P0804 - Impact of prior inadequate response to advanced therapies on early symptomatic improvement with obefazimod induction in moderately to severely active ulcerative colitis: results from the two Phase 3 placebo-controlled ABTECT induction trials

European Crohn's and Colitis Organisation

This poster was presented at the annual ECCO Congress.

to access *all* obefazimod publications at ECCO26

Raja Atreya[1], Bruce E Sands[2], David T Rubin[3], Marla Dubinsky[4], Alessandro Armuzzi[5], Xavier Treton[6], Fabio Cataldi[7], Doug Jacobstein[7], Christopher J Rabbat[7], Kevin Shan[7], Tibor Hlavaty[8], Robert Witek[9], Parambir S Dulai[10], Silvio Danese[11].

[1]University Hospital Erlangen, Germany, [2]Icahn School of Medicine at Mount Sinai, New York, USA, [3]University of Chicago Medicine, Chicago, USA,[4]Pediatric GI and Nutrition Mount Sinai Kravis Children's Hospital, New York, USA, [5]IRCCS Humanitas Research Hospital, Milan, Italy, [6]MICI Institute, Neuilly s/seine, France, [7]Abivax, Paris, France, [8]Cliniq s.r.o., Slovakia, [9]Osrodek Badan Klinicznych Metabolica, Tarnów, Poland, [10]Feinberg School of Medicine Northwestern University - Chicago, USA, [11]IRCCS Ospedale San Raffaele, Italy.

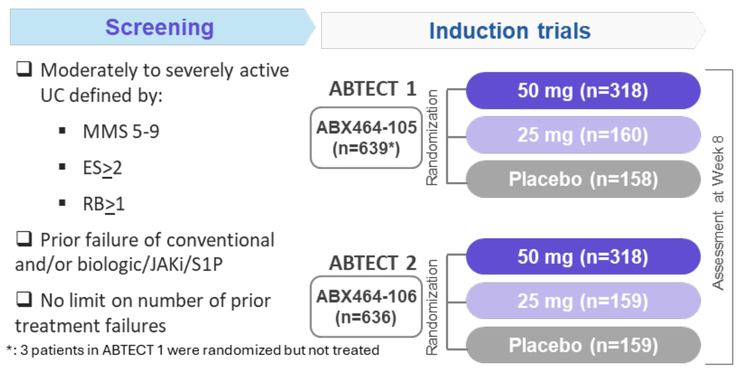
Background

- 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 all clinical, endoscopic and histologic endpoints regardless of prior inadequate response to advanced therapy (ATIR). Here, we report the impact of prior ATIR on early symptomatic improvement with Obe in the ABTECT trials.

Methods

- The multicenter, randomized, double-blind, placebo-controlled ABTECT trials enrolled pts with moderate-to-severe UC (modified Mayo score (MMS)≥ 5, 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 (JAKi) with no limit on the number of prior ATIR. (Fig. 1).

Fig. 1: Design of ABTECT induction trials



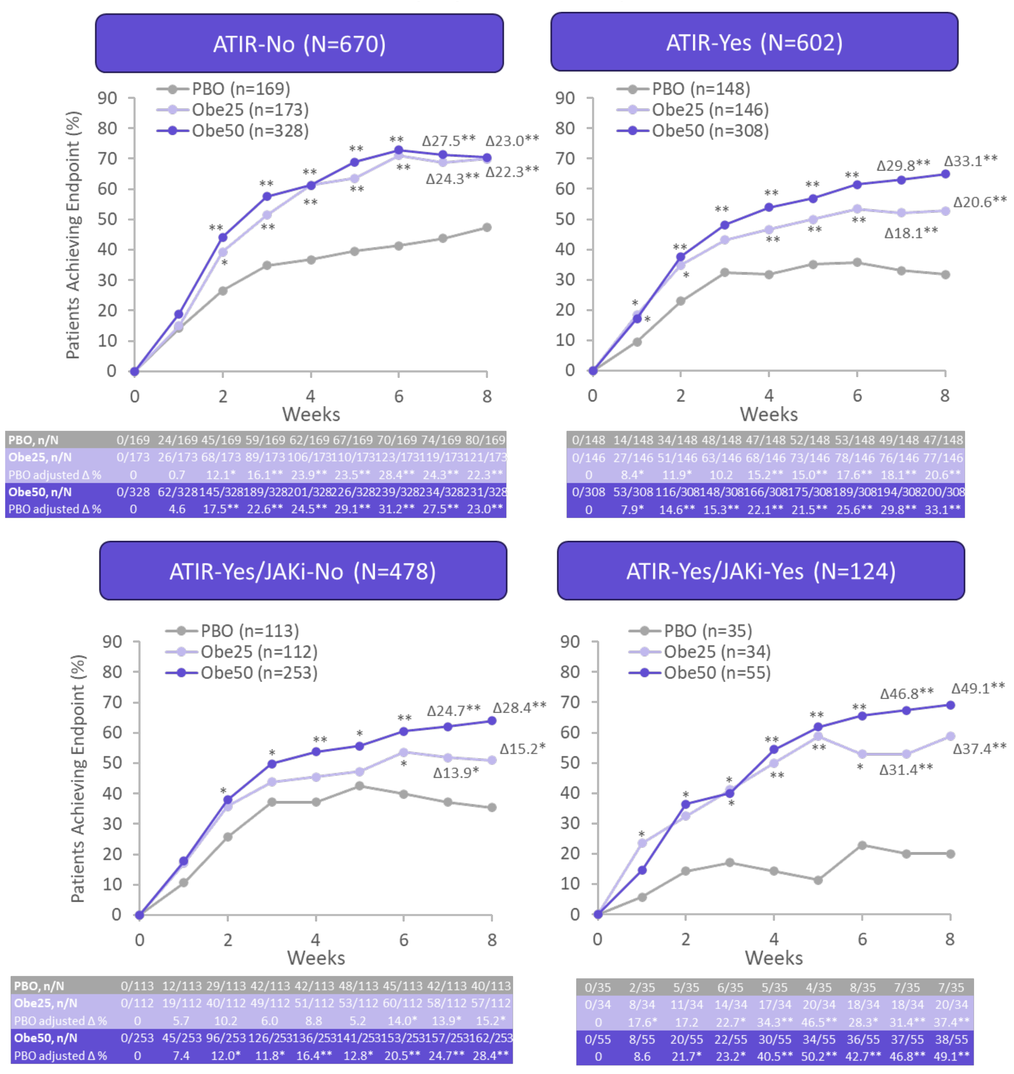
- Pts were randomized 2:1:1 to Obe 50 mg QD (Obe-50), Obe 25 mg QD (Obe-25) or placebo (PBO) for 8 weeks.
- This analysis focuses on proportions of pts achieving symptomatic remission or symptomatic response from week 1 (W1) through week 8 (W8). Pts were categorized as ATIR-No and ATIR-Yes, with the latter further categorized by JAKi IR status (ATIR-Yes/JAKi-No vs. ATIR-Yes/JAKi-Yes). All p-values are nominal.

Results

- Among pts enrolled in the ABTECT trials, 670 were ATIR-No and 602 were ATIR-Yes (478 ATIR/JAKi-No, 124 ATIR/JAKi-Yes).
- In ATIR-No and ATIR-Yes pts, both Obe-50 and Obe-25 led to clinically meaningfully improvements in symptoms vs PBO. A higher proportion of ATIR-No pts receiving Obe achieved symptomatic response and remission from W2 to W8 (Fig. 2).
- In ATIR-Yes pts, symptomatic response was observed as early as W1 with both Obe-25 and Obe-50 (Fig. 2A), and symptomatic remission from W3 with Obe-50 (Fig. 2B). Similar trends were observed in ATIR-Yes/JAKi-No pts with Obe-50.
- Among ATIR-Yes/JAKi-Yes pts, clinically meaningful improvements relative to PBO were observed in symptomatic response from as early as W1. In all ATIR-Yes subgroups, the proportion of pts achieving symptomatic endpoints continued to increase through W8, without evidence of plateauing.

Fig. 2: Rates of symptomatic response (A) and symptomatic remission (B) across subgroups of ATIR pts – pooled ABTECT-1 and ABTECT2

A. Symptomatic response



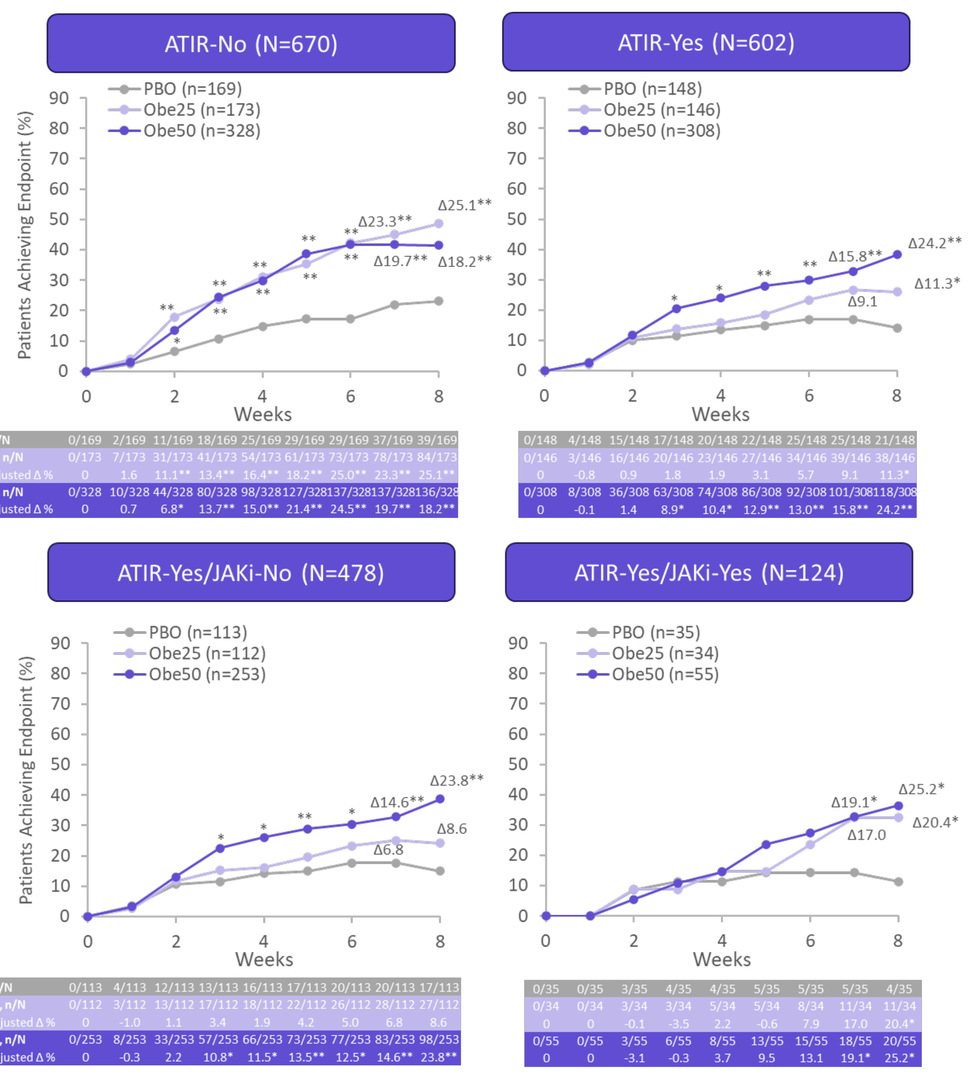
PBO, n/N	0/169	24/169	45/169	59/169	62/169	67/169	70/169	74/169	80/169
Obe25, n/N	0/173	26/173	68/173	89/173	106/173	110/173	123/173	119/173	121/173
PBO adjusted Δ %	0	0.7	12.1*	16.1**	23.9**	23.5**	28.4**	24.3**	22.3**
Obe50, n/N	0/328	62/328	145/328	189/328	201/328	226/328	239/328	234/328	231/328
PBO adjusted Δ %	0	4.6	17.5**	22.6**	24.5**	29.1**	31.2**	27.5**	23.0**

0/148	14/148	34/148	48/148	47/148	52/148	53/148	49/148	47/148
0/146	27/146	51/146	63/146	68/146	73/146	78/146	76/146	77/146
0	8.4*	11.9*	10.2	15.2**	15.0**	17.6**	18.1**	20.6**
0/308	53/308	116/308	148/308	166/308	175/308	189/308	194/308	200/308
0	7.9*	14.6**	15.3**	22.1**	21.5**	25.6**	29.8**	33.1**

PBO, n/N	0/113	12/113	29/113	42/113	42/113	48/113	45/113	42/113	40/113
Obe25, n/N	0/112	19/112	40/112	49/112	51/112	53/112	60/112	58/112	57/112
PBO adjusted Δ %	0	5.7	10.2	6.0	8.8	5.2	14.0*	13.9*	15.2*
Obe50, n/N	0/253	45/253	96/253	126/253	136/253	141/253	153/253	157/253	162/253
PBO adjusted Δ %	0	7.4	12.0*	11.8*	16.4**	12.8*	20.5**	24.7**	28.4**

0/35	2/35	5/35	6/35	5/35	4/35	8/35	7/35	7/35
0/34	8/34	11/34	14/34	17/34	20/34	18/34	18/34	20/34
0	17.6*	17.2	22.7*	34.3**	46.5**	28.3*	31.4**	37.4**
0/55	8/55	20/55	22/55	30/55	34/55	36/55	37/55	38/55
0	8.6	21.7*	23.2*	40.5**	50.2**	42.7**	46.8**	49.1**

B. Symptomatic remission



PBO, n/N	0/169	2/169	11/169	18/169	25/169	29/169	29/169	37/169	39/169
Obe25, n/N	0/173	7/173	31/173	41/173	54/173	61/173	73/173	78/173	84/173
PBO adjusted Δ %	0	1.6	11.1**	13.4**	16.4**	18.2**	25.0**	23.3**	25.1**
Obe50, n/N	0/328	10/328	44/328	80/328	98/328	127/328	137/328	137/328	136/328
PBO adjusted Δ %	0	0.7	6.8*	13.7**	15.0**	21.4**	24.5**	19.7**	18.2**

0/148	4/148	15/148	17/148	20/148	22/148	25/148	25/148	21/148
0/146	3/146	16/146	20/146	23/146	27/146	34/146	39/146	38/146
0	-0.8	0.9	1.8	1.9	3.1	5.7	9.1	11.3*
0/308	8/308	36/308	63/308	74/308	86/308	92/308	101/308	118/308
0	-0.1	1.4	8.9*	10.4*	12.9**	13.0**	15.8**	24.2**

PBO, n/N	0/113	4/113	12/113	13/113	16/113	17/113	20/113	20/113	17/113
Obe25, n/N	0/112	3/112	13/112	17/112	18/112	22/112	26/112	28/112	27/112
PBO adjusted Δ %	0	-1.0	1.1	3.4	1.9	4.2	5.0	6.8	8.6
Obe50, n/N	0/253	8/253	33/253	57/253	66/253	73/253	77/253	83/253	98/253
PBO adjusted Δ %	0	-0.3	2.2	10.8*	11.5*	13.5**	12.5*	14.6**	23.8**

0/35	0/35	3/35	4/35	4/35	5/35	5/35	5/35	4/35
0/34	0/34	3/34	3/34	5/34	5/34	8/34	11/34	11/34
0	0	-0.1	-3.5	2.2	-0.6	7.9	17.0	20.4*
0/55	0/55	3/55	6/55	8/55	13/55	15/55	18/55	20/55
0	0	-3.1	-0.3	3.7	9.5	13.1	19.1*	25.2*

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). 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. Symptomatic remission: RBS=0, SFS ≤1. IE, investigator event; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo; pMMS, partial Modified Mayo Score; RBS, rectal bleeding sub-score; SFS, stool frequency score. * P<0.05; **P<0.01.

Conclusions

- In the ABTECT induction trials, pts with moderately to severely active UC treated with Obe rapidly achieved symptomatic relief (either response or remission) regardless of prior ATIR, including a large number of pts previously treated with JAKi.
- No evidence of a plateau was observed through end of induction at W8 in all ATIR-Yes subgroups.

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 : *RA (consultant or speaker's fees) AbbVie, Abivax, AstraZeneca, Bristol-Myers Squibb, Celltrion Healthcare, Galapagos, J&J, Lilly, MSD, Pfizer, and Takeda Pharma;* 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; *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; 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; FS (consultant or speaker's fees) Janssen, Takeda, Pfizer, MSD, Sandoz, Galapagos, Celltrion, Ferring, Abbvie, Lilly, Alfasigma, Abivax; 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; *XT (consultant or speaker's fees) Celltrion, AbbVie, Johnson & Johnson, Lilly, Takeda, Alpha Sigma, Dr. Falk, Abivax, Biogen, Fresenius Kabi, MSD, Pfizer, Tillotts, and Thabor Therapeutics; PSD (consultant) Abbvie, Abivax, Adiso, Alimentiv, Bristol Meyer Squibb, Celltrion, Genentech, Geneoscopy, Janssen, Pfizer, Takeda;* 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.

ABIVAX

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