

Efficacy of obefazimod in Phase 3 ABTECT-Maintenance trial:

Results of 44-week therapy in subsets of patients
with and without prior inadequate response to
advanced therapies

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Disclosure of Conflicts of Interest

I herewith declare the following paid or unpaid consultancies, business interests, or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

SD served as consultant or received speaker's fees from AbbVie, Abivax, Ferring, Hospira, Johnson & Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, and Boehringer Ingelheim.

Obefazimod is Designed to Restore Intestinal Immune Balance in Ulcerative Colitis Through Physiologic Immunoregulation



Obefazimod MOA

- Obefazimod is an oral, once-daily, small molecule that increases expression of endogenous miR-124
- This helps restore immune balance while maintaining immune surveillance functions



Clinical Evidence

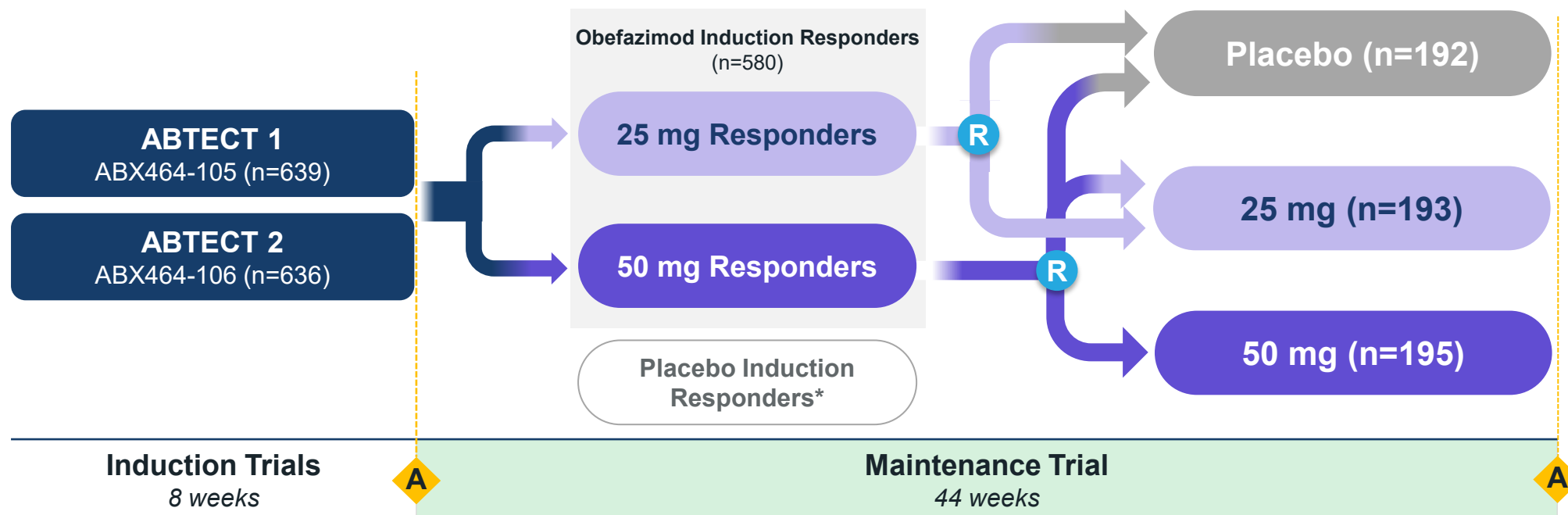
- Phase 2 studies demonstrated clinical activity, with sustained efficacy observed during long-term open-label treatment
- The Phase 3 ABTECT program demonstrated induction efficacy through 8 weeks

Objective

Assess obefazimod efficacy and safety vs. placebo in UC patients who responded to obefazimod induction $\pm$ prior inadequate response to advanced therapies (AT-IR) at Week 52

ABTECT Maintenance: Safety and Efficacy in Obefazimod Induction Responders

ABTECT Phase 3 Responder Re-Randomized Maintenance Trial Design



Primary Endpoint Clinical Remission at Week 52

Defined as SFS = 0 or 1 and RBS = 0, and MES = 0 or 1
(MES of 1 modified to exclude friability)

Secondary Endpoints (Week 52)

- CS-free Clinical Remission
- Sustained Clinical Remission
- Endoscopic Improvement
- Endoscopic Remission
- HEMI Per Geboes

R Randomized
A Assessment

ABTECT Maintenance: Safety and Efficacy in Obefazimod Induction Responders

ABTECT Phase 3 Responder Re-Randomized Maintenance Trial Design



Here we present efficacy endpoints at Week 52 (44 weeks in maintenance trial) for patients with and without prior advanced therapy inadequate response (AT-IR)

AT-IR defined as: inadequate response, loss of response or intolerance to advanced therapies including biologics, JAKs, S1Ps with no upper limit

Primary

Defined as SFS = 0 or 1 and RBS = 0, and MES = 0 or 1
(MES of 1 modified to exclude friability)

- Proportion of Patients Achieving Clinical Response Per MMS
- Proportion of Patients with HEMI Per Geboes

R Randomized
A Assessment

Baseline Characteristics and Maintenance Trial Completion Rate

	Placebo	Obefazimod 25 mg	Obefazimod 50 mg
Patient Characteristics			
Study Participants	192	193	195
Age (Years), Mean (SD)	41.3 (13.4)	43.0 (13.7)	42.3 (14.4)
Induction Baseline			
Baseline Induction MMS, Mean (SD)	6.9 (1.1)	6.7 (1.1)	6.9 (1.2)
Duration of Disease (Years), Mean (SD)	8.1 (7.6)	8.1 (7.4)	7.8 (6.9)
Baseline Induction Fecal Calprotectin (mg/g), Median	1,202	1,585	1,568
Prior and Concomitant UC Therapy			
Prior Advanced Therapy Failure (%)	37.5%	39.4%	46.2%
Corticosteroid Use at Maintenance Baseline (%)	35.9%	41.5%	40.5%
Maintenance Trial Completion Rate			
44-Week Completion Rate*	66 (34.3%)	152 (78.8%)	160 (82.1%)

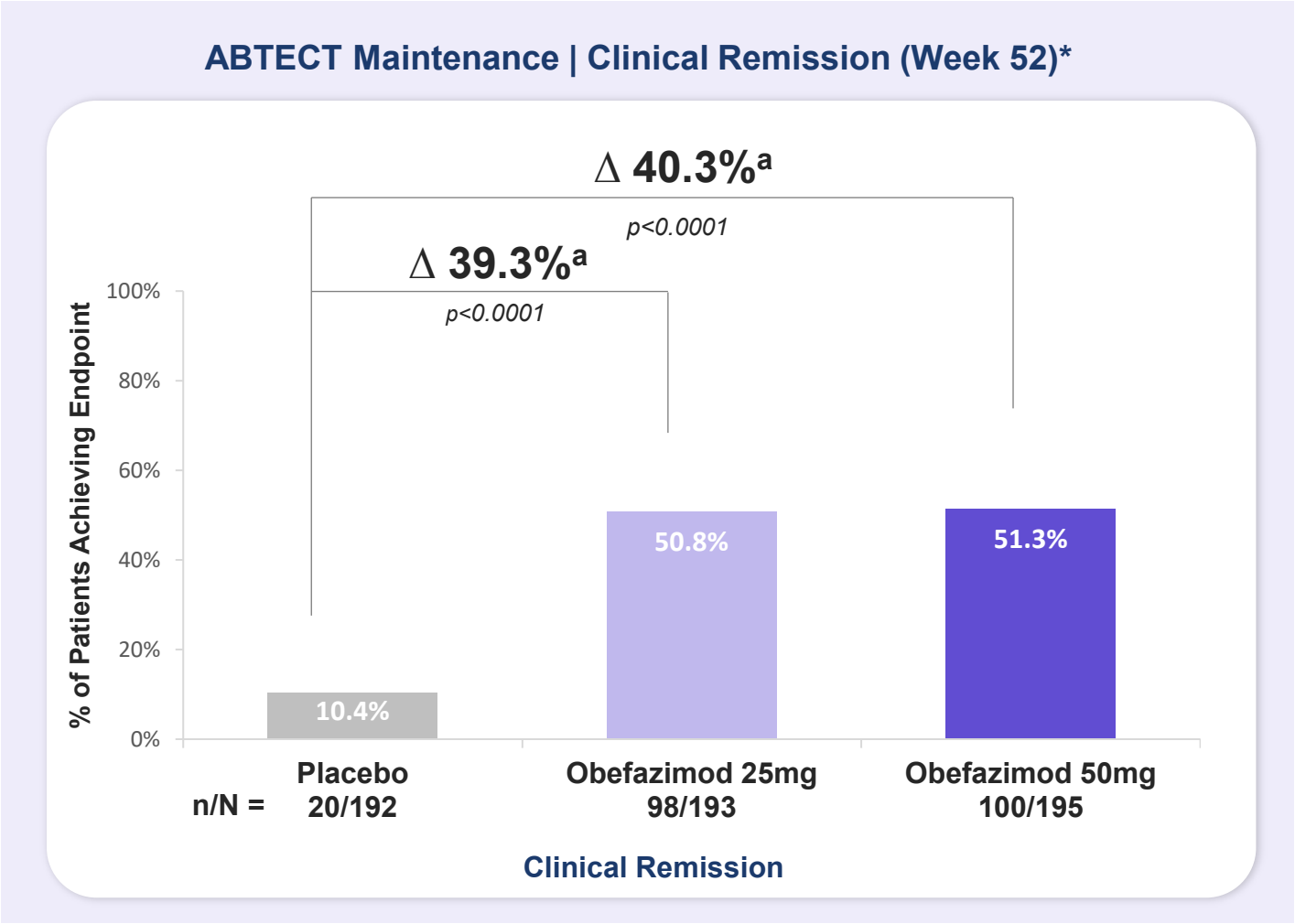
50 mg cohort had a higher percentage of patients with prior advanced therapy failure relative to patients on 25 mg and placebo

Data on File ABX464-107

* Completion without relapse or treatment switch

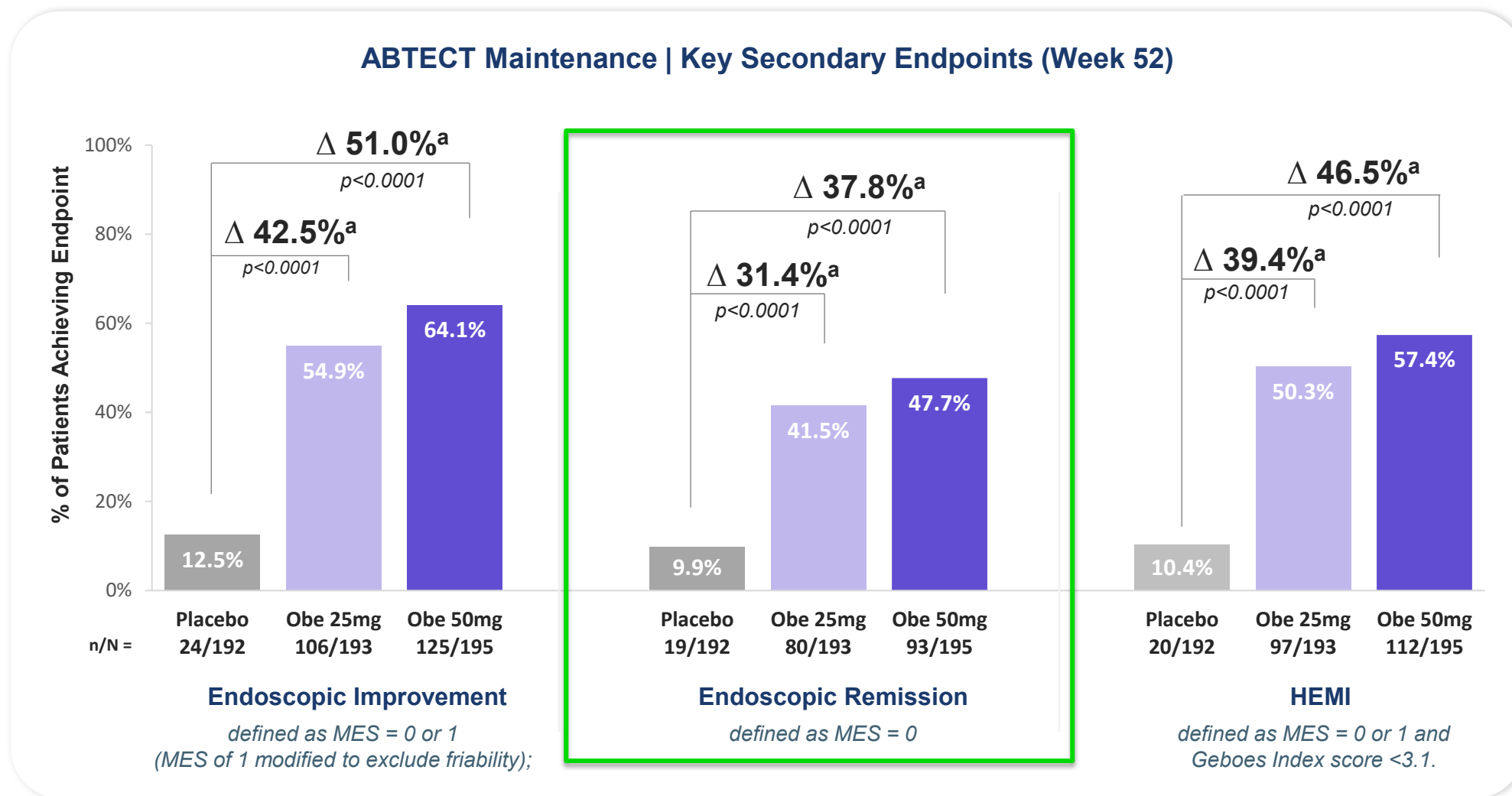
MMS, Modified Mayo Score; SD, standard deviation

Both Obefazimod Doses Met the Primary Endpoint of Clinical Remission at Week 52



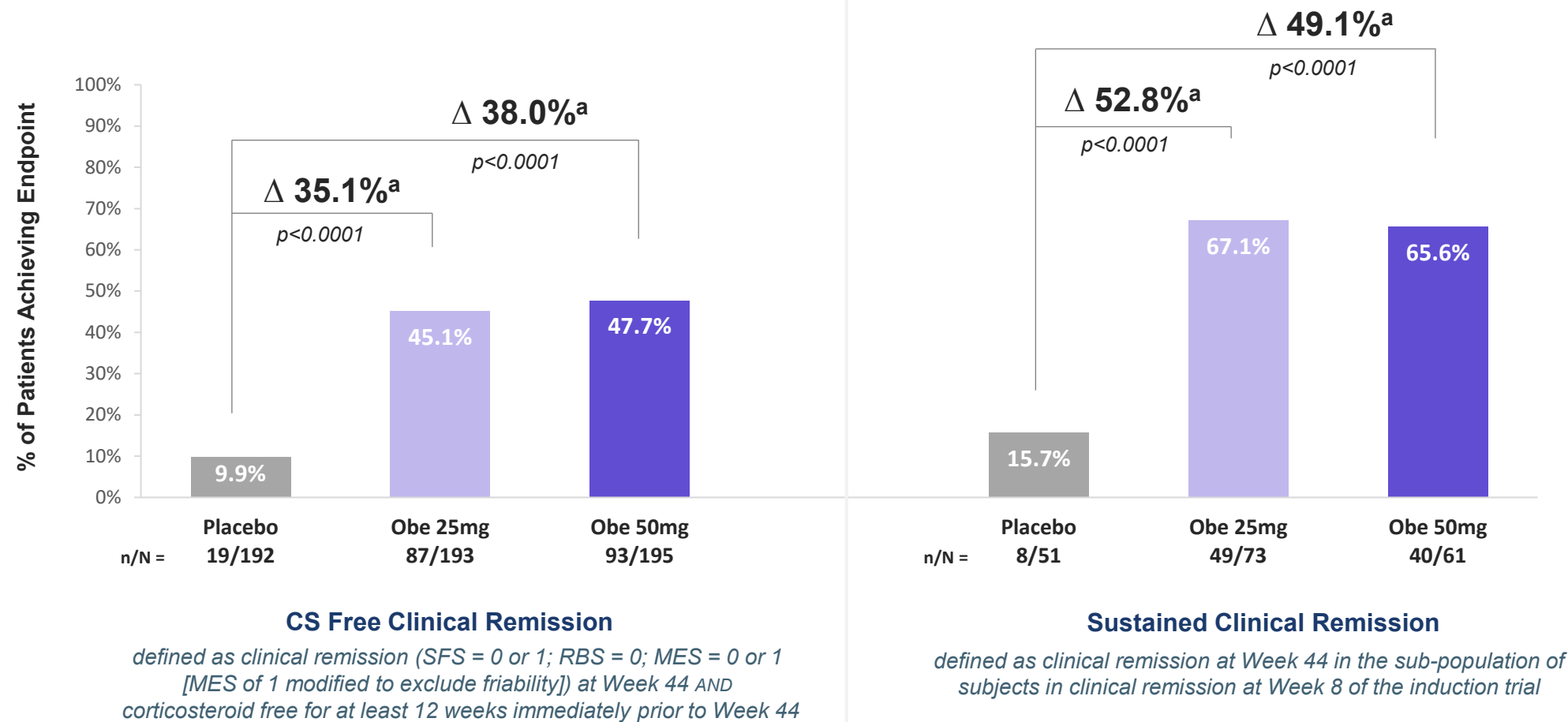
* Week 52 includes the 8-week induction treatment with obefazimod
[a] % Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: clinical remission at maintenance baseline (yes/no), induction treatment (25 mg/50 mg), and maintenance baseline oral corticosteroids usage (yes/no)
Clinical remission is defined as SFS = 0 or 1, and RBS = 0 and MES = 0 or 1 (MES of 1 modified to exclude friability)
Data on File ABX464-107

Both Obefazimod Doses Met All Key Secondary Endpoints at Week 52



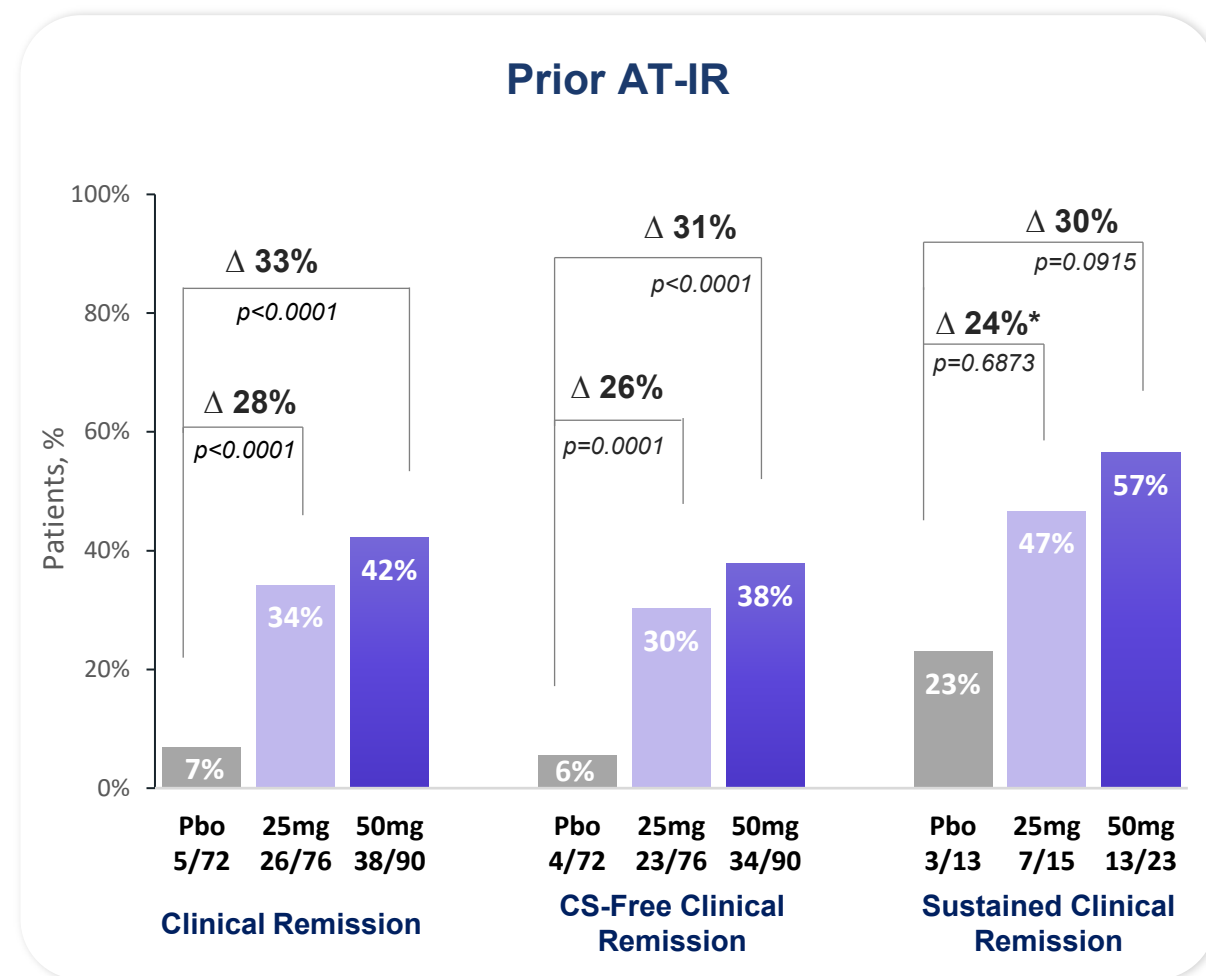
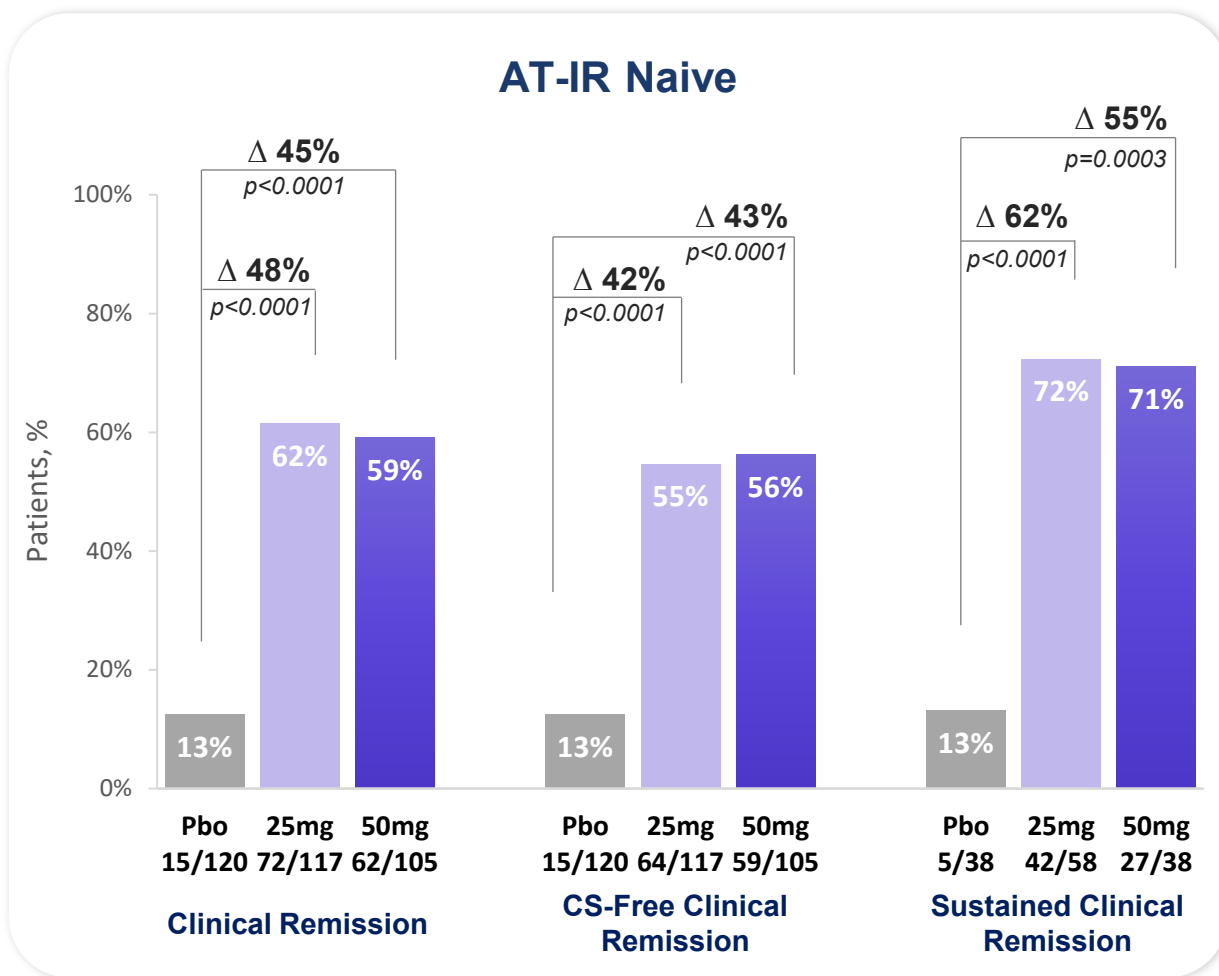
Both Obefazimod Doses Met All Key Secondary Endpoints at Week 52

ABTECT Maintenance | Key Secondary Endpoints (Week 52)



[a] % Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: clinical remission at maintenance baseline (yes/no), induction treatment (25 mg/50 mg), and maintenance baseline oral corticosteroids usage (yes/no) | CS Free = corticosteroid free
Data on File ABX464-107

Clinical Endpoints by Prior Advanced Therapy Inadequate Response (AT-IR)



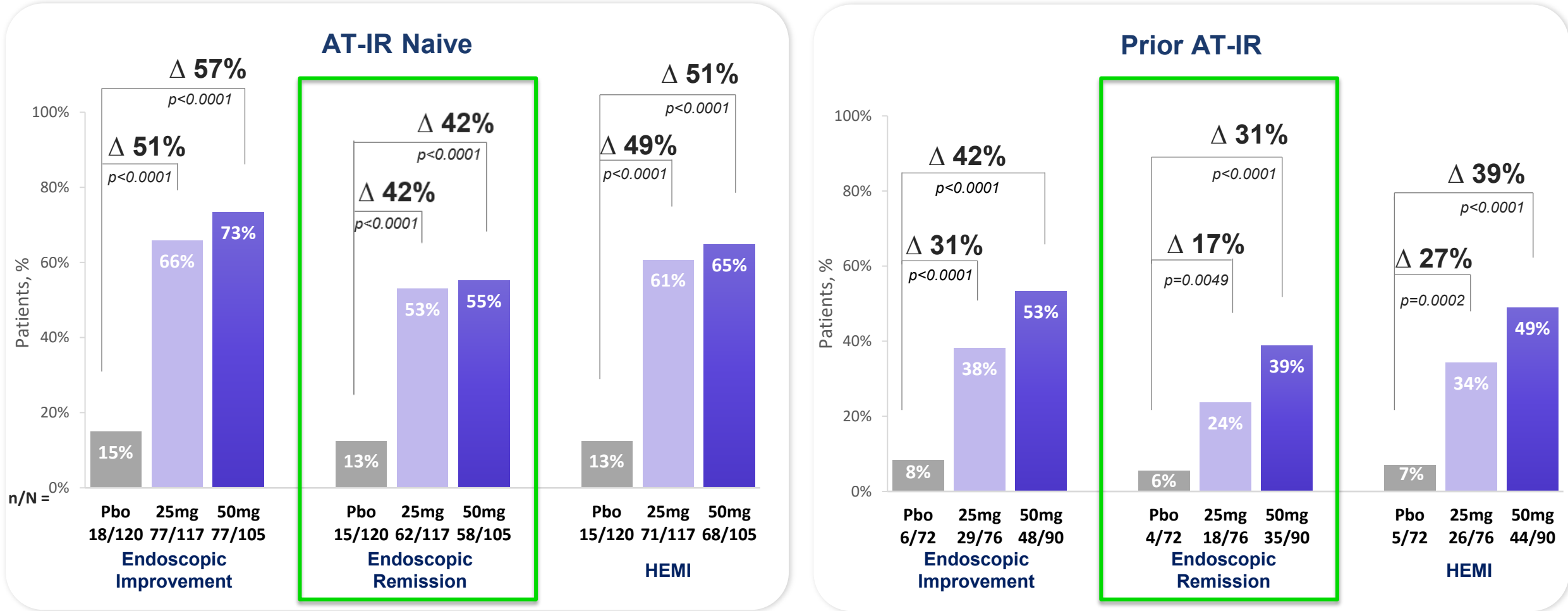
- **Clinical remission:** SFS = 0 or 1, and RBS = 0 and MES = 0 or 1 (MES of 1 modified to exclude friability).
- **CS-free clinical remission:** clinical remission at Week 44 and corticosteroid free for at least 12 weeks immediately prior to Week 44
- **Sustained clinical remission:** clinical remission at Week 44 in the sub-population of subjects in clinical remission at Week 8 of the induction study

Data on File ABX464-107

% Difference shown is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: clinical remission at maintenance baseline (yes/no), induction treatment (25 mg/50 mg), and maintenance baseline oral corticosteroids usage (yes/no). Therefore shown % differences may not match the visual difference between treatment groups. *Δ24% for 25mg in Sustained Clinical Remission endpoint only is based on the unadjusted numerical difference vs placebo (percentage points); not a Mantel-Haenszel stratified estimate. If the Mantel-Haenszel weights is used as described above for this dose and this endpoint, the delta becomes 8% due to the small sample size (n=15).

CS Free = corticosteroid free; MES = Mayo Endoscopic Subscore

Endoscopic and Histologic-Endoscopic Endpoints by Prior Advanced Therapy Inadequate Response (AT-IR)



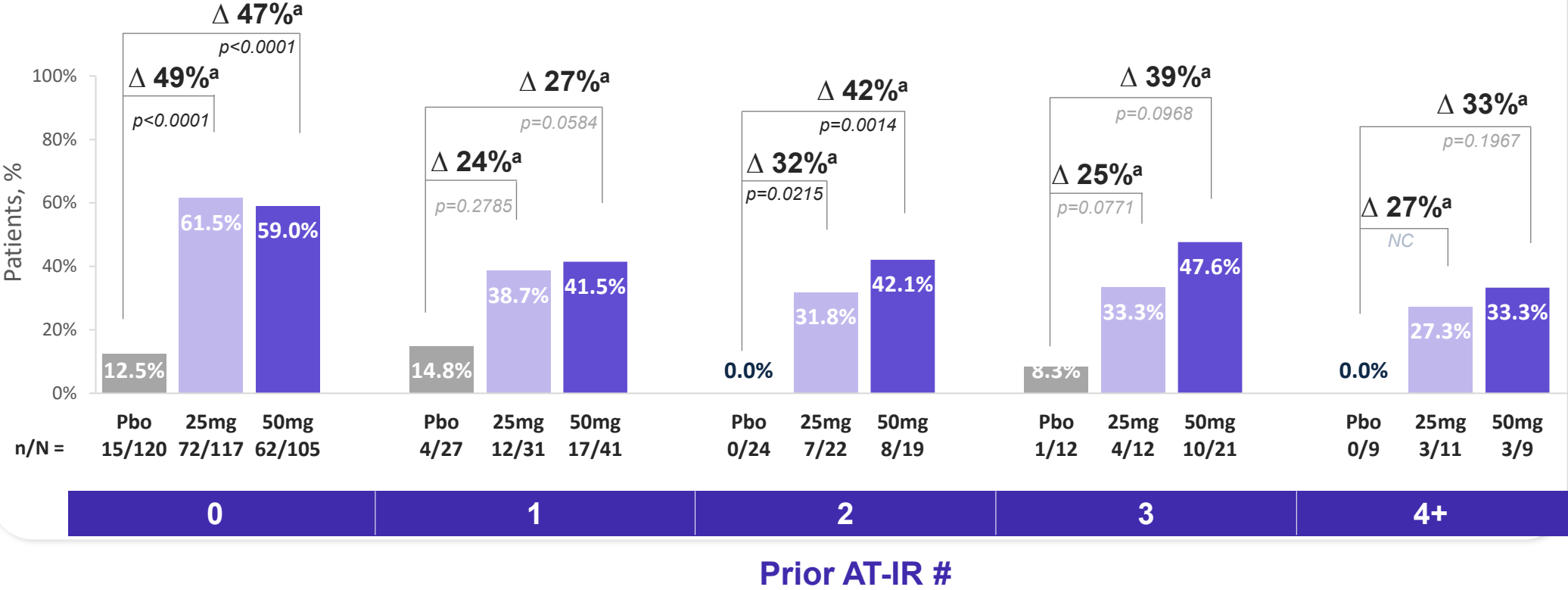
- **Endoscopic improvement:** MES = 0 or 1 (MES of 1 modified to exclude friability)
- **Endoscopic remission:** MES = 0
- **Histologic-endoscopic mucosal healing (HEMI):** MES = 0 or 1 and Geboes Index score ≤ 3.1

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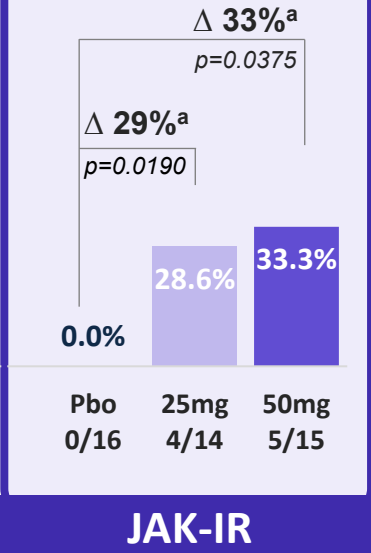
% Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: clinical remission at maintenance baseline (yes/no), induction treatment (25 mg/50 mg), and maintenance baseline oral corticosteroids usage (yes/no)

Clinical Remission by Number of Prior Advanced Therapy Inadequate Responses (AT-IR) and Prior JAK Inhibitor Inadequate Response (JAK-IR)

Clinical Remission by Number of Prior Advanced Therapy Inadequate Response

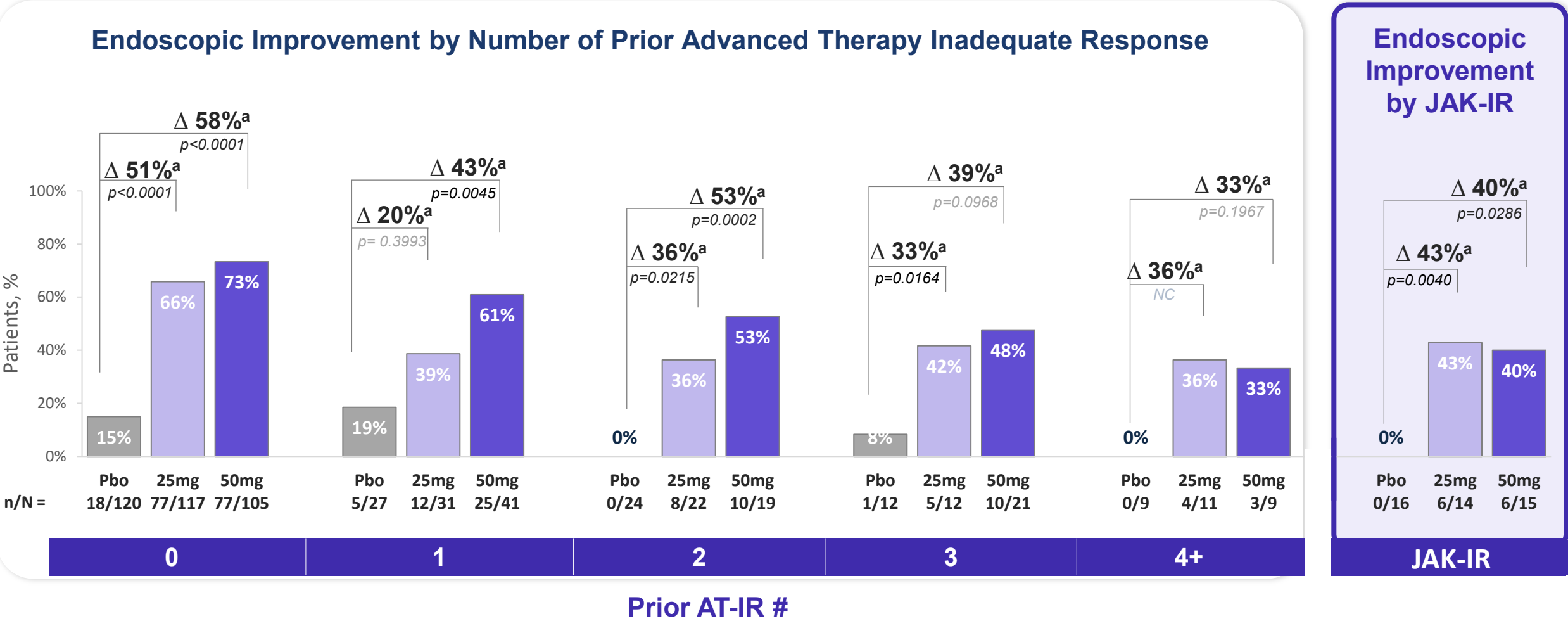


Clinical Remission by JAK-IR



Data on File ABX464-107
Clinical Remission Defined as SFS = 0 or 1 and RBS = 0, and MES = 0 or 1 (MES of 1 modified to exclude friability)
[a] Deltas are unadjusted numerical difference vs placebo (percentage points); not a Mantel-Haenszel stratified estimate.
[b] P-values are nominal and have not been adjusted for multiplicity; therefore, they should be interpreted as descriptive rather than confirmatory.

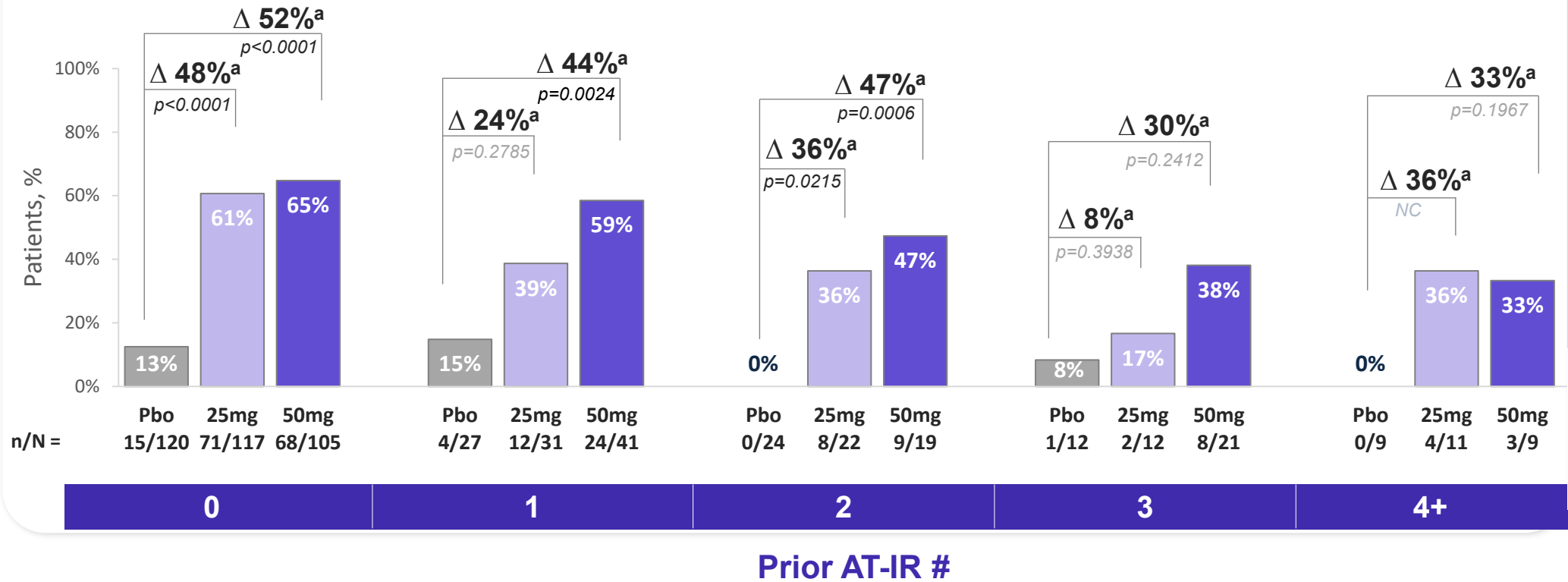
Endoscopic Improvement by Number of Prior Advanced Therapy Inadequate Responses and Prior JAK Inhibitor



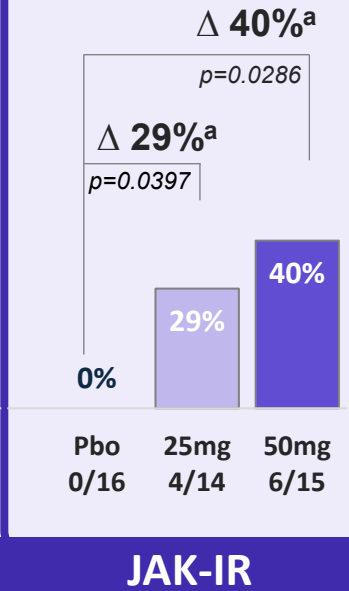
Data on File ABX464-107
Endoscopic improvement is defined as MES = 0 or 1 (MES of 1 modified to exclude friability).
[a] Deltas are unadjusted numerical difference vs placebo (percentage points); not a Mantel-Haenszel stratified estimate.
[b] P-values are nominal and have not been adjusted for multiplicity; therefore, they should be interpreted as descriptive rather than confirmatory.

HEMI by Number of Prior Advanced Therapy Inadequate Responses and Prior JAK Inhibitor

HEMI by Number of Prior Advanced Therapy Inadequate Response



HEMI by JAK-IR



Data on File ABX464-107
HEMI is defined as MES = 0 or 1 and Geboes Index score <= 3.1.
[a] Deltas are unadjusted numerical difference vs placebo (percentage points); not a Mantel-Haenszel stratified estimate.
[b] P-values are nominal and have not been adjusted for multiplicity; therefore, they should be interpreted as descriptive rather than confirmatory.

Safety Results Summary – ABTECT Maintenance

	Placebo N = 192	Obefazimod 25 mg N = 193	Obefazimod 50 mg N = 195
TEAE, n (%)			
Any TEAE	96 (50.0%)	112 (58.0%)	140 (71.8%)
TEAE Leading to Discontinuation	13 (6.8%)	5 (2.6%)	9 (4.6%)
Serious TEAE	8 (4.2%)	5 (2.6%)	11 (5.6%)
Patients with Any Related Serious TEAE	1 (0.5%)	0	0
Death	0	0	0
Pregnancy	0	0	2 (1.1%)
Serious/Severe (Grade ≥3) infections and opportunistic infections¹	2 (1.0%)	2 (1.0%)	1 (0.5%)
Malignancies (other than non-NMSC)			
Breast Cancer	0	0	1 (0.5%)
Prostate Cancer	0	0	1 (0.5%)
Non-Melanoma Skin Cancer (NMSC)			
Basal Cell Carcinoma	1 (0.5%)	0	2 (1.1%)
Squamous Cell Carcinoma	0	1 (0.5%)	2 (1.1%)

1. Serious/Severe Infections and Opportunistic Infections: Placebo = Anal abscess, bronchitis & gastroenteritis, 25 mg = 1 Lymph node tuberculosis, 1 tonsillitis, 50 mg = 1 Appendicitis, focal peritonitis; 2. One case of colonic dysplasia was reported in the obefazimod 50mg arm. No cases of acute pancreatitis were reported

TEAE = Treatment-Emergent Adverse Event

Conclusions

- Treatment differences favored obefazimod over placebo across clinical, endoscopic, symptomatic, and histologic-endoscopic outcomes in AT-IR naïve and in with patients with prior ATIR
- Placebo-adjusted treatment differences were generally numerically larger in AT-IR naïve vs. with patients with prior ATIR
- Clinical remission rates numerically favored both obefazimod doses across 0 to ≥ 4 prior AT-IR therapies and in JAK-IR patients
- Overall favorable safety profile with no evidence of immunosuppression, consistent with the proposed mechanism of action of restoring immune balance while maintaining key components of immune surveillance

