Amiselimod for the Treatment of Active Ulcerative Colitis: A Randomized, Double-Blind, Placebo-Controlled Trial

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Disclosures

- Stephen B. Hanauer reports being a consultant and/or on the speakers' bureau for AbbVie, Bristol Myers Squibb, Janssen (now J & J Innovative Medicine), Pfizer, Prometheus Biosciences (now Merck), and Takeda Pharmaceuticals
- Adam P. Laitman and Zeev Heimanson are employees of Salix Pharmaceuticals
- Robert J. Israel and Jimin Lee are employees of Bausch Health US, LLC
- Stefan Schreiber reports being a clinical investigator for Salix Pharmaceuticals/Bausch Health US, LLC. Fees for consultancy and/or lectures were received from AbbVie Inc., Bristol-Myers Squibb, Celltrion, Dr. Falk Pharma GmbH, Ferring Pharmaceuticals Inc, Galapagos NV, Gilead Sciences, Inc., Merck & Co., Inc., Morphic Therapeutic, Inc., Novartis AG, Pfizer Inc., Roche, Takeda Pharmaceutical Co., Ltd., and Ventyx Biosciences, Inc.

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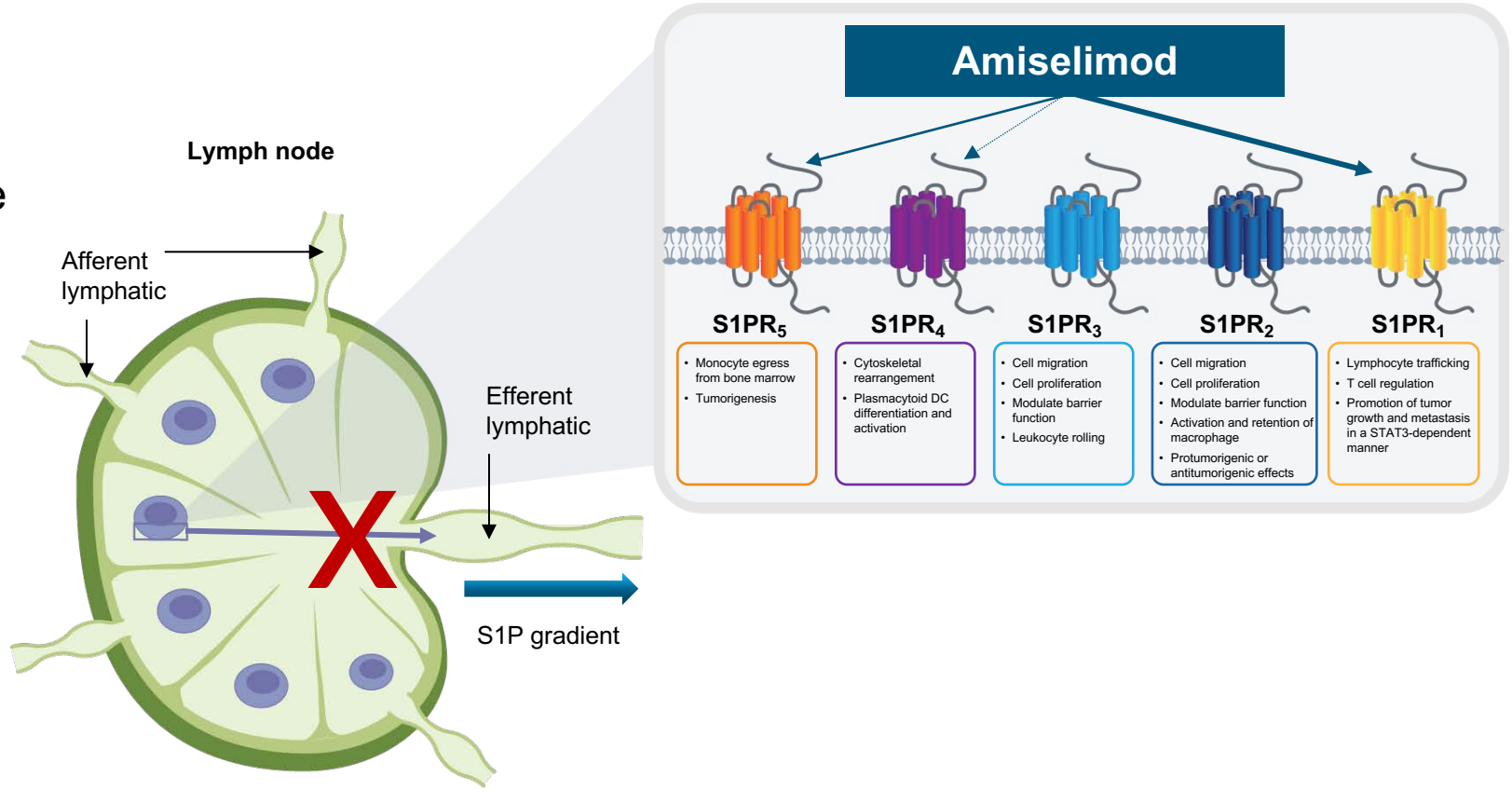
Background

- **Advances have been made in the treatment of patients with UC[1,2]**
  - However, lack of response and treatment-related AEs highlight a need for new safe and effective therapies
- **Amiselimod**
  - Investigational oral S1P receptor modulator with greatest affinity for receptor $S1P_1$, followed by $S1P_5$[3]
  - Immunomodulatory mechanism of action includes decreasing circulating peripheral lymphocytes

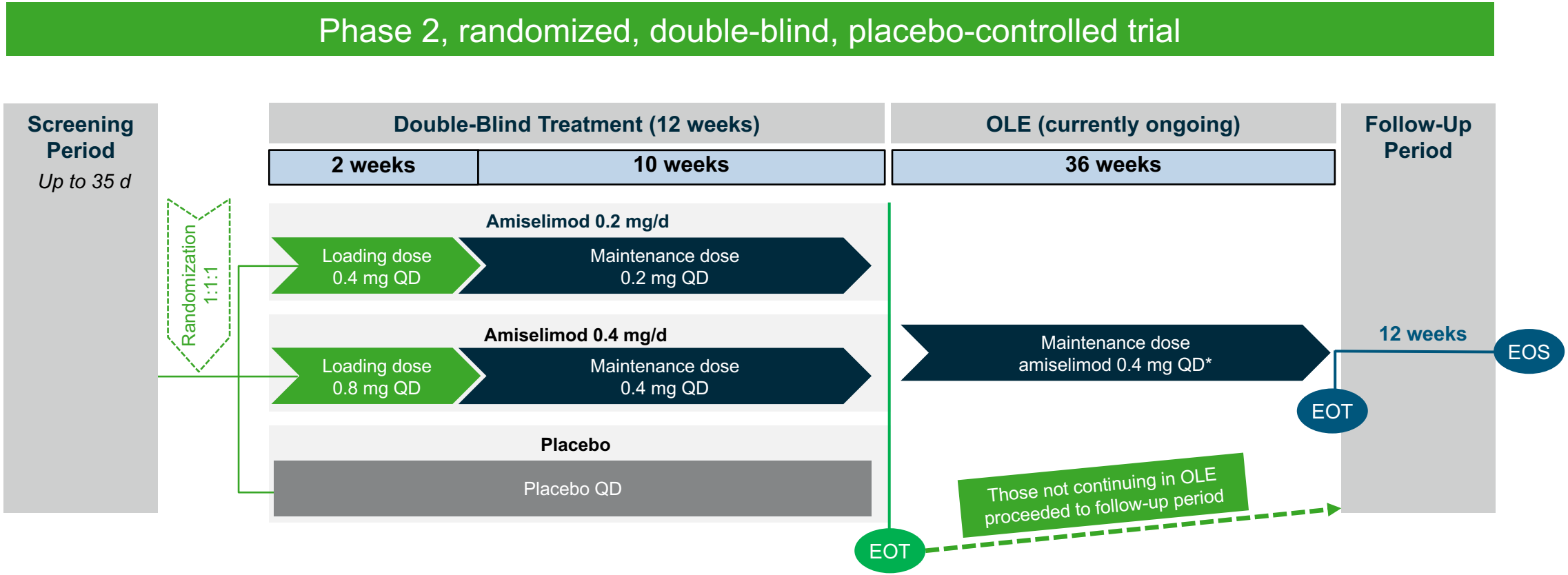


AEs = Adverse events; DC = dendritic cell; S1P = sphingosine 1-phosphate; S1PR = sphingosine 1-phosphate receptor; STAT3 = signal transducer and activator of transcription 3; UC = ulcerative colitis.

1. La Berre C, et al. *Lancet. 2023*;402(10401):571-584. 2. Ko CW, et al. *Gastroenterology*. 2019;156(3):748-764. 3. Sugahara K, et al. *Br J Pharmacol.* 2017;174(1):15-27.

Objective and Study Design

- **Objective:** to assess the 12-week efficacy and safety of 2 amiselimod doses compared with placebo for the induction of remission of active, mild to moderate UC



*Patients in any of the 3 double-blind treatment arms who completed study through Day 85 (Week 12) were eligible to continue in OLE phase and receive amiselimod 0.4 mg QD (no loading dose).
EOS = end of study; EOT = end of treatment; OLE = open-label extension; QD = once daily; UC = ulcerative colitis.

Key Inclusion Criteria

- **Adults (18-75 y) with active mild to moderate UC***
  - Modified Mayo score (MMS) of 3-8
  - Endoscopic subscore from screening colonoscopy of ≥2†
  - Active disease extending ≥15 cm from anal verge, confirmed by screening colonoscopy
- **Concomitant oral/rectal 5-ASAs or oral corticosteroids (≤20 mg prednisolone equivalent/day) for treatment of UC permitted if dose stable for ≥28 days prior to randomization**
- **No history/evidence of ≥2 failures with biologic treatment for UC**
- **No recent‡ history of fulminant colitis, abdominal abscess, toxic megacolon, bowel obstruction, or bowel perforation**
- **No history/evidence of colonic resection or subtotal colectomy within 1 year prior to randomization**
- **No history/evidence of ileostomy, colostomy, or known fixed symptomatic intestinal stenosis**

*Confirmed ≥12 weeks prior to randomization by clinical and endoscopic evidence (corroborated by histopathology).
†Determined by central reviewer.
‡Within 12 weeks prior to randomization.
5-ASA = 5 aminosalicylate; MMS = modified Mayo score; UC = ulcerative colitis.

Assessments

- **Primary endpoint**
  - Change from baseline in MMS* at Week 12
- **Secondary endpoints**
  - Percentage of patients achieving endoscopic improvement at Week 12
    - Endoscopic improvement defined as MMS endoscopic subscore ≤1
  - Percentage of patients achieving clinical remission[1] at Week 12, defined as MMS
    - Endoscopy subscore of ≤1 (excluding friability) and
    - Rectal bleeding subscore = 0 and
    - Stool frequency subscore of ≤1
- **Safety, including adverse events, was monitored throughout the study**

*MMS is the sum of endoscopy subscore (excludes friability) plus rectal bleeding subscore, plus stool frequency subscore.

1. US Food and Drug Administration. 2022. https://www.fda.gov/media/158016/download. Accessed May 1, 2024.

MMS = modified Mayo score.

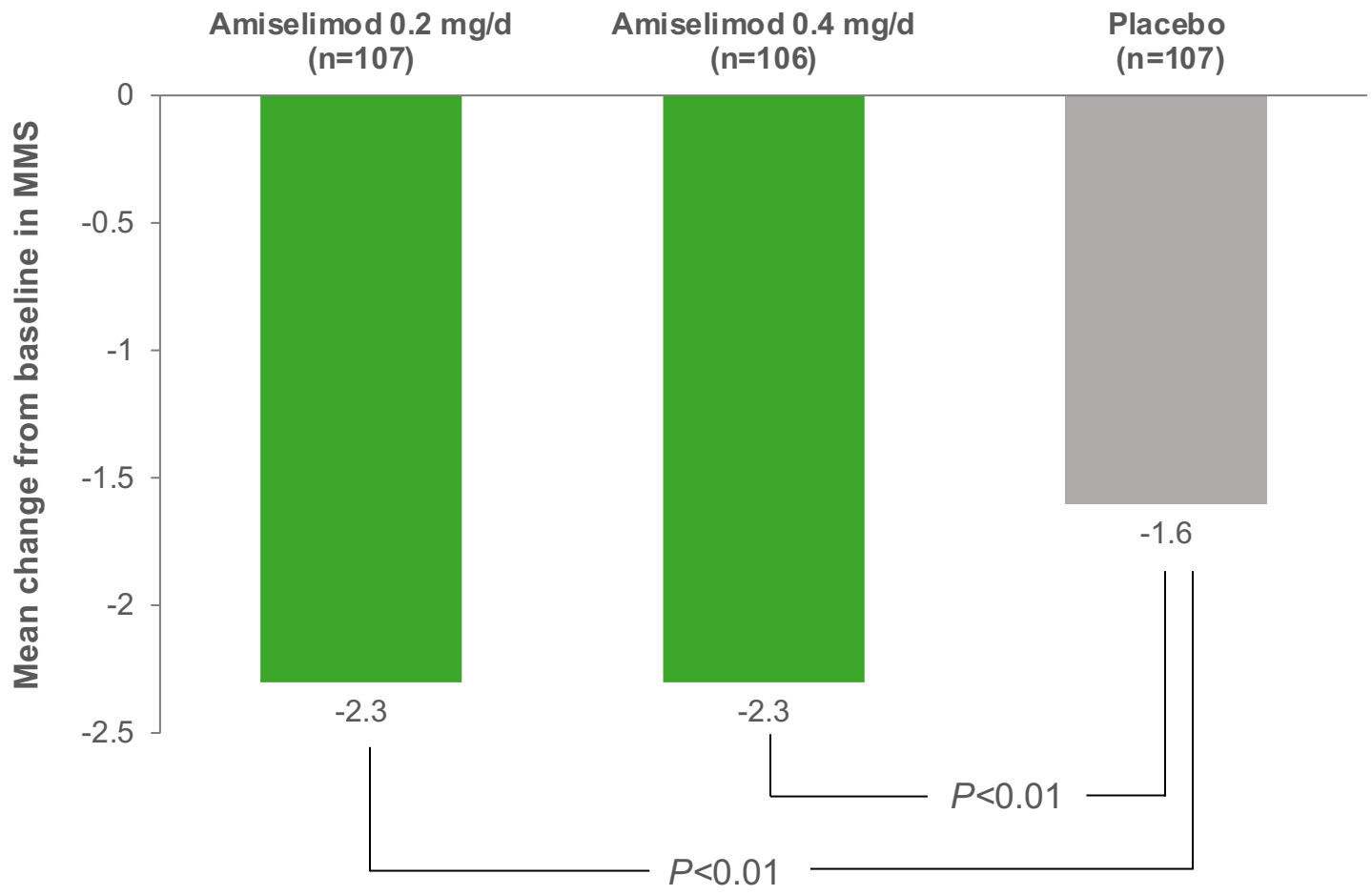
Patient Demographics and Baseline Characteristics

Parameter	Amiselimod 0.2 mg/d (n=107)	Amiselimod 0.4 mg/d (n=106)	Placebo (n=107)
Age, y, median (range)	39.0 (18-73)	41.5 (18-70)	38.0 (18-70)
Gender, n (%)			
Male	63 (58.9)	63 (59.4)	61 (57.0)
Female	44 (41.1)	43 (40.6)	46 (43.0)
Race, n (%)			
White	89 (83.2)	97 (91.5)	98 (91.6)
Asian	16 (15.0)	9 (8.5)	9 (8.4)
Not reported	2 (1.9)	0	0
UC severity, n (%)			
Mild (MMS score, 3-4)	21 (19.6)	22 (20.8)	22 (20.6)
Moderate (MMS score, 5-8)	86 (80.4)	84 (79.2)	85 (79.4)
Baseline MMS, mean (SD)	5.8 (1.4)	5.7 (1.5)	5.8 (1.4)

- **87.9%, 90.6%, and 88.8% of patients in the amiselimod 0.2 mg/d, amiselimod 0.4 mg/d, and placebo groups, respectively, completed the double-blind treatment phase**

MMS = modified Mayo score; UC = ulcerative colitis.

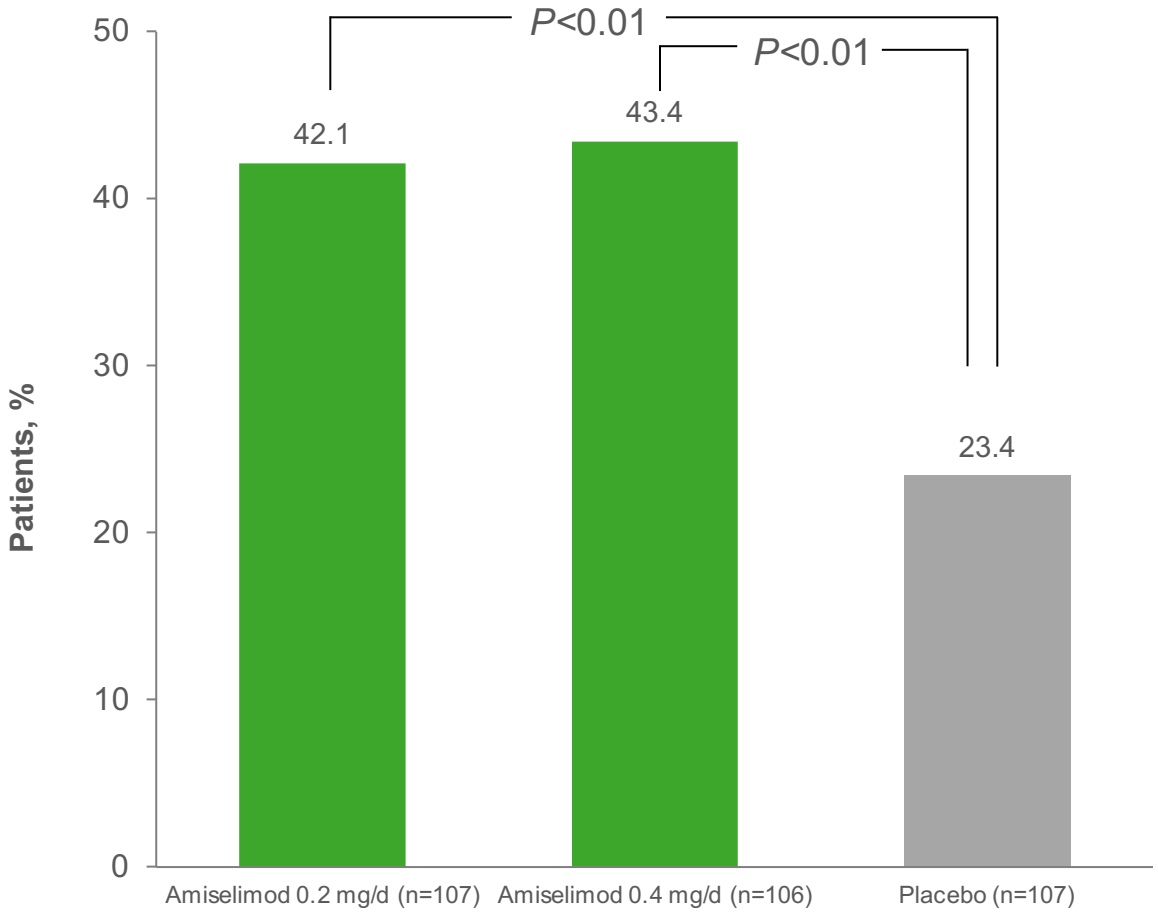
Primary Endpoint: Change From Baseline in MMS (Week 12)



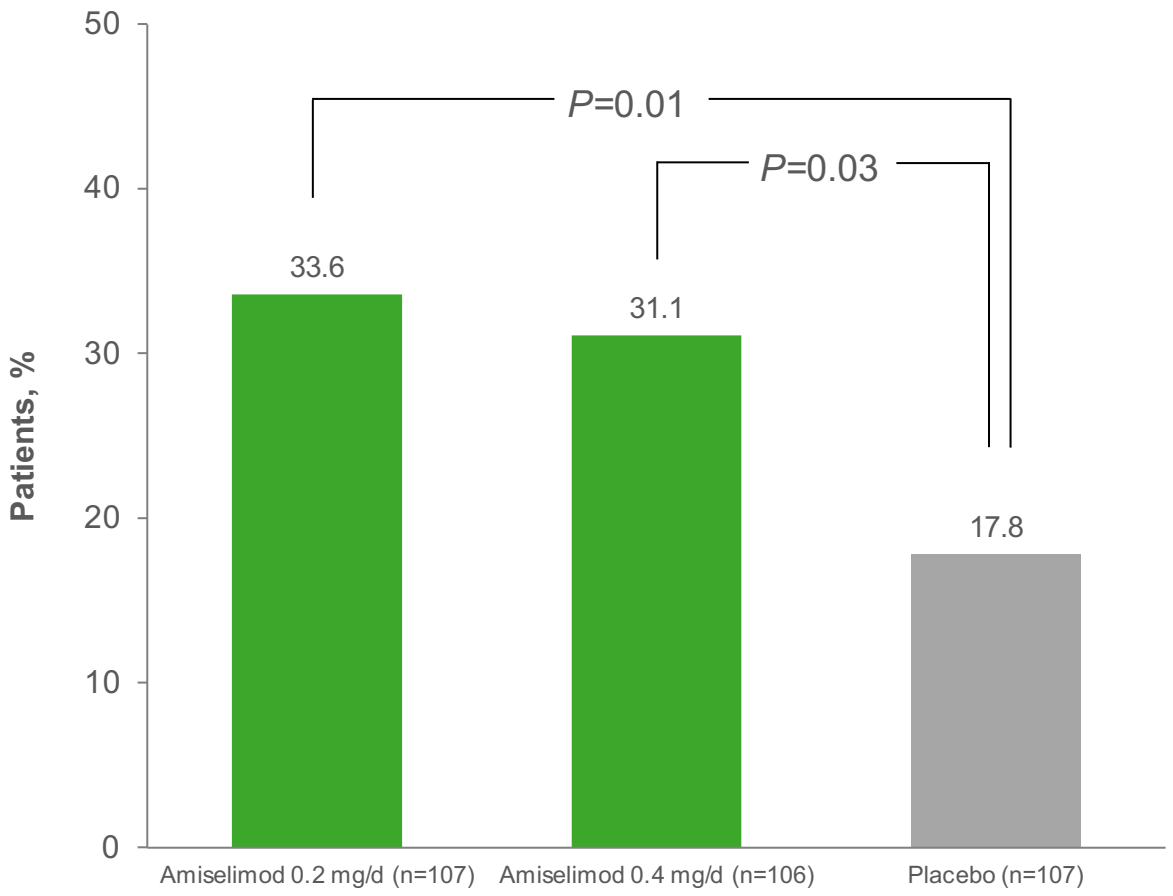
MMS = modified Mayo score.

Secondary Endpoints (Week 12)

Endoscopic improvement*

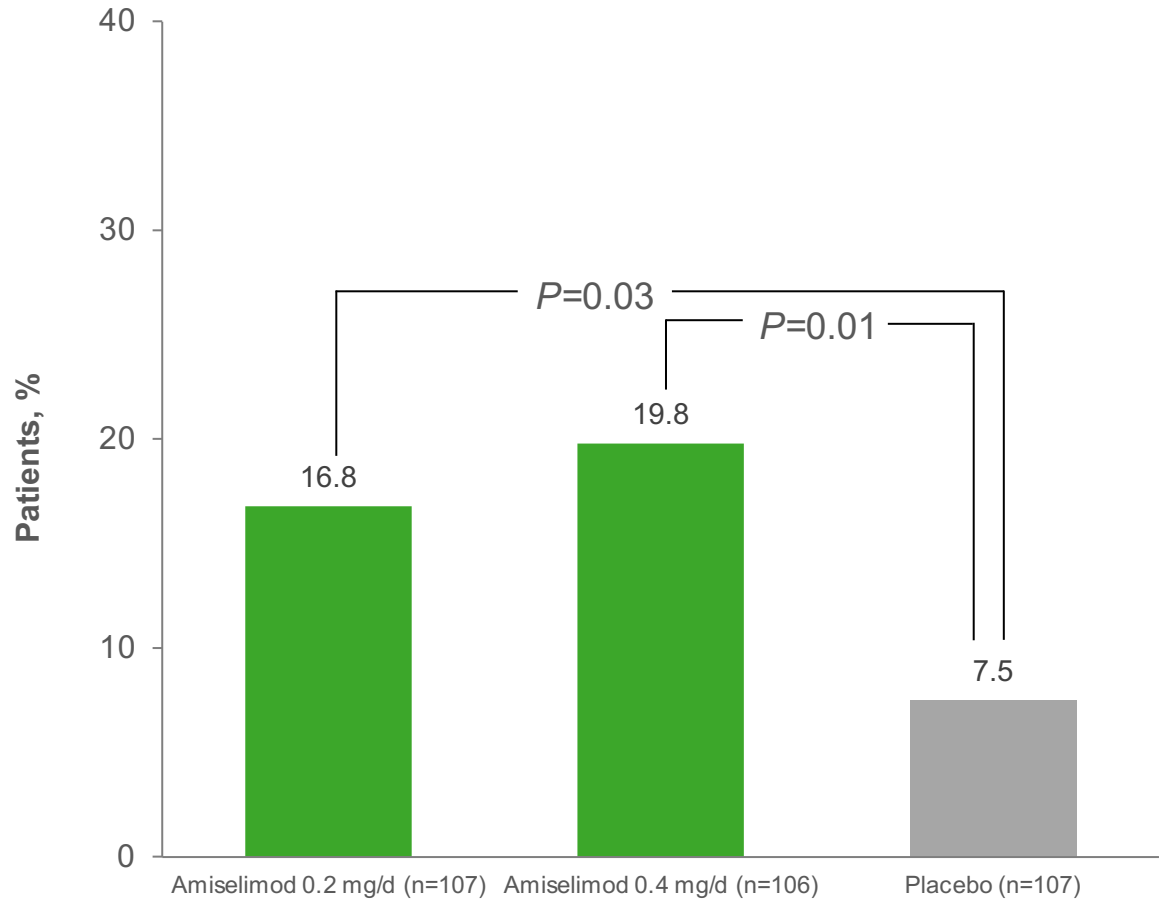


Clinical remission†



*MMS endoscopic subscore of ≤1 at Week 12.
†Endoscopy subscore of ≤1 (excluding friability), rectal bleeding subscore of 0, and a stool frequency subscore of ≤1 at Week 12.
MMS = modified Mayo Score.

Exploratory Endpoint: Histological Remission at Week 12*



*Geboes index score of <2.0 (Original Geboes Score).

Summary of Treatment-Emergent Adverse Events

Parameter, n (%)	Amiselimod 0.2 mg/d (n=107)	Amiselimod 0.4 mg/d (n=106)	Placebo (n=107)
Any AEs	56 (52.3)	62 (58.5)	46 (43.0)
AEs leading to discontinuation	5 (4.7)	5 (4.7)	3 (2.8)
Drug-related AEs	23 (21.5)	25 (23.6)	5 (4.7)
Serious AEs	2 (1.9)	2 (1.9)	1 (0.9)
Mortality	0	0	0
Most common AEs*			
Infection	18 (16.8)	14 (13.2)	18 (16.8)
COVID-19	4 (3.7)	5 (4.7)	6 (5.6)
Leukopenia	11 (10.3)	17 (16.0)	0
Anemia	6 (5.6)	5 (4.7)	5 (4.7)
Neutropenia	2 (1.9)	7 (6.6)	0 (0)

*Occurring in ≥5.0% of patients in any group, excluding UC.
AE = adverse event; UC = ulcerative colitis.

Conclusions

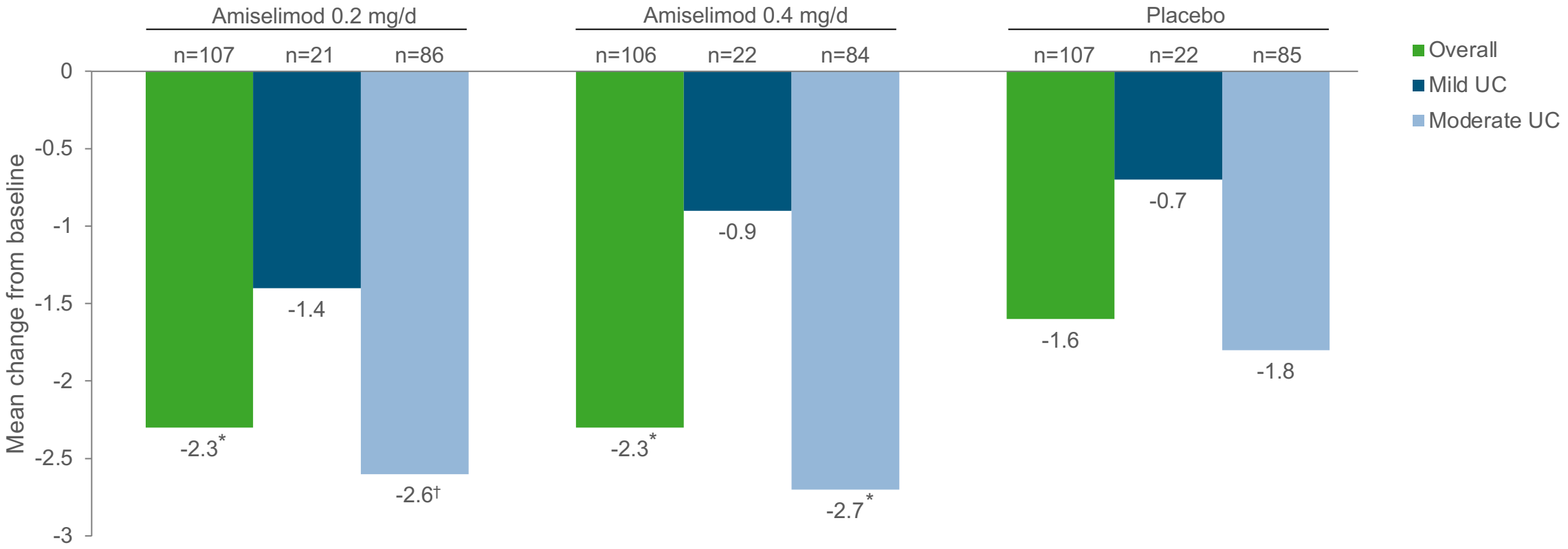
- **Treatment with amiselimod for 12 weeks was well tolerated and efficacious as a potential therapy for induction of UC remission**
  - Both amiselimod dose levels (0.2 and 0.4 mg/d) were significantly more effective than placebo
  - Both had a similar tolerability profile, except for incidence of leukopenia and neutropenia, which were more common with 0.4 mg/d versus 0.2 mg/d dosing
- **OLE (maintenance) phase is ongoing (estimated completion, early 2025)**
- **Phase 3 trial is planned**

OLE = open-label extension; UC = ulcerative colitis.

Thank You

Backup Slides

Primary Endpoint: Change From Baseline in MMS at Week 12, by Baseline UC Severity



*P<0.01 vs placebo.
†P=0.02 vs placebo.
MMS = modified Mayo score; UC = ulcerative colitis.