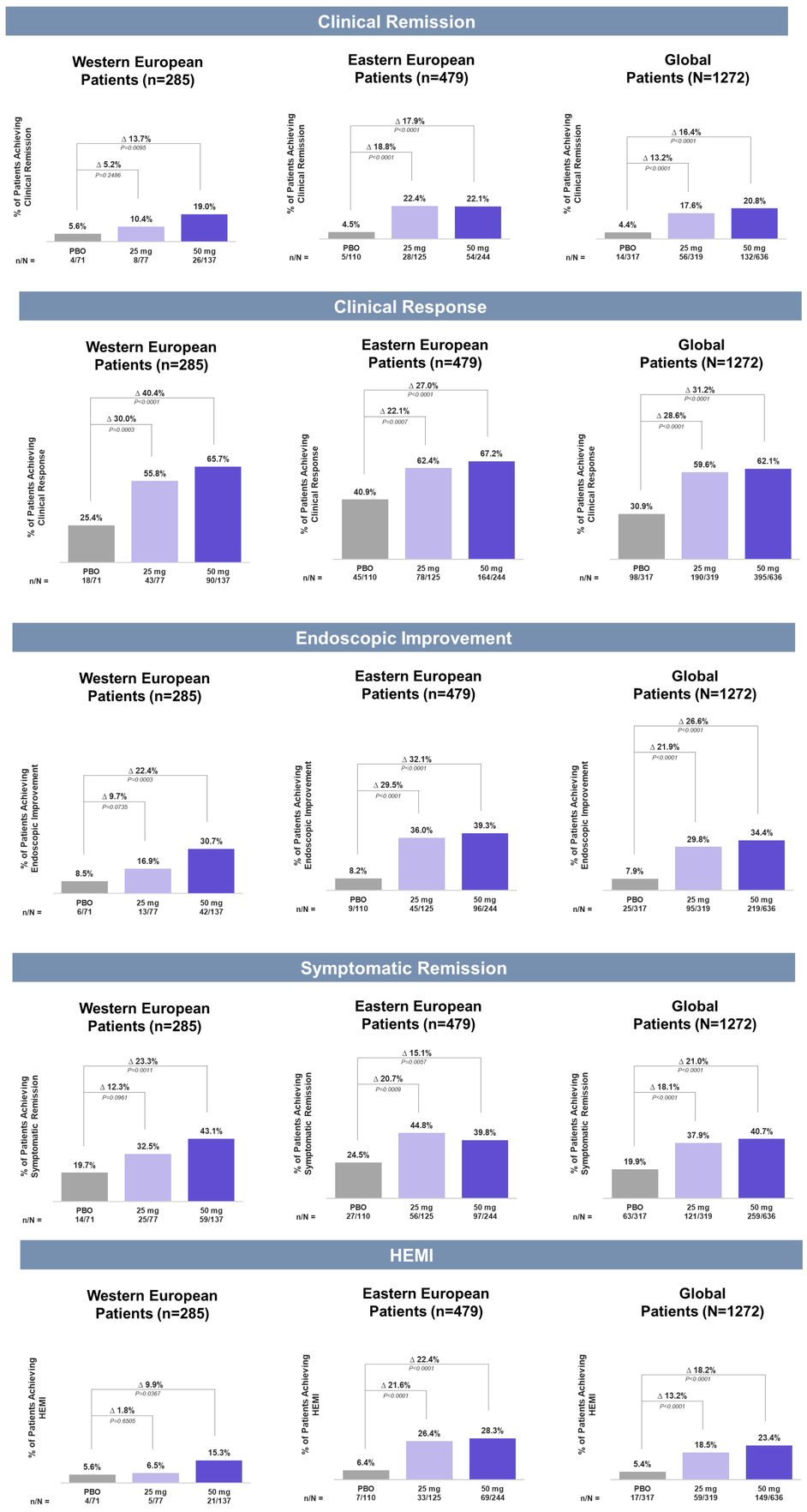


Fig. 2: Eight-week efficacy of Obe in European vs global population: pooled ABTECT trials



Analyses not powered for statistical significance in 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 ≥ or an absolute RBS ≤1. Endoscopic improvement: endoscopic subscore ≤1. Symptomatic remission: RBS=0, SFS ≤1. HEMI: MES=0 or 1 and Geboes Index score ≤3.1. HEMI, histo-endoscopic mucosal improvement; IE, intercurrent event; MES, Mayo Endoscopic Subscore; MMS, Modified Mayo Score; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo; RBS, rectal bleeding subscore; SFS, stool frequency score.

Disclosures : *FS (consultant/speaker's fees) Janssen, Takeda, Pfizer, MSD, Sandoz, Galapagos, Celltrion, Ferring, Abbvie, Lilly, Alfasigma, Abivax. US (consultant/speaker's fees) AbbVie, Abivax, Amgen, Galapagos, Janssen, Eli Lilly; speaker for Abivax, Amgen, Galapagos, Eli Lilly, Janssen; (grants) Abbvie, Abivax, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead Sciences, Galapagos, Janssen, Pfizer, Roche, and Takeda Pharmaceuticals. XT (consultant/speaker's fees) Celltrion, AbbVie, Johnson & Johnson, Lilly, Takeda, Alpha Sigma, Dr. Falk, Abivax, Biogen, Fresenius Kabi, MSD, Pfizer, Tillotts, Thabor Therapeutics. FDA (consultant/speaker's fees) Abbvie, Alfasigma, Ferring, Lilly, Sandoz, Janssen, Fresenius Kabi, Galapagos, Giuliani, MSD, Pfizer, Takeda, Tillotts, Omega Pharma, AnaptysBio, Nestlé. AA (consultant/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, AG Pharma, Novartis; (grants) Biogen, MSD, Takeda, Pfizer. SH (consultant/speaker's fees) Alfa sigma, Amgen, Abbvie, Galapagos, Lilly, Janssen, Takeda, Shire, Pfizer, AstroPharma, Falk, Ferring, Gilead, MSD, Roche, Stada, Vifor. RA (consultant/speaker's fees) AbbVie, Abivax, AstraZeneca, Bristol-Myers Squibb, Celltrion Healthcare, Galapagos, Johnson&Johnson, Lilly, MSD, Pfizer, and Takeda Pharma. FB (consultant/speaker's fees) AbbVie, Arena Pharmaceuticals, Celltrion Ferring, Galapagos, Janssen, MSD, Pfizer Inc, Takeda, Amgen, Celgene, Fresenius Kabi, J&J, Sandoz; (grants) AbbVie, Amgen, Eurogenerics, J&J, Takeda. HT (consultant/speaker's fees) Abbvie, Abivax, Dr Falk Pharma, ferring, Galapagos, Microbiotica, MSD, Pfizer, Takeda*

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