P0923 - Early symptomatic improvement with obefazimod in patients with moderately to severely active ulcerative colitis: pooled results from the ABTECT-1 and ABTECT-2 Phase 3, double-blind, placebo-controlled induction trials

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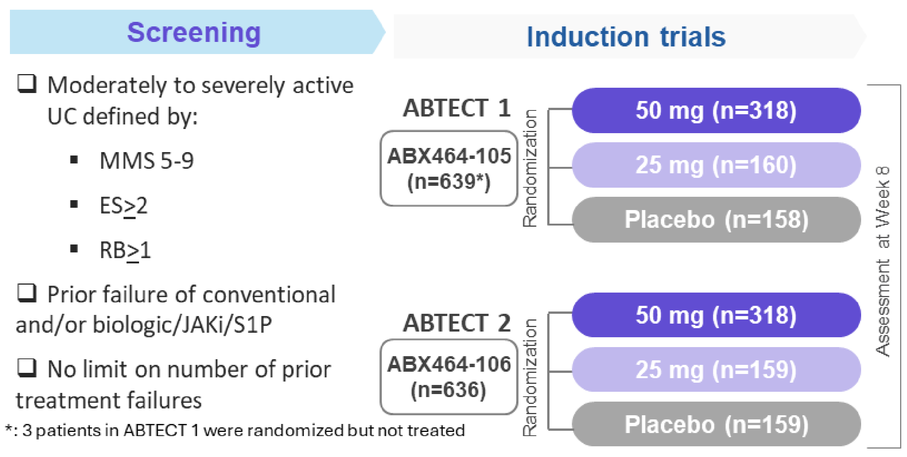
Background

- 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. .
- Here, we report the onset of symptomatic improvement with Obe in pts with UC enrolled in 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 (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

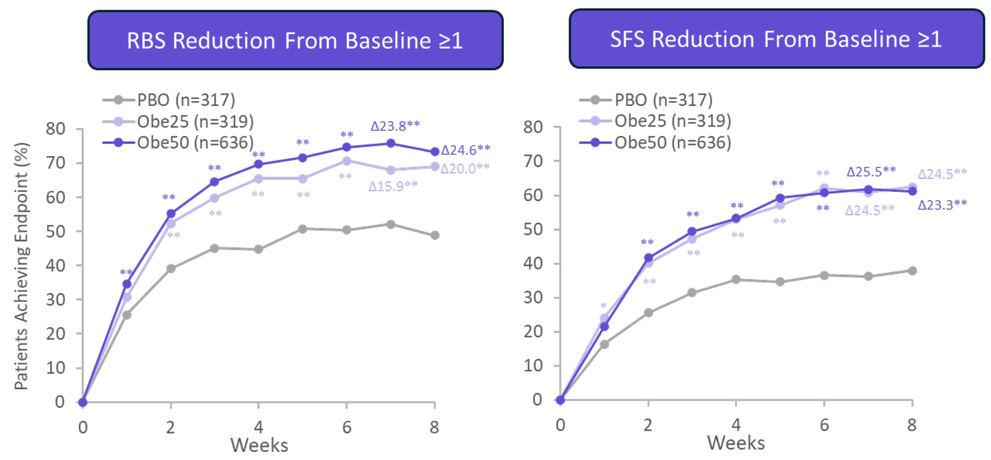


- This analysis assessed symptom improvement from W1 through W8, including change from baseline in stool frequency subscore (SFS) and RBS, and the proportion of pts achieving symptomatic response and remission.

Results

- 1272 pts were randomized and treated in ABTECT trials, with balanced baseline characteristics across treatment groups.
- In this pooled analysis, Obe-25 and Obe-50 produced reductions in RBS and SFS vs PBO, starting from W1, reaching a nominally significant difference relative to PBO by W2, with symptom improvements consistently increasing through W8.
- From W1, a greater proportion of pts receiving Obe achieved reductions in RBS of ≥ 1 point and SFS of ≥ 1 point from baseline vs PBO (Fig.2).
- Greater proportions of pts receiving Obe achieved RBS=0 from W2 at both doses, while achievement of SFS= 0 or 1 occurred by W2 for Obe-50 and by W4 for Obe-25 (Fig.3).
- Greater proportions of pts receiving Obe achieved symptomatic response from W1 and symptomatic remission from W2 increasing through W8 with no evidence of a plateau (Fig.4).

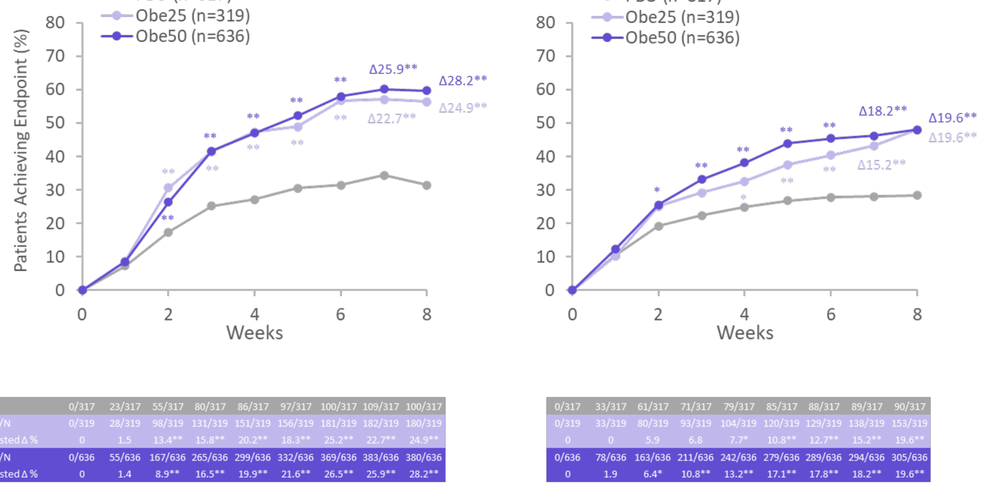
Fig. 2: RBS and SFS reduction from baseline ≥1 pooled ABTECT-1 and ABTECT-2 studies



PBO, n/N	0/317	81/317	124/317	143/317	142/317	161/317	160/317	165/317	155/317
Obe25, n/N	0/319	98/319	167/319	191/319	209/319	209/319	226/319	217/319	220/319
PBO adjusted Δ %	0	5.2	13.2**	14.8**	20.7**	14.7**	20.3**	15.9**	20.0**
Obe50, n/N	0/636	221/636	351/636	411/636	443/636	456/636	475/636	482/636	467/636
PBO adjusted Δ %	0	9.2**	16.1**	19.5**	24.9**	20.9**	24.3**	23.8**	24.6**

0/317	52/317	81/317	100/317	112/317	110/317	116/317	115/317	120/317
0/319	77/319	128/319	151/319	169/319	182/319	198/319	194/319	199/319
0	7.7*	14.6**	15.8**	17.6**	22.3**	25.4**	24.5**	24.5**
0/636	137/636	265/636	314/636	339/636	377/636	386/636	393/636	389/636
0	5.2	16.2**	17.9**	18.0**	24.6**	24.1**	25.5**	23.3**

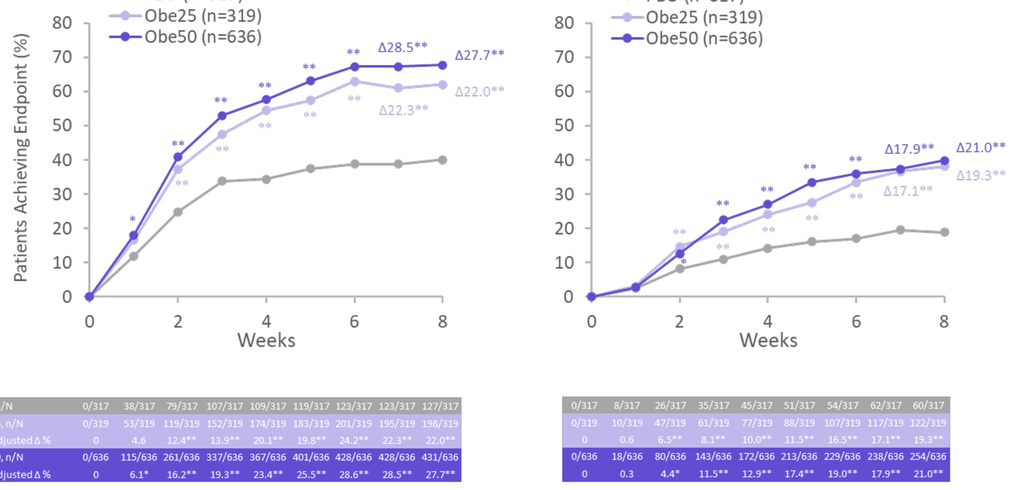
Fig. 3: Proportion of pts achieving RBS = 0, SFS = 0 or 1 pooled ABTECT-1 and ABTECT-2 studies



PBO, n/N	0/317	23/317	55/317	80/317	86/317	97/317	100/317	109/317	100/317
Obe25, n/N	0/319	28/319	98/319	131/319	151/319	156/319	181/319	182/319	180/319
PBO adjusted Δ %	0	1.5	13.4**	15.8**	20.2**	18.3**	25.2**	22.7**	24.9**
Obe50, n/N	0/636	55/636	167/636	265/636	299/636	332/636	369/636	383/636	380/636
PBO adjusted Δ %	0	1.4	8.9**	16.5**	19.9**	21.6**	26.5**	25.9**	28.2**

0/317	33/317	61/317	71/317	79/317	85/317	88/317	89/317	90/317
0/319	33/319	80/319	93/319	104/319	120/319	129/319	138/319	153/319
0	0	5.9	6.8	7.7*	10.8**	12.7**	15.2**	19.6**
0/636	78/636	163/636	211/636	242/636	279/636	289/636	294/636	305/636
0	1.9	6.4*	10.8**	13.2**	17.1**	17.8**	18.2**	19.6**

Fig. 4: Proportion of pts achieving symptomatic response, symptomatic remission - pooled ABTECT-1 and ABTECT-2 studies



PBO, n/N	0/317	38/317	79/317	107/317	109/317	119/317	123/317	123/317	127/317
Obe25, n/N	0/319	53/319	119/319	152/319	174/319	183/319	201/319	195/319	198/319
PBO adjusted Δ %	0	4.6	12.4**	13.9**	20.1**	19.8**	24.2**	22.3**	22.0**
Obe50, n/N	0/636	115/636	261/636	337/636	367/636	401/636	428/636	428/636	431/636
PBO adjusted Δ %	0	6.1*	16.2**	19.3**	23.4**	25.5**	28.6**	28.5**	27.7**

0/317	8/317	26/317	35/317	45/317	51/317	54/317	62/317	60/317
0/319	10/319	47/319	61/319	77/319	88/319	107/319	117/319	122/319
0	0.6	6.5**	8.1**	10.0**	11.5**	16.5**	17.1**	19.3**
0/636	18/636	80/636	143/636	172/636	213/636	229/636	238/636	254/636
0	0.3	4.4*	11.5**	12.9**	17.4**	19.0**	17.9**	21.0**

Statistical inferences are exploratory, and all P values are nominal and 2-sided. NRI is used for subjects with missing outcome and subjects reporting any IE; % 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. Symptomatic remission was an "other secondary" endpoint, not multiplicity controlled, for the FDA and health authorities other than the EMA. EMA, European Medicines Agency; FDA, Food and Drug Administration; 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 in pts with moderately to severely active UC, both Obe doses demonstrated rapid and clinically meaningful symptoms improvement versus PBO, evident as early as W1.

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 : *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; RA (consultant or speaker's fees) AbbVie, Abivax, AstraZeneca, Bristol-Myers Squibb, Celltrion Healthcare, Galapagos, J&J, Lilly, MSD, Pfizer, and Takeda Pharma; MS (consultant or speaker's fees) Gilead, Celltrion, Janssen, Abbvie, Ferring, Takeda, Pfizer, Eli Lilly, Dr. Falk Pharma,Celgene, MSD, Emerge Health, BMS, Alimentiv; SM (speaker's fees) Abivax; CLB (consultant or speaker's fees) Abbvie, Amgen, Celltrion, Ferring, Fresenius Kabi, Galapagos, Gielad, Janssen, Lilly, MSD, Nordic Pharma, Pfizer, Sandoz, Takeda; TH (consultant or speaker's fees) Pfizer, Abbvie, Takeda, Janssen Pharmaceuticals, Amgen; XT (consultant or speaker's fees) Abbvie, Celltrion, MSD, J&J, Takeda, Amgen, Alphasigma, Lilly, Thabor Therapeutics; 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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