P0922 - Impact of obefazimod treatment on histologic and combined histologic-endoscopic outcomes in patients with moderately to severely active ulcerative colitis: results from the ABTECT-1 and ABTECT-2 Phase 3, double-blind, placebo-controlled induction trials

European Crohn's and Colitis Organisation
This poster was presented at the annual ECCO Congress.
to access *all* obefazimod publications at ECCO26

Fernando Magro[1], Bruce E Sands[2], Silvio Danese[3], Marla Dubinsky[4], Fabio Cataldi[5], Doug Jacobstein[5], Christopher J Rabbat[5], Kevin Shan[5], Luciana Harlacher[6], Franco Scaldaferri[7], Geert D'Haens[8], Luc Biedermann[9], Laurent Peyrin-Biroulet[10]

[1]CINTESIS@RISE, Faculty of Medicine, University of Porto, Portugal, [2]Icahn School of Medicine at Mount Sinai, New York, USA, [3]IRCCS Ospedale San Raffaele, Italy, [4]Pediatric GI and Nutrition Mount Sinai Kravis Children's Hospital, New York, USA, [5]Abivax, Paris, France,[6]Hospital de Clínicas de Porto Alegre, Brazil, [7] Fondazione Policlinico A. Gemelli IRCCS - Università Cattolica del Sacro Cuore, Roma, Italy [8]Amsterdam University Medical Center, The Netherlands, [9]University Hospital Zurich, Switzerland, [10]INFINY Institute, INSERM NGERE, CHRU Nancy, Vandœuvre-lès-Nancy, France.

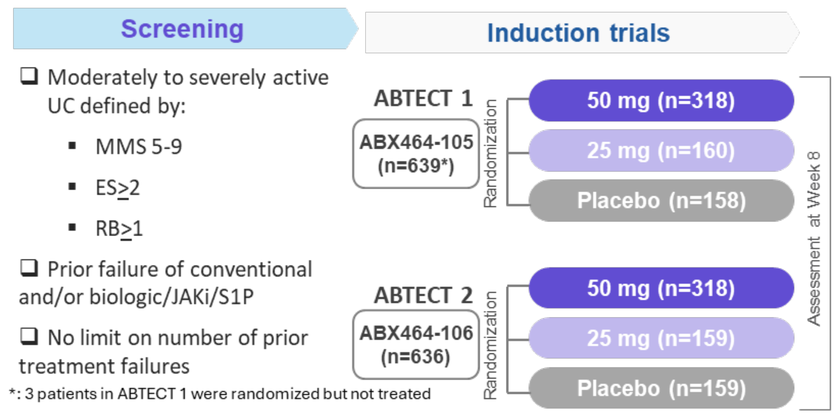
Background

- 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.
- UC treatment goals are shifting from symptomatic treatment (i.e. clinical remission) to achieving mucosal healing [4]. Here we report proportions of pts that met endoscopic, histologic and combined histologic-endoscopic outcomes in ABTECT trials.

Methods

- The 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

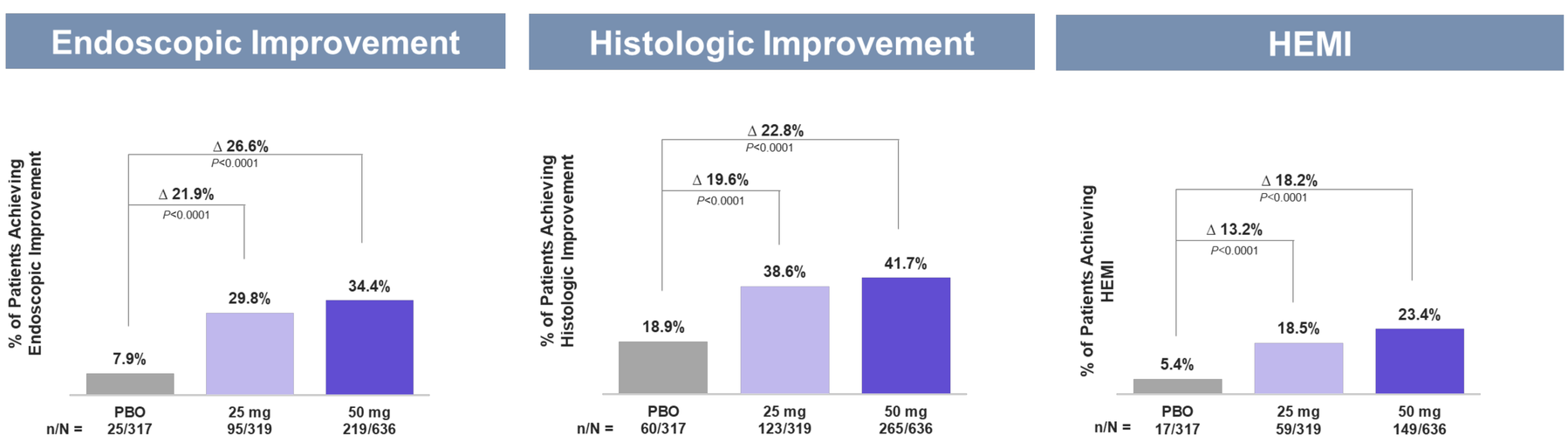


- Rectal or sigmoidal biopsies from the most affected segment were collected during endoscopy at screening and Week 8 (W8) to evaluate treatment effect of Obe vs PBO on histopathology scores using the Geboes index. Endoscopic improvement/remission, histologic improvement/remission, histo-endoscopic mucosal improvement (HEMI) and remission (HEMR), and endoscopic improvement histological remission (EIHR) were evaluated using non-responder imputation (NRI).

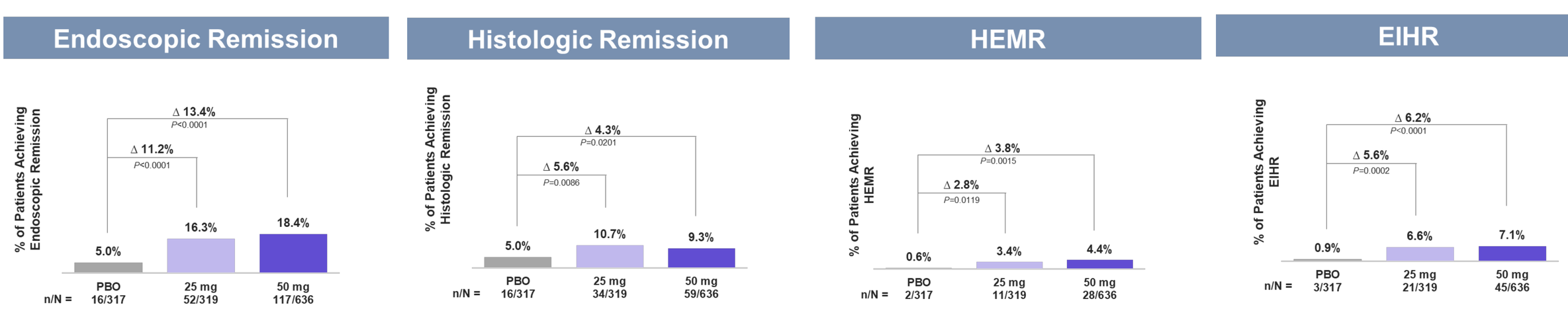
Results

- 1272 pts were randomized and treated in the two ABTECT trials.
- In a pooled analysis, higher proportions of pts receiving either Obe-25 or Obe-50 versus PBO achieved all endoscopic and histologic endpoints (endoscopic improvement: Obe-25-PBO difference=21.9%; Obe-50-PBO difference=26.6% - histologic improvement: Obe-25-PBO difference=19.6%; Obe-50-PBO difference=22.8%), and combined endoscopic-histologic with nominal significance, including the most stringent endpoint of HEMR (Fig.2).

Fig. 2: 8-week histologic and combined histologic-endoscopic outcomes - pooled ABTECT trials



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), and pivotal study (ABX464-105/ABX464-106). All P values are 2-sided. Endoscopic improvement: endoscopic subscore ≤1. Endoscopic remission: endoscopic subscore=0. Histological improvement: neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes histologic score ≤3.1). Histological remission: absence of neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue, according to the Geboes grading system (ie, Geboes histologic score <2.0). HEMI: endoscopic subscore ≤1 and Geboes Index score ≤3.1. HEMR: absence of neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue, according to the Geboes grading system (ie, Geboes histologic score <2.0), and endoscopy subscore of 0. EIHR: endoscopic subscore ≤1 and Geboes Index score <2.0. EIHR, Endoscopic Improvement histological remission; HEMI, Histo-endoscopic mucosal improvement; HEMR, Histo-endoscopic mucosal remission; IE, intercurrent event; MES, Mayo Endoscopic Subscore; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo.



Conclusions

- In the ABTECT induction trials in pts with moderately to severely active UC, Obe treatment led to clinically meaningful improvements in endoscopic, histologic, and combined histologic-endoscopic endpoints at W8.

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: Kobayashi T, et al. Nat Rev Dis Primers. 2020 Sep 10;6(1):74 doi: 10.1038/s41572-020-0205-x

Disclosures : *FM (consultant or speaker's fees) AbbVie, Amgen, Biogen, Celgene, Celltrion, Dr Falk Pharma, Ferring Pharmaceuticals, Hospira, Janssen, Laboratórios Vitória, MSD, Pfizer, Sandoz, Takeda, UCB, Vifor (Grant) GEDII and National Science Foundation; 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; 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; MD (consultant or speaker's fees) Abbvie, Abivax, Arena Pharmaceuticals, Astra Zeneca, Boehringer Ingelheim International GmbH, BMS, Eli Lilly and Company, F. Hoffmann-La Roche Ltd, Genentech Inc, Gilead, Janssen Pharmaceuticals, Merck, Pfizer Inc, Prometheus Biosciences, Takeda Pharmaceuticals; LH (consultant or speaker's fees) J&J, AbbVie, Takeda, Ventyx, Abivax, BMS, Lilly, MSD, Sanofi; FS (consultant or speaker's fees) Janseen, Takeda, Pfizer, MSD, Sandoz, Galapagos, Celltrion, Ferring, Abbvie, Lilly, Alfasigma, Abivax; GDH: (consultant or speaker's fees) Abbvie, Abivax, Agomab, Alimentiv, Anaptys Bio, AstraZeneca, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom Biosciences, Galapagos, GSK, 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; LB (consultant or speaker's fees) Abbvie, MSD, Vifor, Falk, Esocap, Calypso, Ferring, Pfizer, Shire, Takeda, Janssen, Ewopharma; 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.*

.

ABIVAX
7-11 Blvd Haussmann- 75009 Paris, France
E-mail: info@abivax.com - www.abivax.com