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

Fernando Magro, Bruce E Sands, Silvio Danese, Marla Dubinsky, Fabio Cataldi, Doug Jacobstein, Christopher J Rabbat, Kevin Shan, Luciana Harlacher, Franco Scaldaferri, Geert D'Haens, Luc Biedermann, Laurent Peyrin-Biroulet

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SPEAKER DISCLOSURE

Fernando Magro

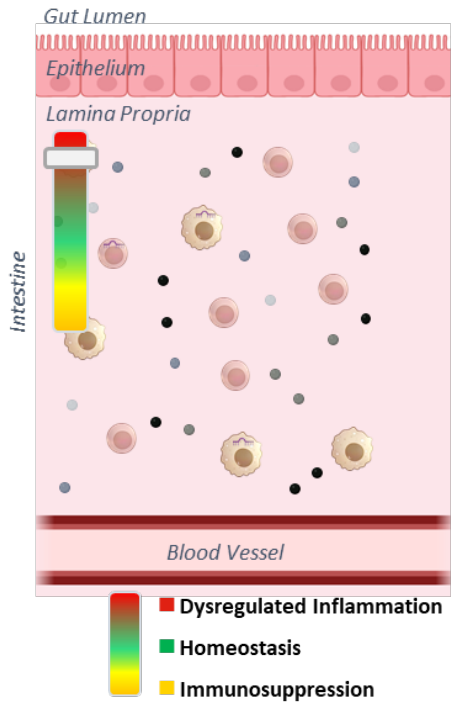
- *Grant support:*
  GEDII and National Science Foundation

- *Personal fees:*
  AbbVie, Amgen, Biogen, Celgene, Celltrion, Dr Falk Pharma, Ferring Pharmaceuticals, Hospira, Janssen, Laboratórios Vitória, MSD, Pfizer, Sandoz, Takeda, UCB, and Vifor

Obefazimod
Mechanism of action

Active UC

Inflammatory Th17 cells & macrophages are elevated in the mucosa: key disease drivers



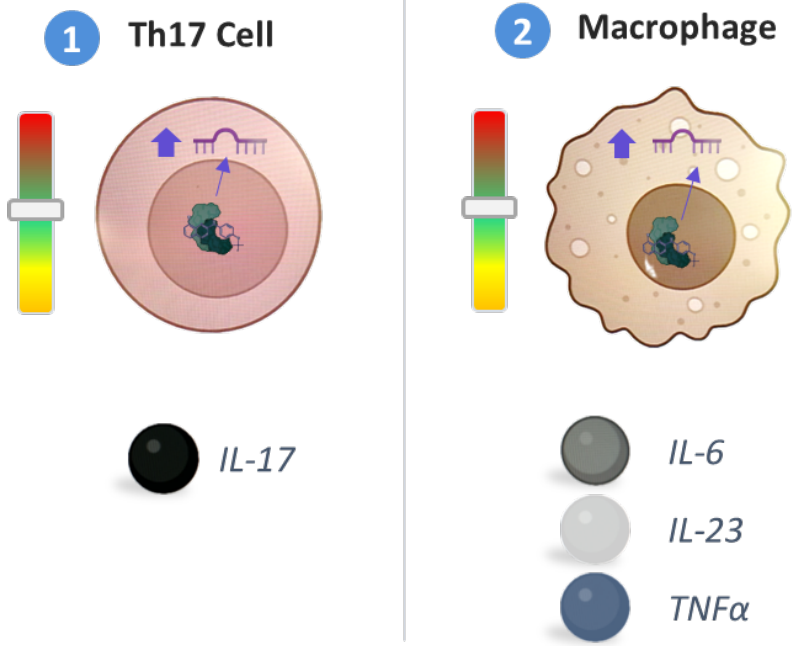
Obe ↑ miR-124

miR-124 is an endogenous regulator of cell behavior

↑ miR-124 normalizes the levels of inflammatory cells

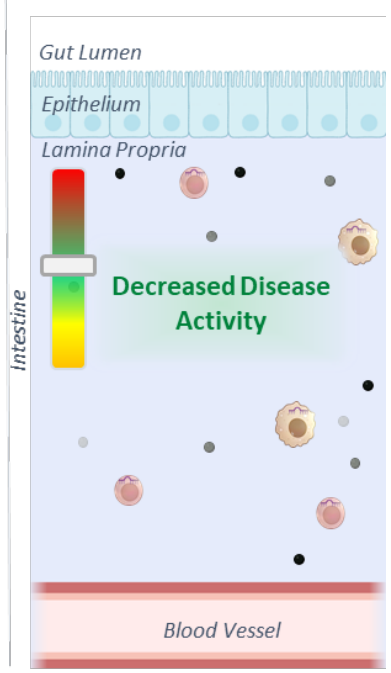
Normalizes Th17 T cells and IL-17 levels

Reduces macrophage recruitment while balancing levels of IL-23, IL-6 and TNFα



Balance restored

Restores mucosal immune balance



CBC: Cap Binding Complex - Apolit et al. Clin Transl Gastroenterol, 2023 | Vermeire et al., J Crohns Colitis, 2023 | Abivax Data on File | Images made with BioRender

Obefazimod restores mucosal immune balance in ulcerative colitis through regulation of Th17 cells and macrophages

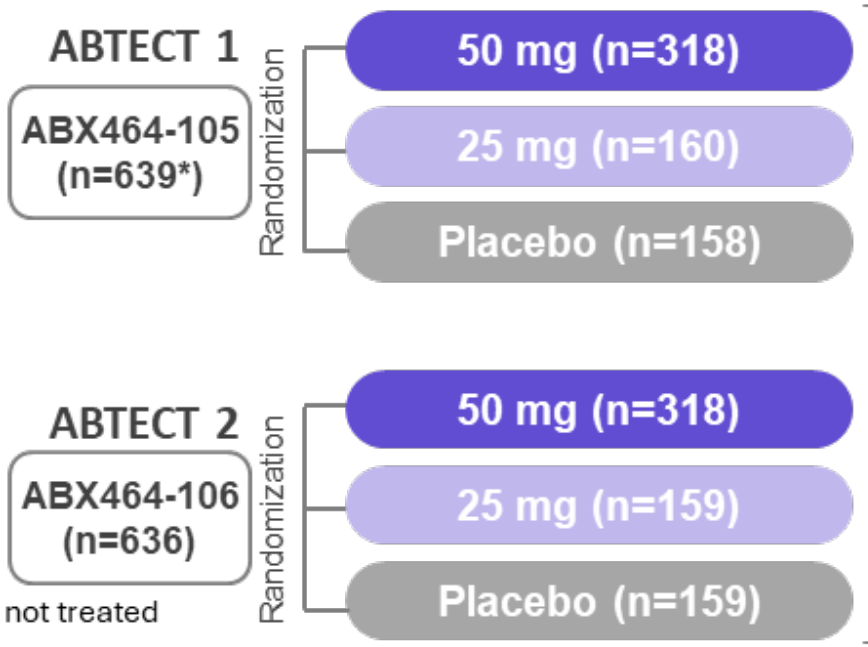
Design of ABTECT induction trials

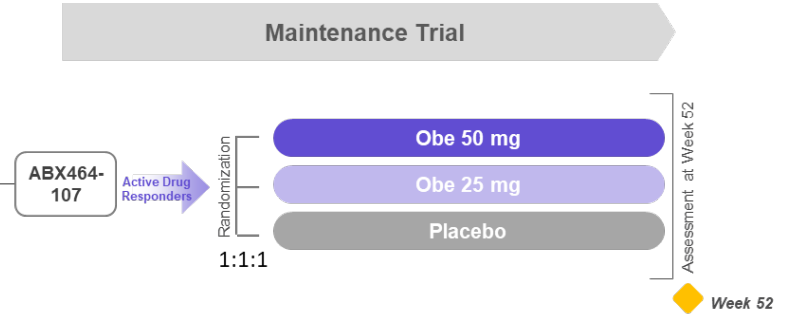
Screening

- ❑ Moderately to severely active UC defined by:
  - MMS 5-9
  - ES≥2
  - RB≥1
- ❑ Prior failure of conventional and/or biologic/JAKi/S1P
- ❑ No limit on number of prior treatment failures

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

Induction trials





Rectal or sigmoidal biopsies from the most affected segment were collected during endoscopy at screening and Week 8

Objective of the presentation

Here, we report the proportions of patients that met endoscopic, histologic and combined histologic-endoscopic outcomes at Week 8

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Baseline characteristics

	Pooled ABTECT 1 & 2			ABTECT 1 (105)			ABTECT 2 (106)		
	Placebo (N=317)	Obe 25 mg (N=319)	Obe 50 mg (N=636)	Placebo (N=158)	Obe 25 mg (N=160)	Obe 50 mg (N=318)	Placebo (N=159)	Obe 25 mg (N=159)	Obe 50 mg (N=318)
Age (years), mean (SD)	42.3 (14.1)	41.4 (13.2)	42.1 (14.0)	43.1 (13.6)	41.5 (13.5)	42.7 (14.3)	41.6 (14.7)	41.3 (12.8)	41.4 (13.6)
Baseline MMS, mean (SD)	6.9 (1.0)	6.9 (1.0)	6.9 (1.1)	6.9 (1.0)	6.8 (1.0)	6.9 (1.1)	6.8 (1.0)	7.0 (1.0)	6.9 (1.1)
Endoscopic subscore 3, n (%)	189 (59.6)	194 (60.8)	378 (59.4)	94 (59.5)	91 (56.9)	190 (59.7)	95 (59.7)	103 (64.8)	188 (59.1)
Extensive Colitis	130 (41.0)	131 (41.1)	236 (37.1)	59 (37.3)	63 (39.4)	110 (34.6)	71 (44.7)	68 (42.8)	126 (39.6)
Fecal Calprotectin (μg/g), median	1902	1762	1564	1969	1499	1581	1792	2041	1499
Concomitant Corticosteroids	126 (39.7)	120 (37.6)	262 (41.2)	61 (38.6)	61 (38.1)	132 (41.5)	65 (40.9)	59 (37.1)	130 (40.9)
AT-IR* Yes	148 (46.7)	146 (45.8)	308 (48.4)	69 (43.7)	70 (43.8)	149 (46.9)	79 (49.7)	76 (47.8)	159 (50.0)
Number of prior JAK-IR (% of AT-IR Yes Patients)	35 (23.6)	34 (23.3)	55 (17.9)	15 (21.7)	15 (21.4)	22 (14.8)	20 (25.3)	19 (25.0)	33 (20.8)
Number of prior AT-IR by medication name†, n (%)									
1	62 (19.6)	45 (14.1)	150 (23.6)	31 (19.6)	23 (14.4)	70 (22.0)	31 (19.5)	22 (13.8)	80 (25.2)
2	34 (10.7)	45 (14.1)	64 (10.1)	16 (10.1)	20 (12.5)	35 (11.0)	18 (11.3)	25 (15.7)	29 (9.1)
3	28 (8.8)	33 (10.3)	52 (8.2)	12 (7.6)	18 (11.3)	25 (7.9)	16 (10.1)	15 (9.4)	27 (8.5)
4+	24 (7.6)	23 (7.2)	42 (6.6)	10 (6.3)	9 (5.6)	19 (6.0)	14 (8.8)	14 (8.8)	23 (7.2)

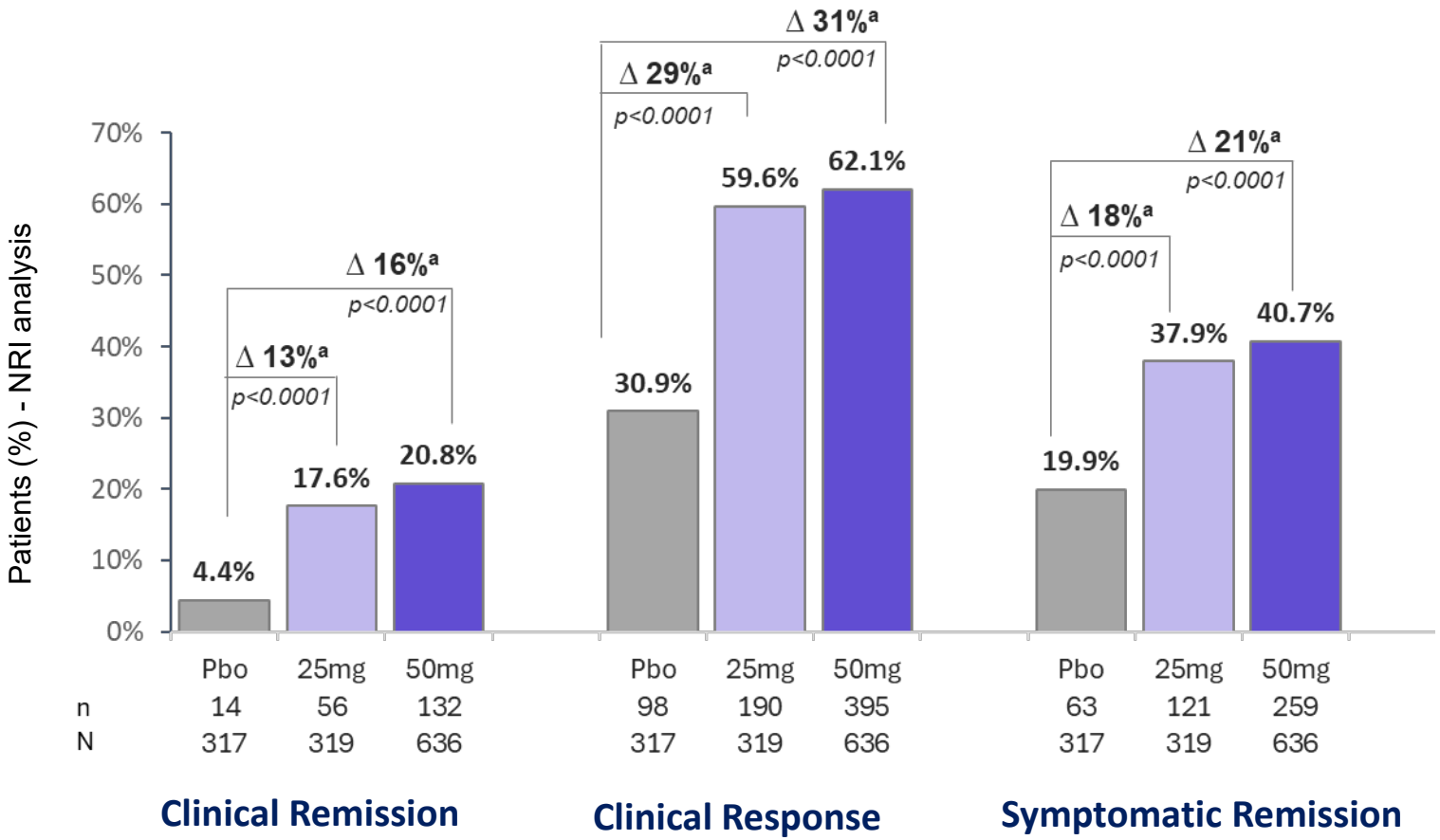
*: Inadequate Response to Advanced Therapies
†: Medication name results in each individual advanced therapy being counted as a unique medication; e.g. infliximab + adalimumab would be counted as 2

Baseline characteristics were generally well balanced in ABTECT trials, with a slightly more severe and refractory population in the 25mg group in ABTECT 2 vs. ABTECT 1

Pooled ABTECT 1 & 2

Clinical and symptomatic endpoints at Week 8

Primary Endpoint | **Key Secondary Endpoints**

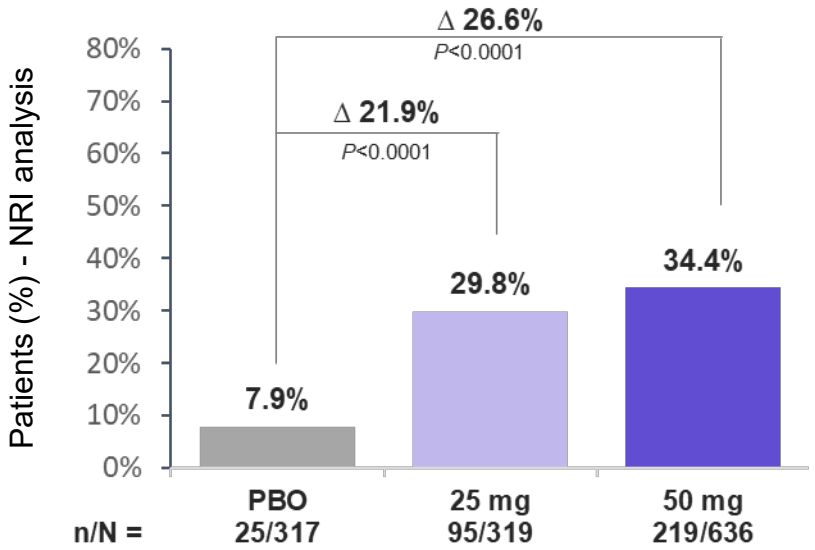


Both doses of obefazimod achieved clinically meaningful significant* improvements across clinical and symptomatic endpoints

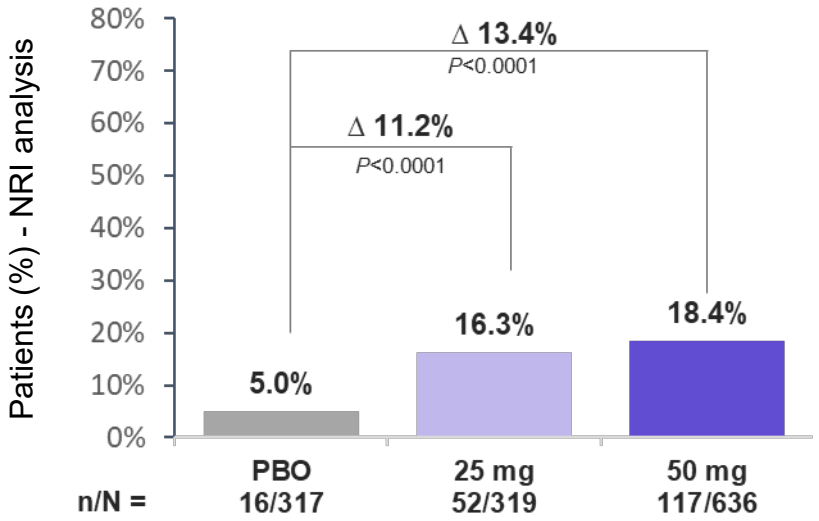
*: All p-values are nominal
[a] % Difference is for obefazimod minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), Baseline oral corticosteroids usage (yes/no). P-values are two sided. NRI is used for subjects with missing outcome at Week 8 and subjects reporting any IE prior to Week 8. Clinical remission is defined as SFS = 0 or 1, and RBS = 0 and MES = 0 or 1 (MES of 1 modified to exclude friability. Clinical response is defined as a reduction from Baseline in MMS >= 2 points and a relative reduction from Baseline in MMS >= 30%, and a reduction from Baseline in RBS >= 1 point and/or RBS = 0 or 1. Symptomatic remission is defined as RBS=0 and SFS= 0 or 1

Pooled ABTECT 1 & 2
Endoscopic endpoints at Week 8

Endoscopic improvement



Endoscopic remission



The pooled analysis showed significantly* higher proportions of patients treated with obefazimod 25 mg or 50 mg *versus* placebo achieving endoscopic endpoints

* All p-values are nominal

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. IE, intercurrent event; MES, Mayo Endoscopic Subscore; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo.

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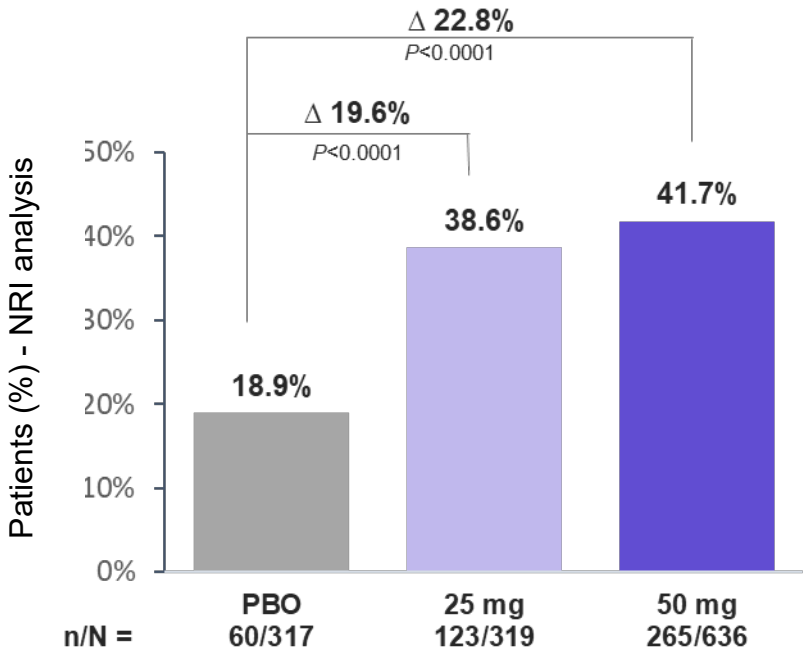
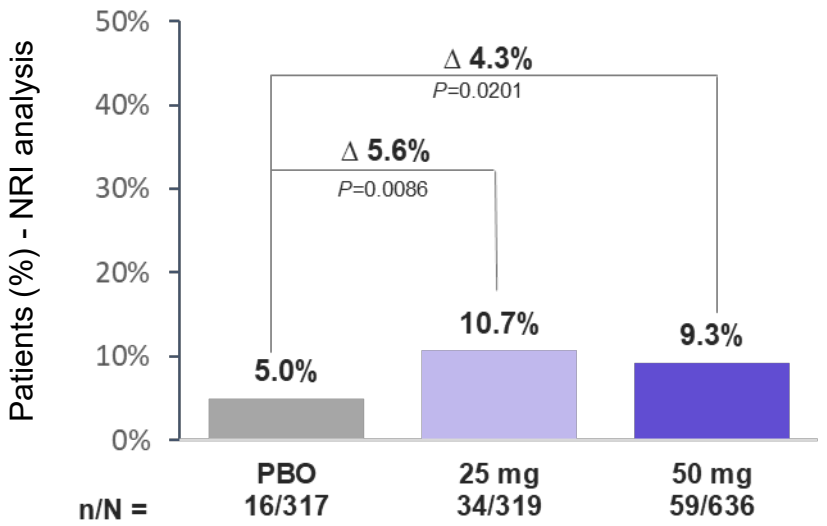
Pooled ABTECT 1 & 2
Histologic endpoints at Week 8

Histologic improvement
(Geboes histologic score ≤3.1)



Histologic remission
(Geboes histologic score <2A.0)



The pooled analysis showed significantly* higher proportions of pts receiving either obefazimod 25 mg or 50 mg *versus* placebo achieving histologic endpoints

*: All p-values are nominal; 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. 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 <2A.0). IE, intercurrent event; MES, Mayo Endoscopic Subscore; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo.

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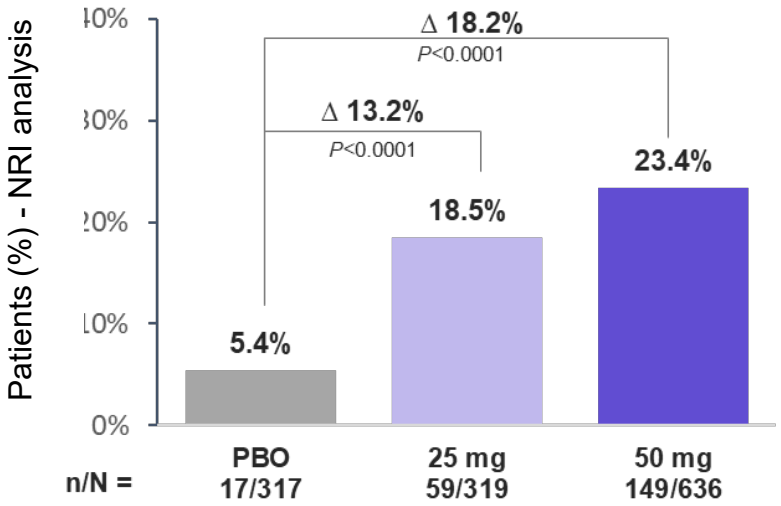
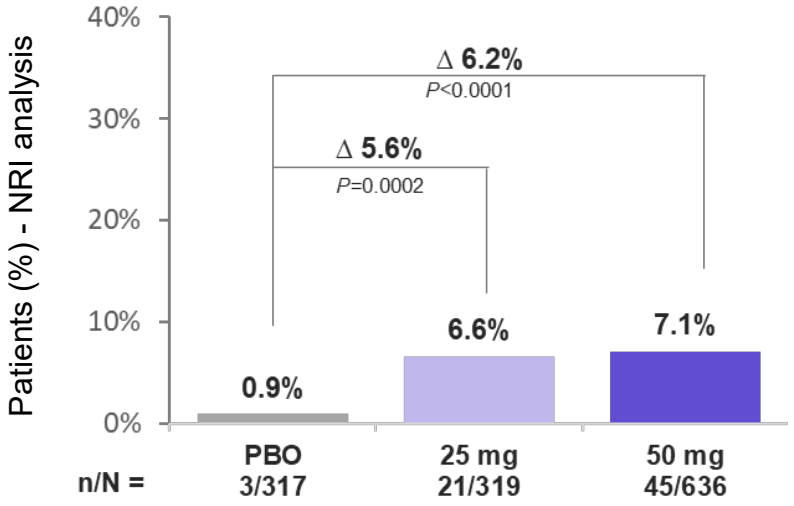
Pooled ABTECT 1 & 2
Combined histologic-endoscopic outcomes at Week 8

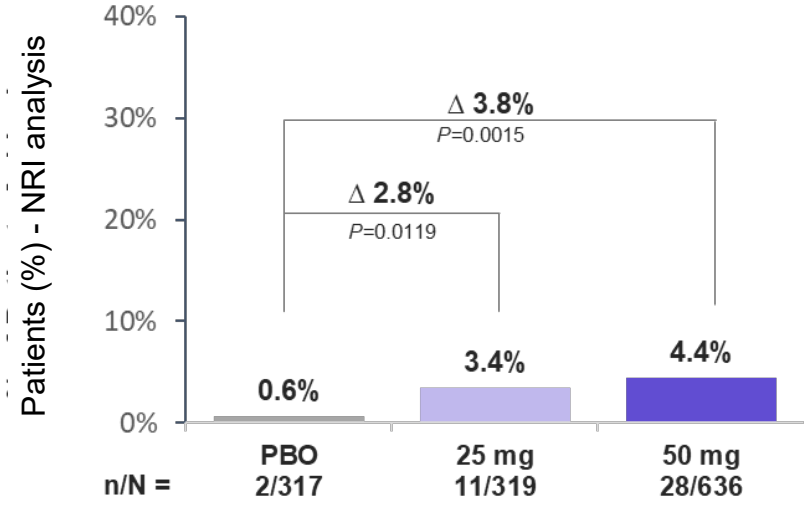
HEMI
(Endoscopic subscore ≤1 + Geboes score ≤3.1)



EIHR
(Endoscopic subscore ≤1 + Geboes score <2A.0)



HEMR
(Endoscopic subscore =0 + Geboes score <2A.0)



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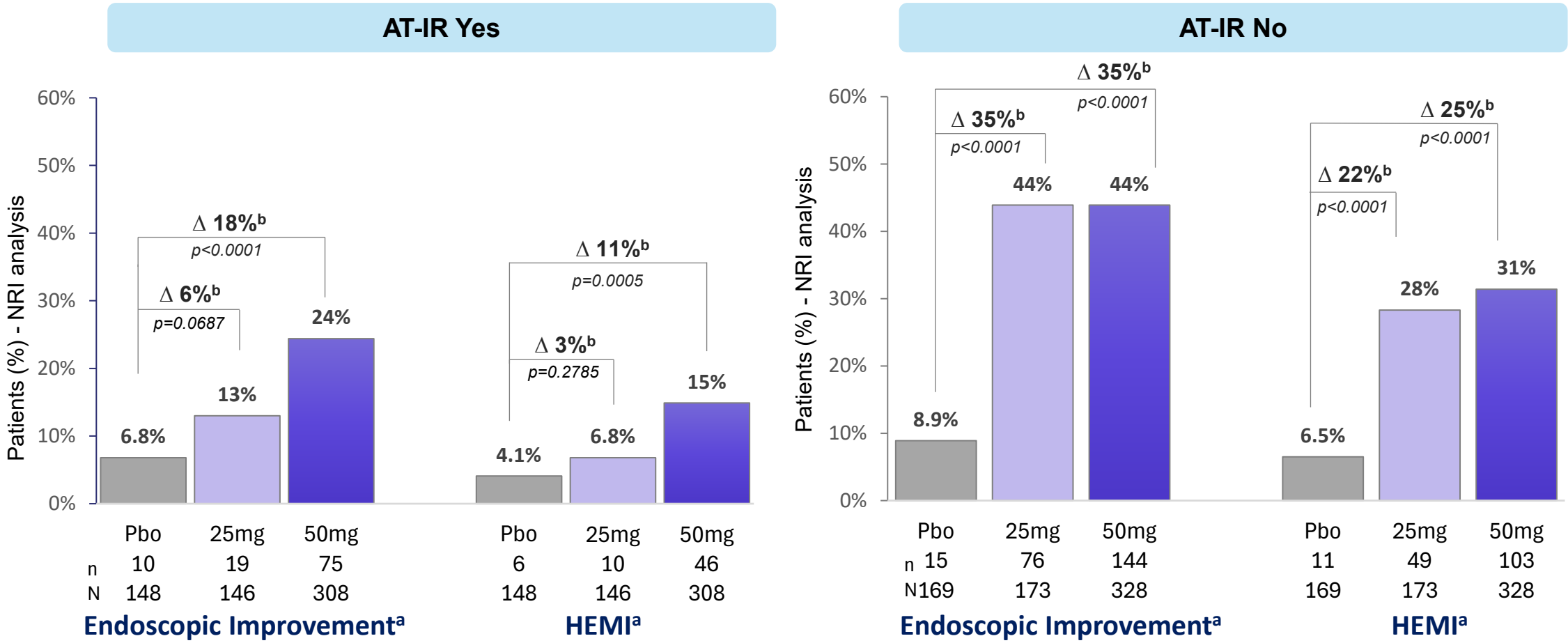
Pooled ABTECT 1 & 2

Obefazimod 50 mg improved endoscopic & histologic outcomes in both AT-IR subgroups, with stronger effects in AT-IR No patients at Week 8



AT-IR: inadequate response to advanced therapies

All p-values are nominal; [a] Endoscopic improvement is defined as MES = 0 or 1 (MES of 1 modified to exclude friability). HEMI is defined as MES = 0 or 1 and Geboes Index score ≤3.1; [b] % Difference is for obefazimod 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). P-values are two sided. NRI is used for subjects with missing outcome at Week 8 and subjects reporting any IE prior to Week 8.

Conclusions

In the ABTECT induction trials, obefazimod treatment led to clinically meaningful improvements in endoscopic, histologic, and combined histologic-endoscopic endpoints at week 8

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Thank you

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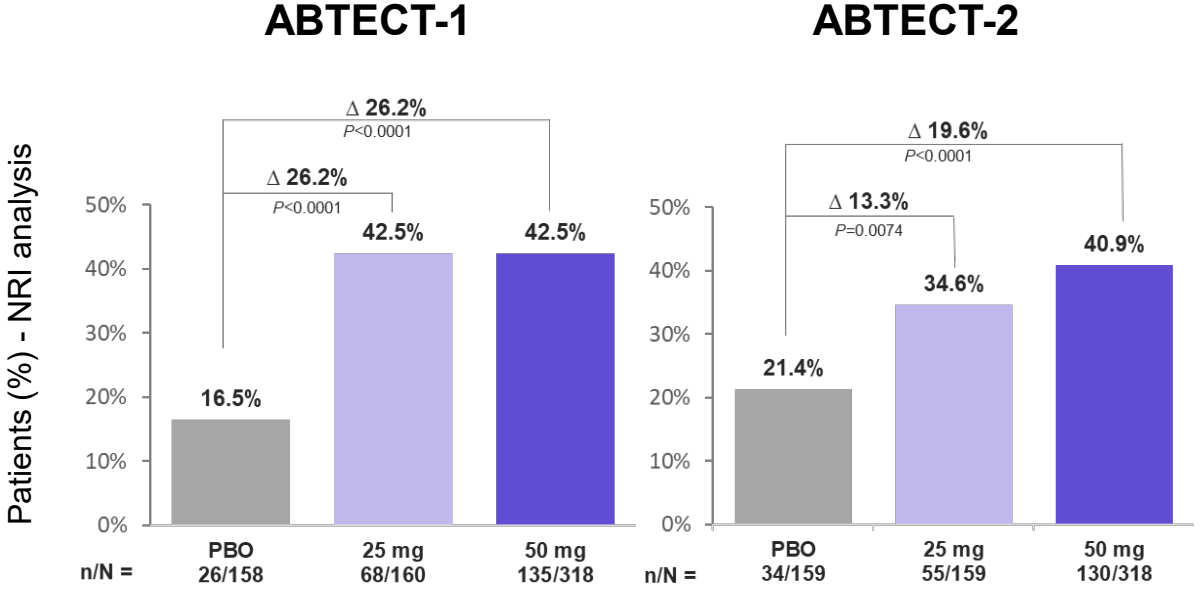
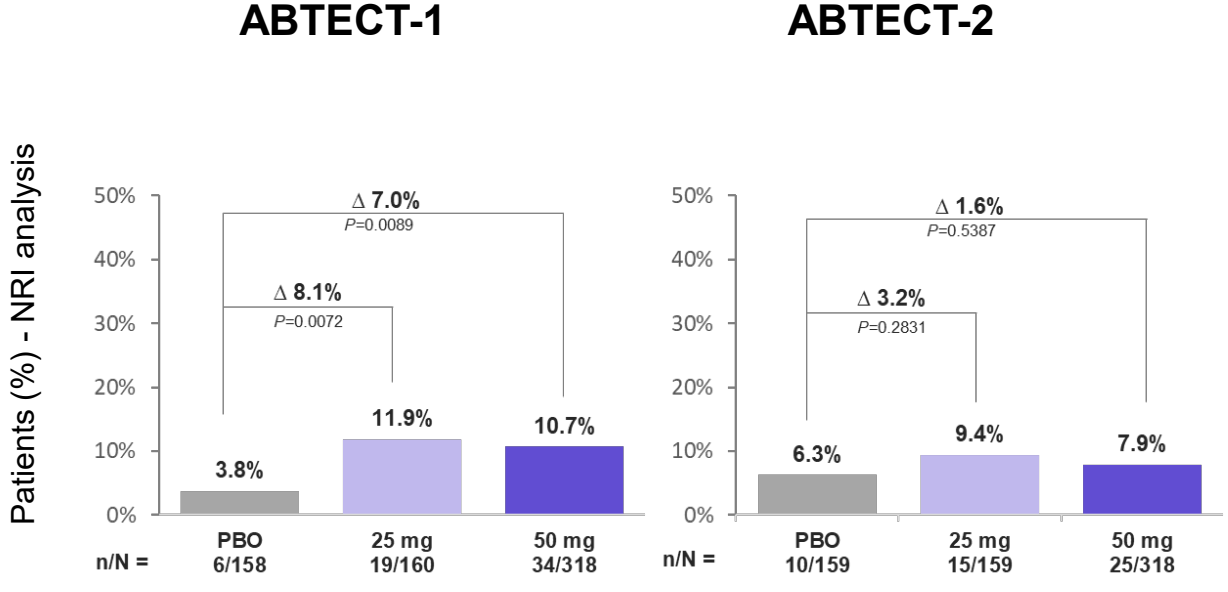
BACK-UP SLIDES

ABTECT 1 & 2
Histologic endpoints

Histologic improvement
(Geboes histologic score ≤3.1)



Histologic remission
(Geboes histologic score <2A.0)



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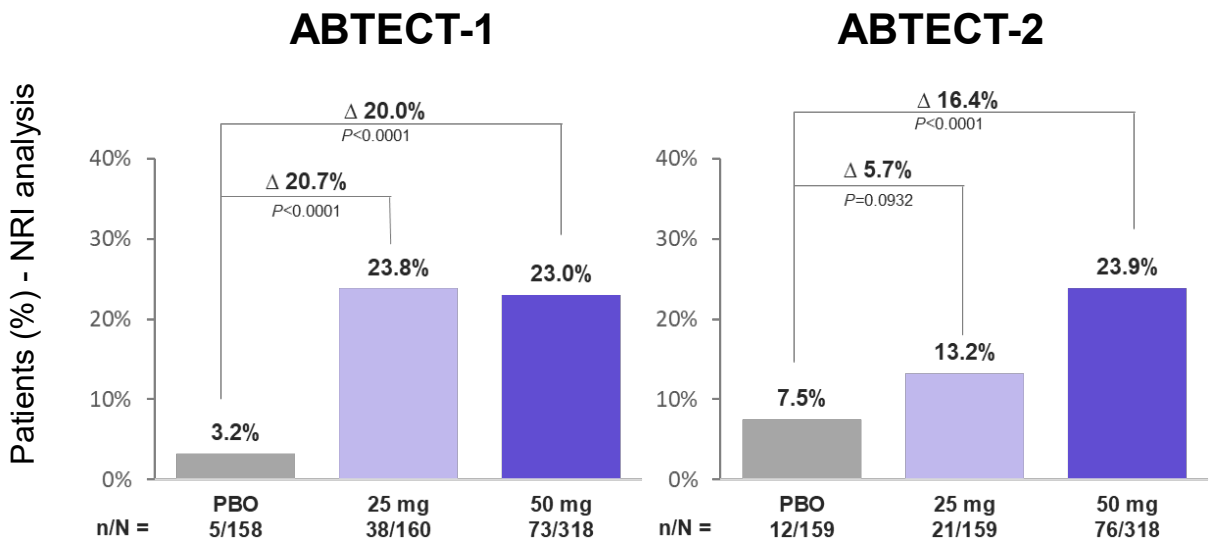
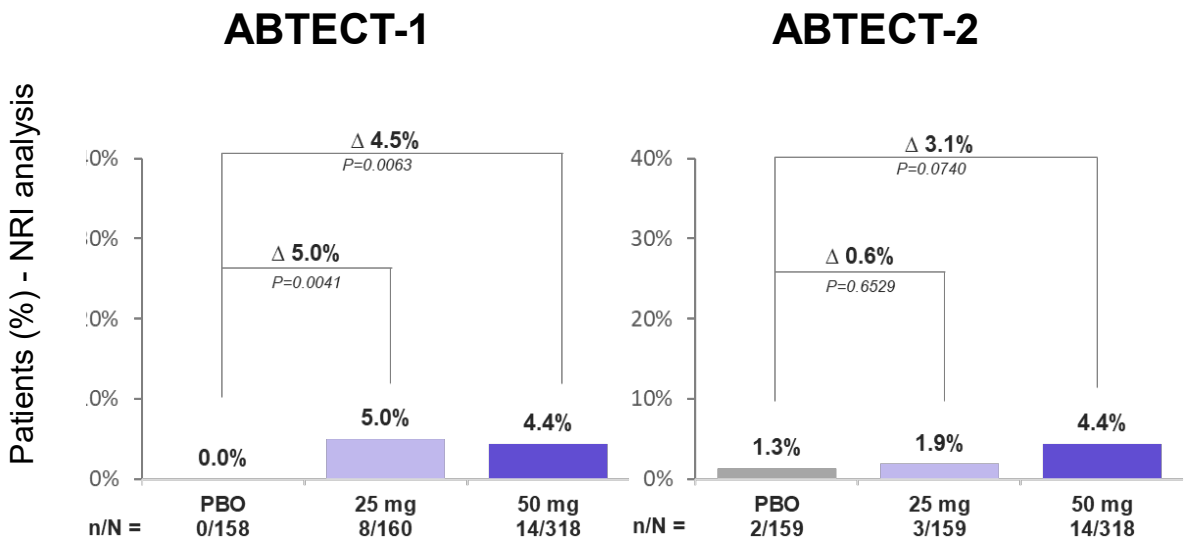
ABTECT 1 & 2
Combined histologic-endoscopic outcomes

HEMI
(Endoscopic subscore ≤1 + Geboes score ≤3.1)



HEMR
(Endoscopic subscore =0 + Geboes score <2A.0)



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