Impact of baseline disease duration on the efficacy of once-daily oral obefazimod in moderately to severely active ulcerative colitis: week 8 results from the ABTECT-1 and ABTECT-2 Phase 3, double-blind, placebo-controlled induction trials

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Disclosure of Conflicts of Interest

Consulting and/or speaking fees from:

Geert D'Haens GDA (consultant or speaker's fees) Abbvie, Abivax, Agomab, Alimentiv, Anaptys Bio, AstraZeneca, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exeliom Biosciences, Galapagos, Glaxo Smith Kline, Dr Falk Pharma, Pfizer, J&J, Merck, Mirador, Polpharma, Procise Diagnostics, Prometheus Biosciences, Sorriso Pharma, Spyre, Takeda, Ventyx.

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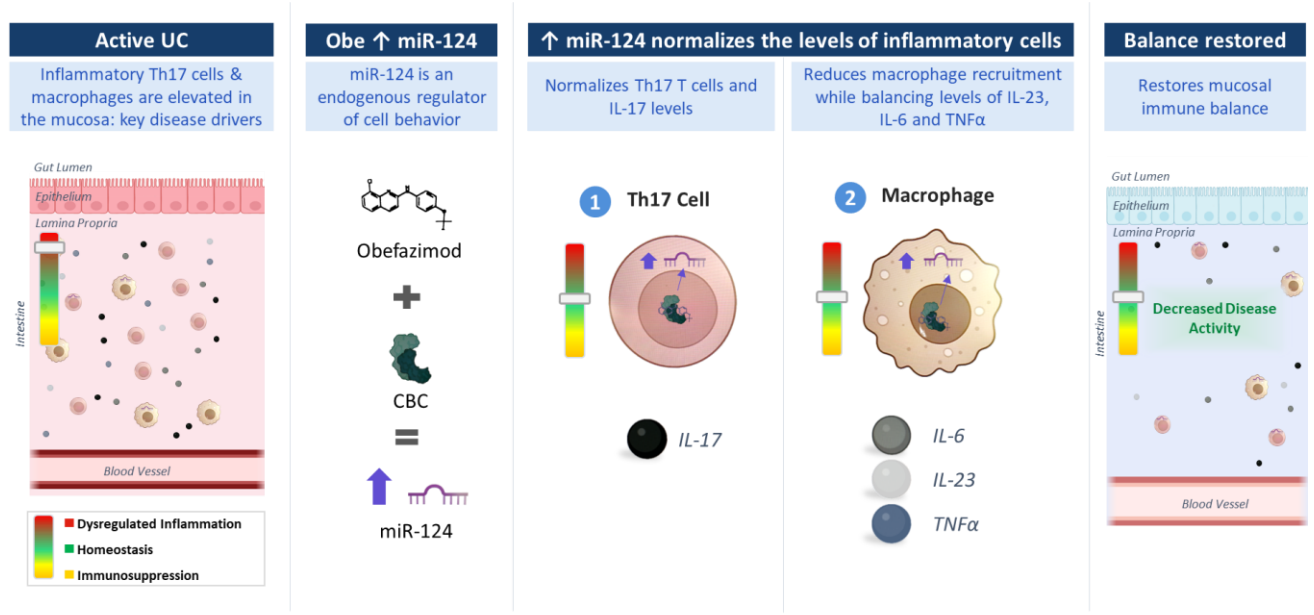
Obefazimod MOA

Obefazimod restores mucosal immune balance in ulcerative colitis (UC) through physiologic immunoregulation of Th17 cells and macrophages

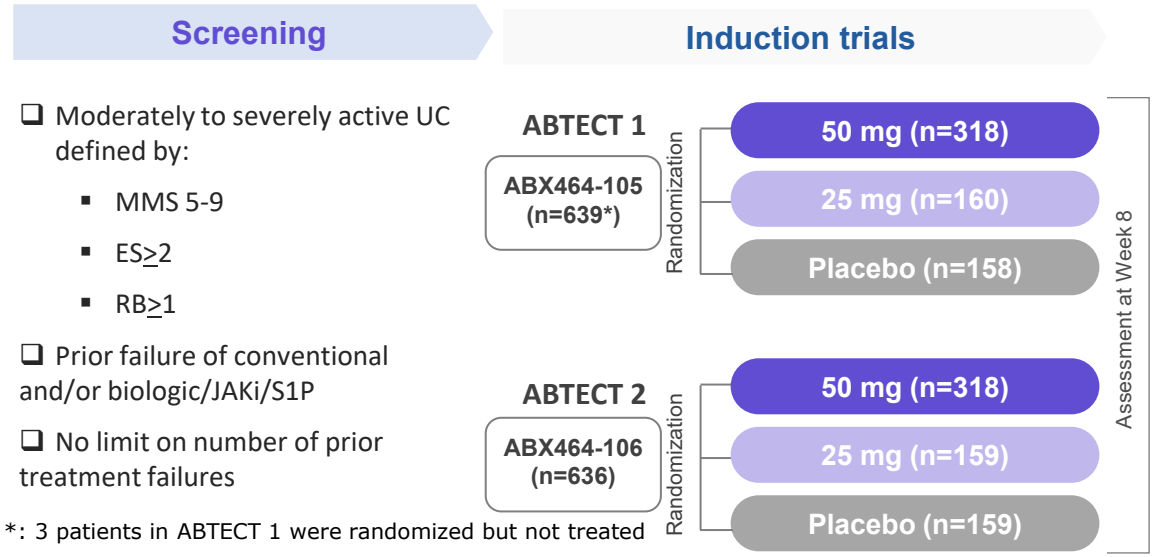


Apolit et al. Clin Transl Gastroenterol, 2023 | Vermeire et al., J Crohns Colitis, 2023 | Abivax Data on File | Images made with BioRender

Design of ABTECT induction trials

Patients (pts) stratified based on baseline disease duration (BDD) since UC diagnosis:

- <2 years (BDD<2)
- 2 to <10 years (BDD2-10)
- ≥10 years (BDD≥10)



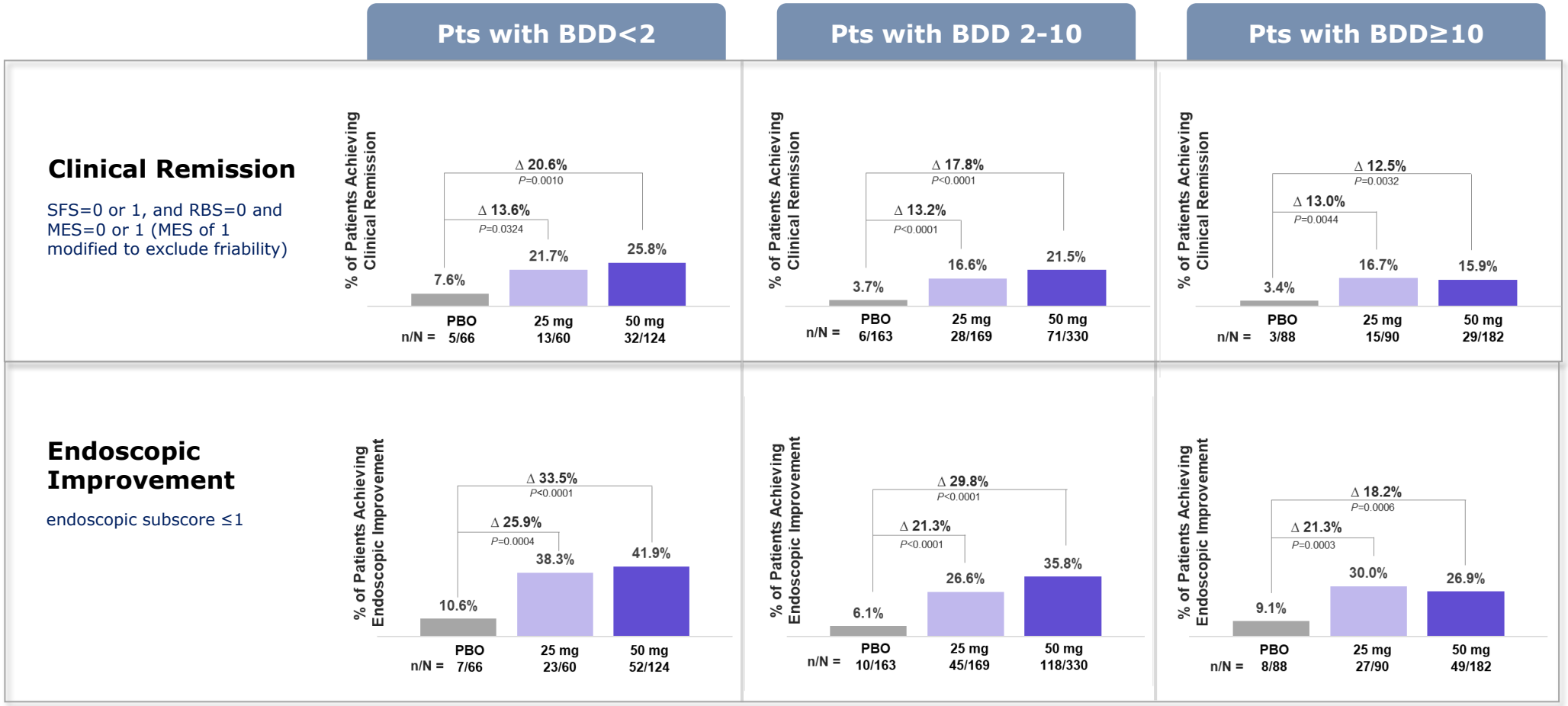
*: 3 patients in ABTECT 1 were randomized but not treated

Demographic and baseline characteristics

Baseline disease duration:		Pts with BDD<2 (N1=250)			Pts with BDD 2-10 (N1=662)			Pts with BDD≥10 (N1=360)		
		Obe-25 (N=60)	**Obe-50 (N=124)**	**PBO (N=66)**	**Obe-25 (N=169)**	**Obe-50 (N=330)**	**PBO (N=163)**	**Obe-25 (N=90)**	**Obe-50 (N=182)**	**PBO (N=88)**
Age (yr), mean (SD)		35.4 (12.5)	36.8 (14.6)	37.6 (14.1)	40.7 (12.7)	41.2 (14.0)	41.5 (14.1)	46.7 (12.5)	47.1 (11.9)	47.5 (12.6)
Baseline MMS, mean (SD)		6.7 (1.0)	6.8 (1.1)	6.7 (1.0)	7.0 (1.1)	6.9 (1.0)	7.0 (1.0)	6.8 (1.0)	6.9 (1.1)	6.8 (1.0)
Endoscopic subscore 3, n (%)		25 (41.7)	65 (52.4)	32 (48.5)	111 (65.7)	198 (60)	104 (63.8)	58 (64.4)	115 (63.2)	53 (60.2)
Fecal Calprotectin (mg/g), median		1836.650	1565.570	1610.480	1752.780	1718.870	1842.930	1768.630	1200.785	2215.080
Concomitant Corticosteroids, n (%)		26 (43.3)	65 (52.4)	23 (34.8)	63 (37.3)	127 (38.5)	68 (41.7)	31 (34.4)	70 (38.5)	35 (39.8)
ATIR-No, n (%)		44 (73.3)	93 (75)	48 (72.7)	84 (49.7)	161 (48.8)	85 (52.1)	45 (50)	74 (40.7)	36 (40.9)
ATIR-Yes, n (%)		16 (26.7)	31 (25)	18 (27.3)	85 (50.3)	169 (51.2)	78 (47.9)	45 (50)	108 (59.3)	52 (59.1)
Number of prior JAK-IR (% ATIR-Yes pts), n (%)		2 (12.5)	3 (9.7)	5 (27.8)	23 (27.1)	33 (19.5)	19 (24.4)	9 (20)	19 (17.6)	11 (21.2)
Number of prior AT-IR†, n (%)	0	44 (73.3)	93 (75)	48 (72.7)	84 (49.7)	161 (48.8)	85 (52.1)	45 (50)	74 (40.7)	36 (40.9)
	1	11 (18.3)	27 (21.8)	11 (16.7)	25 (14.8)	78 (23.6)	31 (19)	9 (10)	45 (24.7)	20 (22.7)
	2	4 (6.7)	2 (1.6)	3 (4.5)	25 (14.8)	30 (9.1)	19 (11.7)	16 (17.8)	32 (17.6)	12 (13.6)
	3	1 (1.7)	2 (1.6)	2 (3)	23 (13.6)	38 (11.5)	18 (11)	9 (10)	12 (6.6)	8 (9.1)
	4+	0	0	2 (3)	12 (7.1)	23 (7)	10 (6.1)	11 (12.2)	19 (10.4)	12 (13.6)

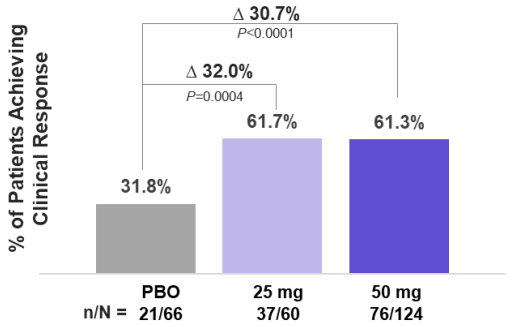
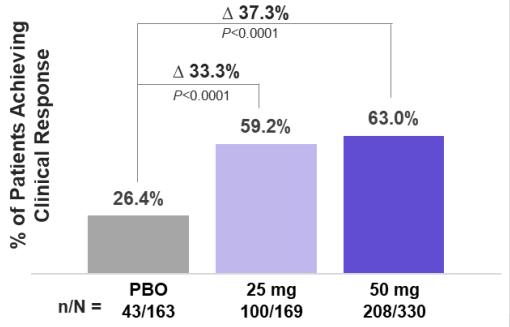
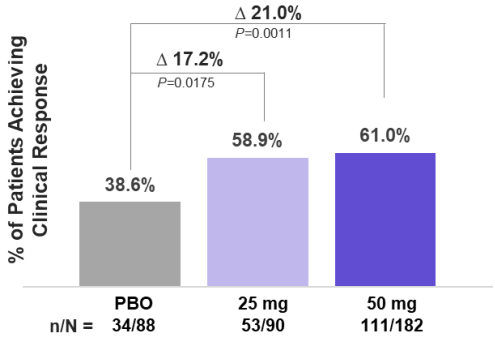
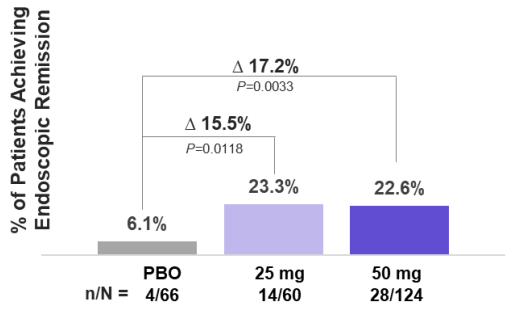
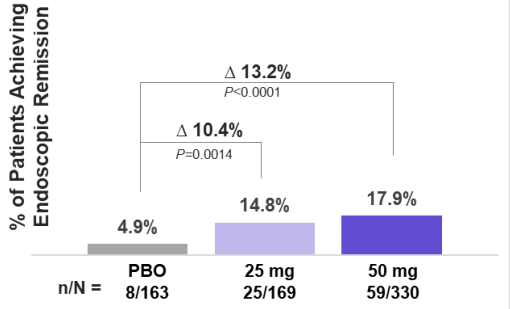
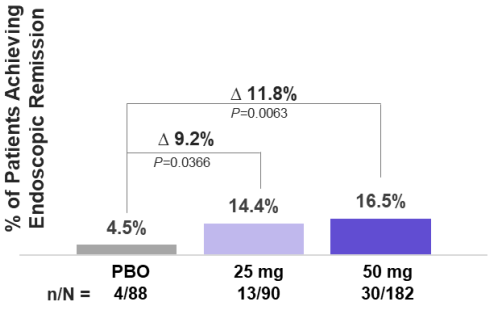
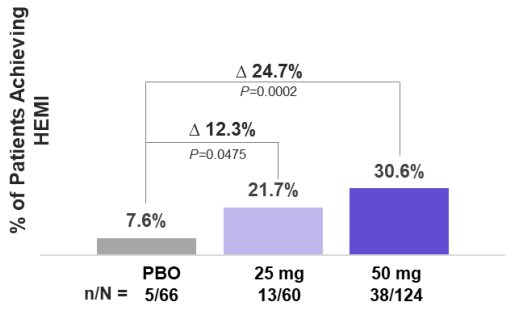
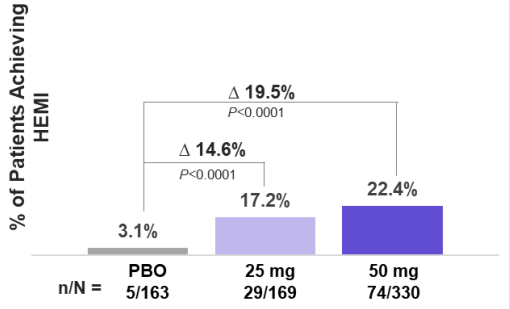
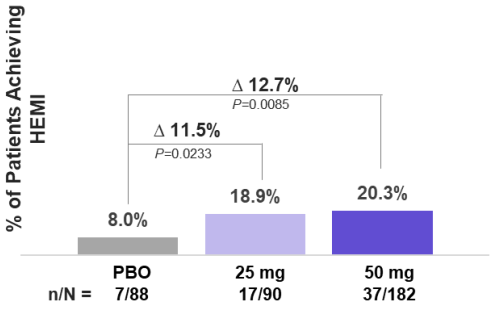
ATIR: inadequate response to advanced therapies; JAK: janus kinase; MMS: modified Mayo score; SD: standard deviation; %: n/N*100; N1 represents number of pts in each subgroup; †: ATIRs are counted by unique medication name (e.g. infliximab and adalimumab would be counted as 2 ATIRs)

Efficacy (1)



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).

Efficacy (2)

	Pts with BDD<2	Pts with BDD 2-10	Pts with BDD≥10
Clinical Response decrease from baseline in the MMS ≥2 points and ≥30% from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1			
Endoscopic Remission endoscopic subscore=0			
HEMI histo-endoscopic mucosal improvement is defined as MES=0 or 1 and Geboes Index score ≤3.1			

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Conclusions

- In the ABTECT induction trials of obefazimod for moderately to severely active UC, disease duration did not impact clinical, endoscopic, or histo-endoscopic improvements.
- Numerically higher remission rates were seen in pts with early disease.