

Efficacy and Safety of Obefazimod in Patients with Moderately to Severely Active Ulcerative Colitis:

Results from the Phase 3, Randomized, Double-blind, Placebo-Controlled, 44-week Maintenance Trial (ABTECT-Maintenance)

BE Sands, S Danese, L Peyrin-Biroulet, MC Dubinsky, T Hisamatsu, H Tilg, R Atreya, A Armuzzi, X Treton, F Baert, U Seidler, G D'Haens, F Cataldi, D Jacobstein, CJ Rabbat, K Shan, GA Duvall, B Siegmund, PS Dulai, DT Rubin, S Vermeire

Dr. Henry D. Janowitz Division of Gastroenterology
Icahn School of Medicine at Mount Sinai, New York, USA



UNITED EUROPEAN
GASTROENTEROLOGY

uegweek

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:

I received consultancy fees from Aclaris Therapeutics, Adaxion Therapeutics, Adiso Therapeutics, Agomab Therapeutics, Alfasigma, Alimentiv, Amgen, AnaptysBio, AstraZeneca, Attovia Therapeutics, Biologic Design, BiomeBank, Biora Therapeutics, Boehringer-Ingelheim, Caldera Therapeutics, Cellarity, Cytoki Pharma, Disc Medicine, Eil Lilly & Company, Ensho Therapeutics, Enthera, Enveda Biosciences, Equilium, Evommune, Ferring, Fzata, Galapagos, Genentech (Roche), Genesis Therapeutics, Gilead Sciences, GlaxoSmithKline, Globalport, Ignite Biomedical, Imedex, Imhotex, Immunitas Therapeutics, Immunyx Pharma, Kallyope, Kyowa Kirin, LifeMine Therapeutics, Merck & Co., Merck Sharp & Dohme, Microba, Microbiotica, Mirador Therapeutics, Mitsubishi Tanabe Pharma, Mobius Care, Morphic Therapeutic, MRM Health, Nexus Therapeutics, Nimbus Discovery, Novartis, Numab Therapeutics, Odyssey Therapeutics, ONO Pharmaceutical, OSE Immunotherapeutics, Palisade Bio, Pioneering Medicines Explorations, Prometheus Biosciences, Protagonist Therapeutics, Q32 Bio, Quotient Therapeutics, Rasayana Therapeutics, Recludix Pharma, Reistone Biopharma, Sanofi, Slate Bio, Sorriso Pharmaceuticals, Spyre Therapeutics, Synlogic, Target RWE, Televant, Teva, Thetis Pharmaceuticals, SRT Therapeutics, TR1X, Trex Bio, Union Therapeutics, VectivBio, Vedanta Biosciences, Vividion Therapeutics, Xencor; honoraria for consulting and speaking and other support from AbbVie, Abivax, Bristol Myers Squibb, Celltrion, Eli Lilly & Company, Genentech (Roche), J&J Innovative Medicine/Janssen, Merck & Company, Pfizer, Takeda, Teva; honoraria for consulting, stock options from Caldera Therapeutics, Mirador Therapeutics and SRT Therapeutics; and stock from Doximity.

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
- Restores immune balance while maintaining immune surveillance functions



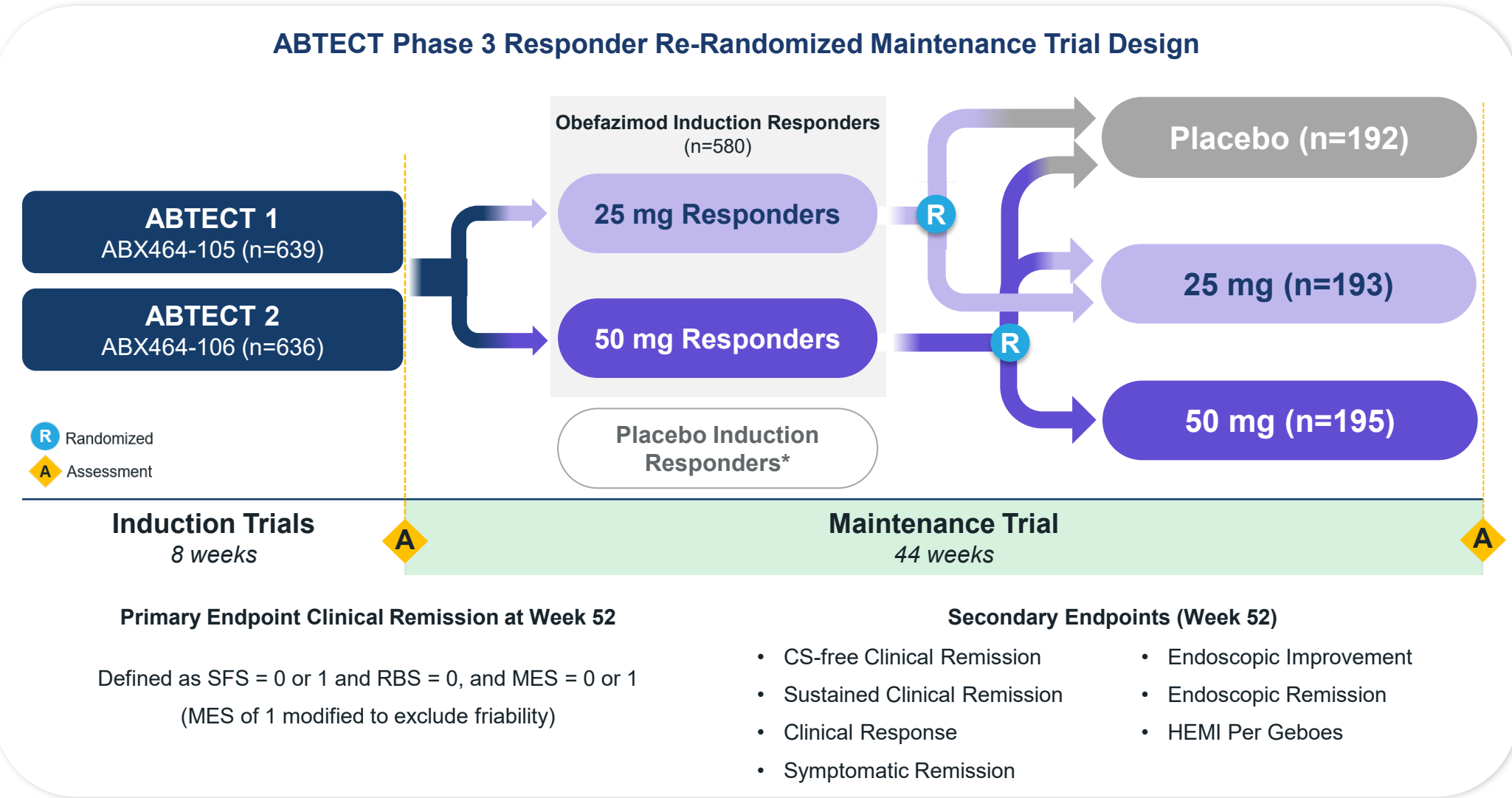
Clinical Evidence

- 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 patients with moderately to severely active UC who responded to obefazimod induction after 52 weeks of treatment overall

ABTECT Maintenance: Safety and Efficacy in Obefazimod Induction Responders



Induction Clinical Response defined as decrease in the MMS ≥ 2 points and $\geq 30\%$ from baseline, with a decrease in RBS ≥ 1 or an absolute RBS ≤ 1

Randomization stratification factors: clinical remission at maintenance baseline (yes/no), induction treatment (25 mg/50 mg), and maintenance baseline oral corticosteroids usage (yes/no)

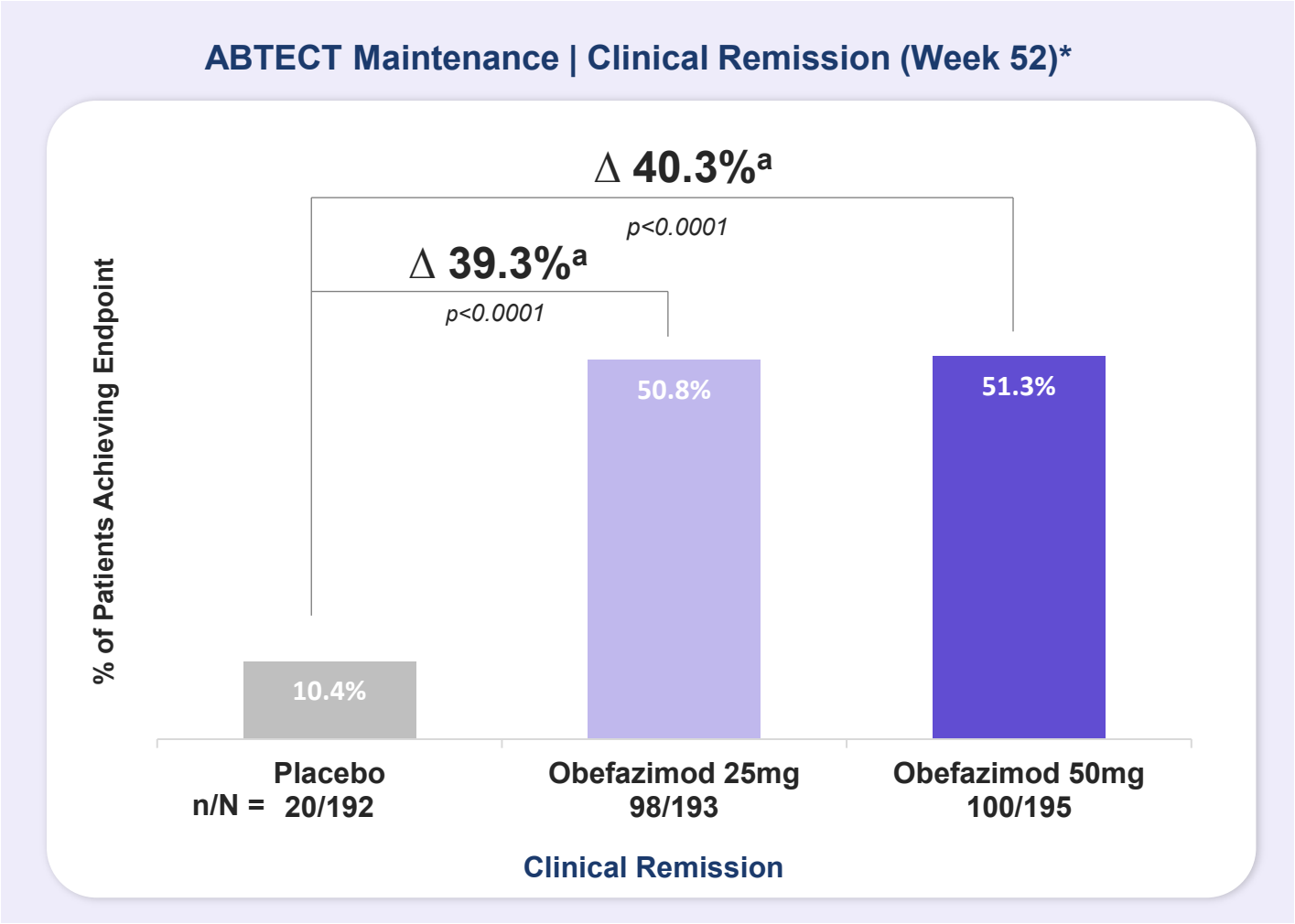
ueg * Placebo induction responders were maintained on blinded placebo in maintenance | **HEMI**, Histologic-Endoscopic Mucosal Improvement; **MES**, Mayo Endoscopic Score; **MMS**, modified Mayo score; **RBS**, rectal bleeding score; **SFS**, stool frequency subscore

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
Stratification Factors			
Corticosteroid Use at Maintenance Baseline (%)	35.9%	41.5%	40.5%
Maintenance Baseline Clinical Remission Rate	27.1%	37.8%	32.3%
Prior Advanced Therapy Failure (%)	37.5%	39.4%	46.2%
Maintenance Trial W44 Completion Rate*	66 (34.3%)	152 (78.8%)	160 (82.1%)

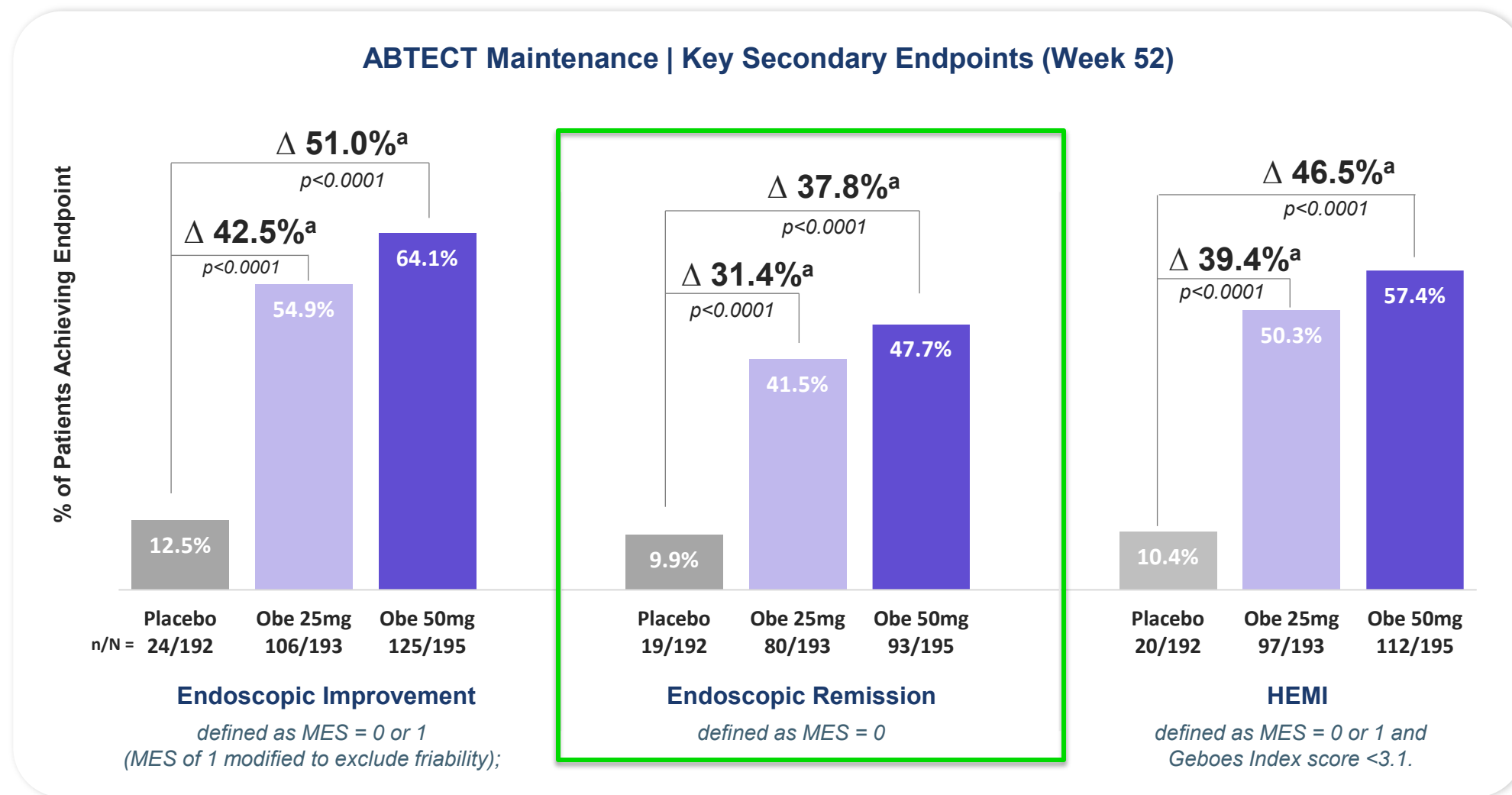
50 mg cohort had a higher percentage of patients with prior advanced therapy failure relative to patients on 25 mg and placebo

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



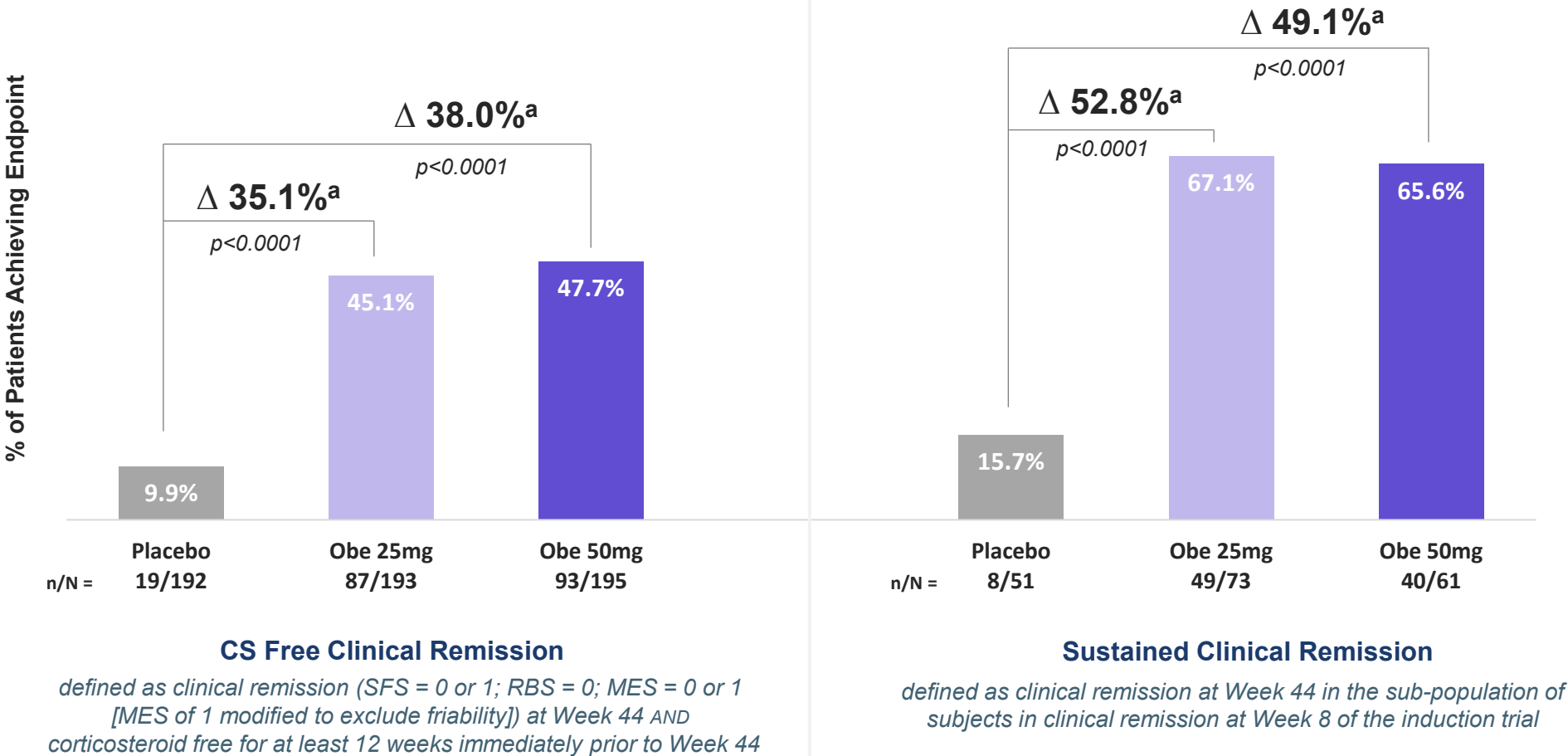
* Week 52 includes the 8-week induction treatment with obefazimod
[a] % Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: clinical remission at maintenance baseline (yes/no), 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



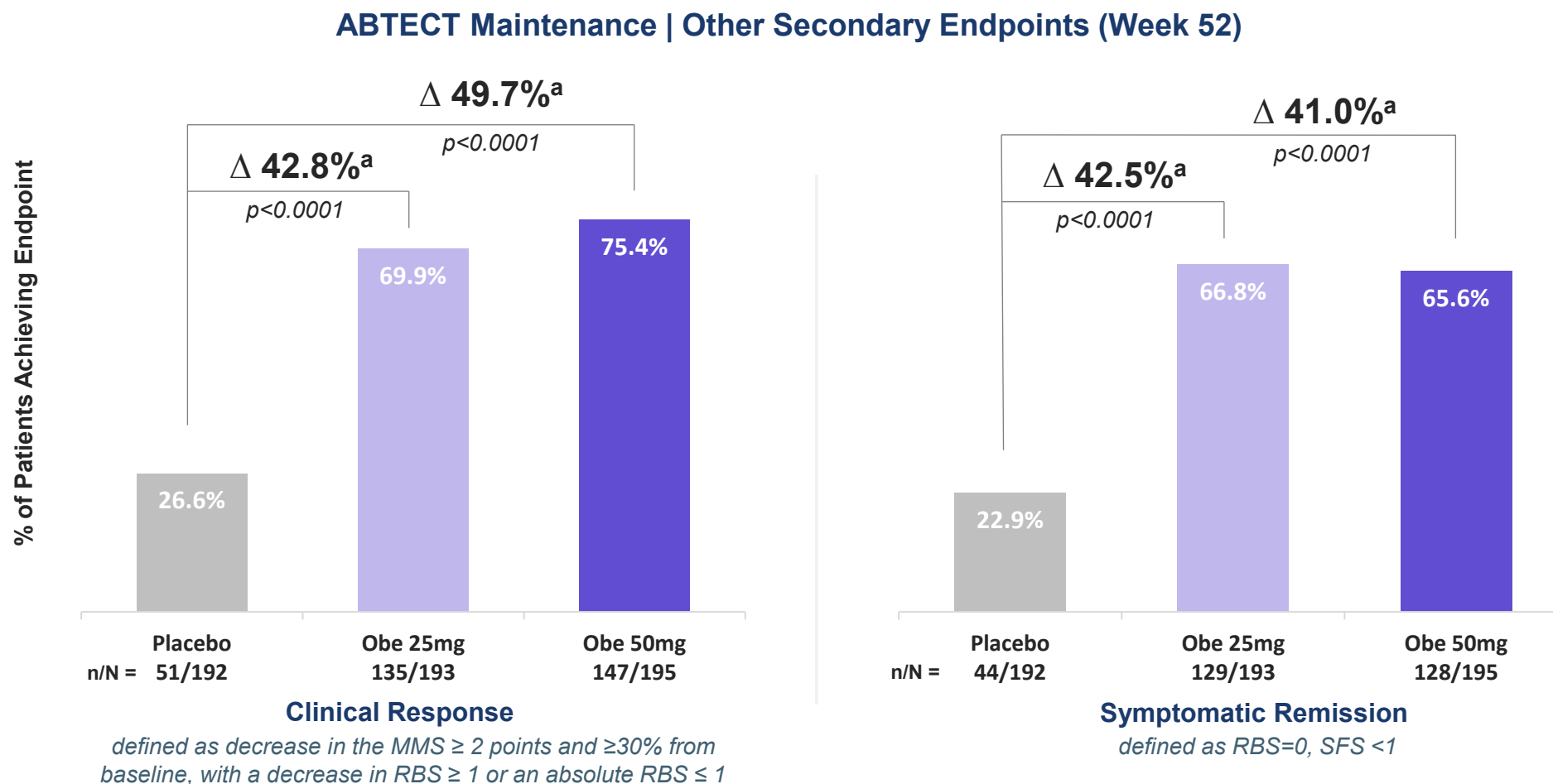
Both Obefazimod Doses Met All Key Secondary Endpoints at Week 52

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

At Week 52, Higher Proportions of Patients Achieved Clinical Response and Symptomatic Remission With Both Obefazimod Doses than With Placebo



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

- Both obefazimod doses met the primary endpoint of clinical remission at Week 52 with **50.8%** and **51.3%** of patients receiving 25 mg and 50 mg, respectively, **versus 10.4%** receiving placebo (adjusted differences, 39.3 and 40.3 percentage points; both $p < 0.0001$)
- Both obefazimod doses met all multiplicity-controlled key secondary endpoints (all $p < 0.0001$)
- **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

