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

Stephen B. Hanauer, MD[1]; Adam P. Laitman, MD[2]; Zeev Heimanson, PharmD[2]; Robert J. Israel, MD[3]; Jimin Lee, MD, PhD[3]; Stefan Schreiber, MD[4]

[1]Northwestern University, Chicago, IL, USA; [2]Salix Pharmaceuticals, Bridgewater, NJ, USA; [3]Bausch Health US, LLC, Bridgewater, NJ, USA; [4]University Hospital Schleswig-Holstein, Kiel, Germany

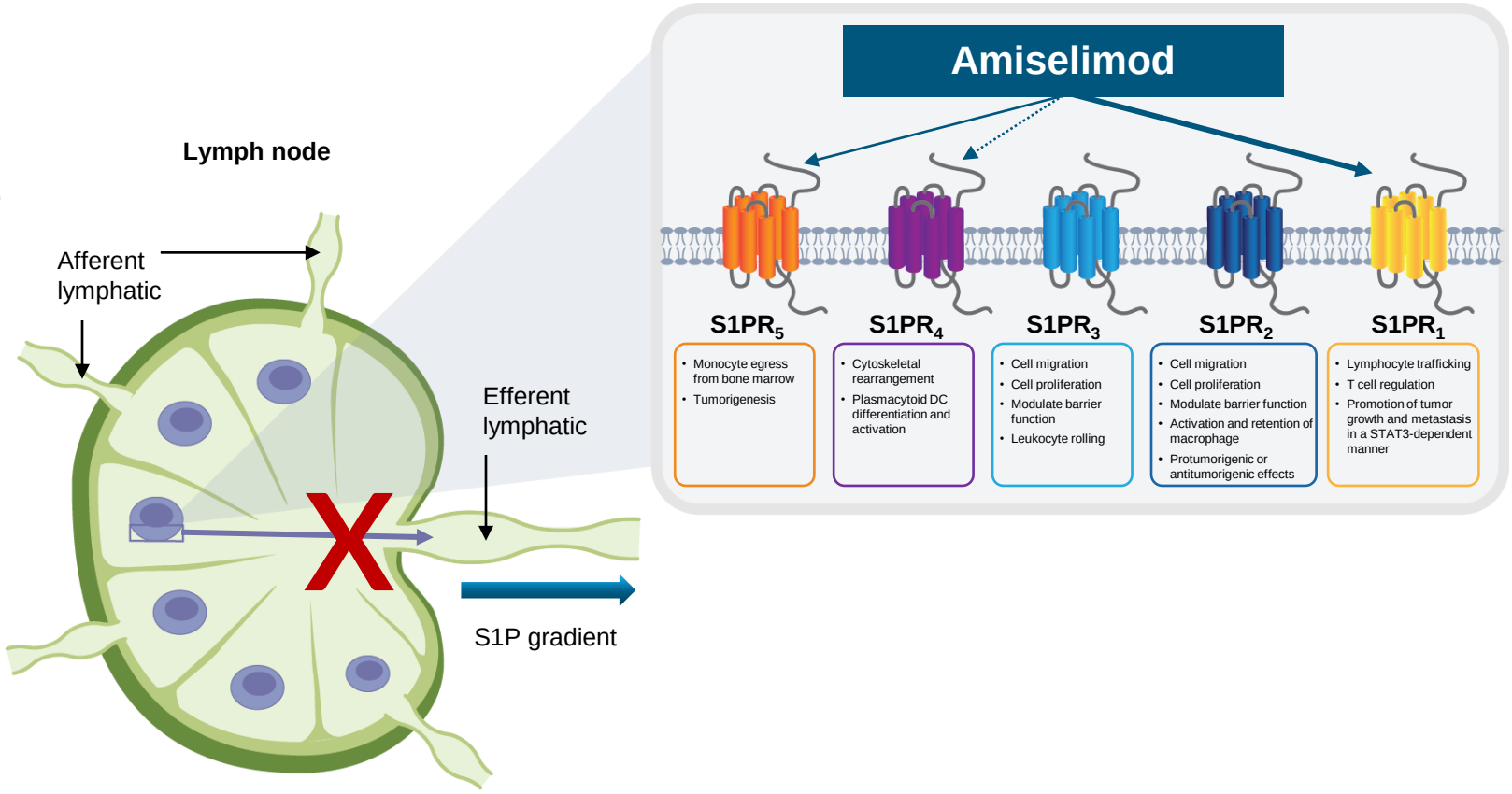
Disclosures

- 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.

The study was supported by Salix Pharmaceuticals. Technical editorial assistance was provided under direction of the authors by Synchrony Medical Communications, West Chester, PA, with support from Salix Pharmaceuticals.

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



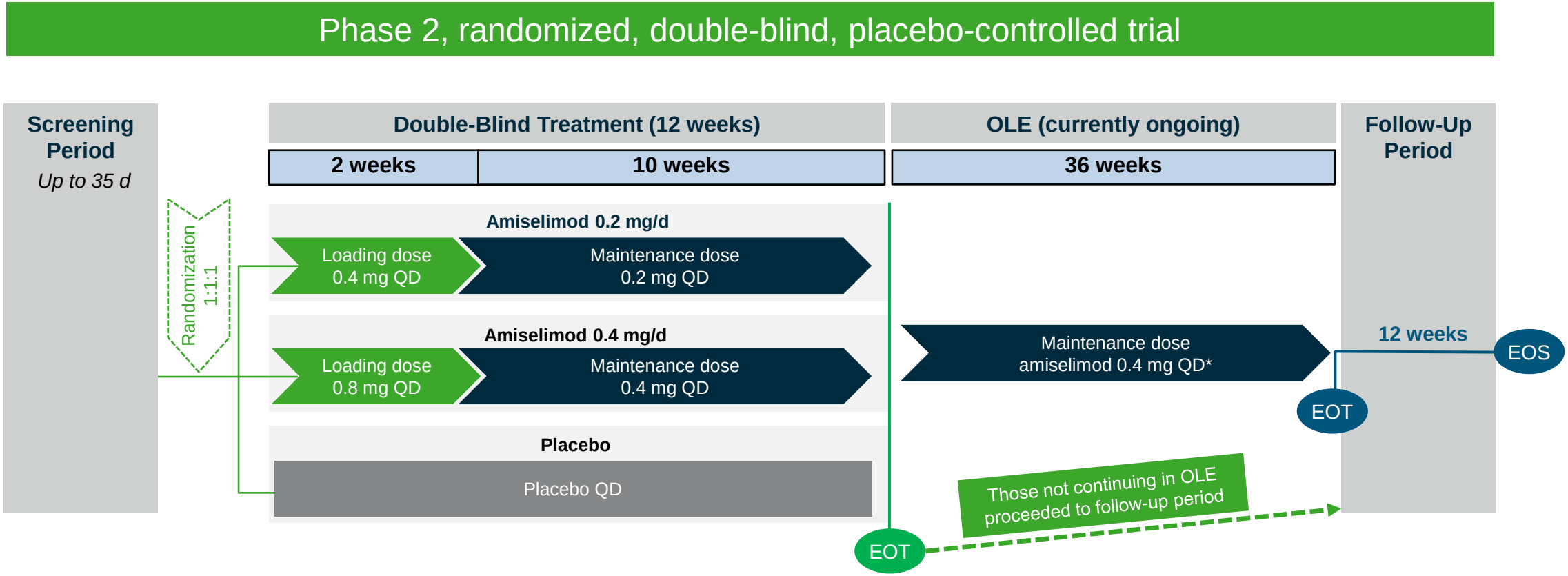
AEs = Adverse events; DC = dendritic cell; S1P = sphingosine 1-phosphate; S1PR = sphingosine 1-phosphate receptor; STAT3 = signal transducer and activator of transcription 3; UC = ulcerative colitis.

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.

Figure adapted with permission from Bencardino S, et al. *J Clin Med.* 2023;12(15):5014, via a CC-BY Creative Commons license.

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.

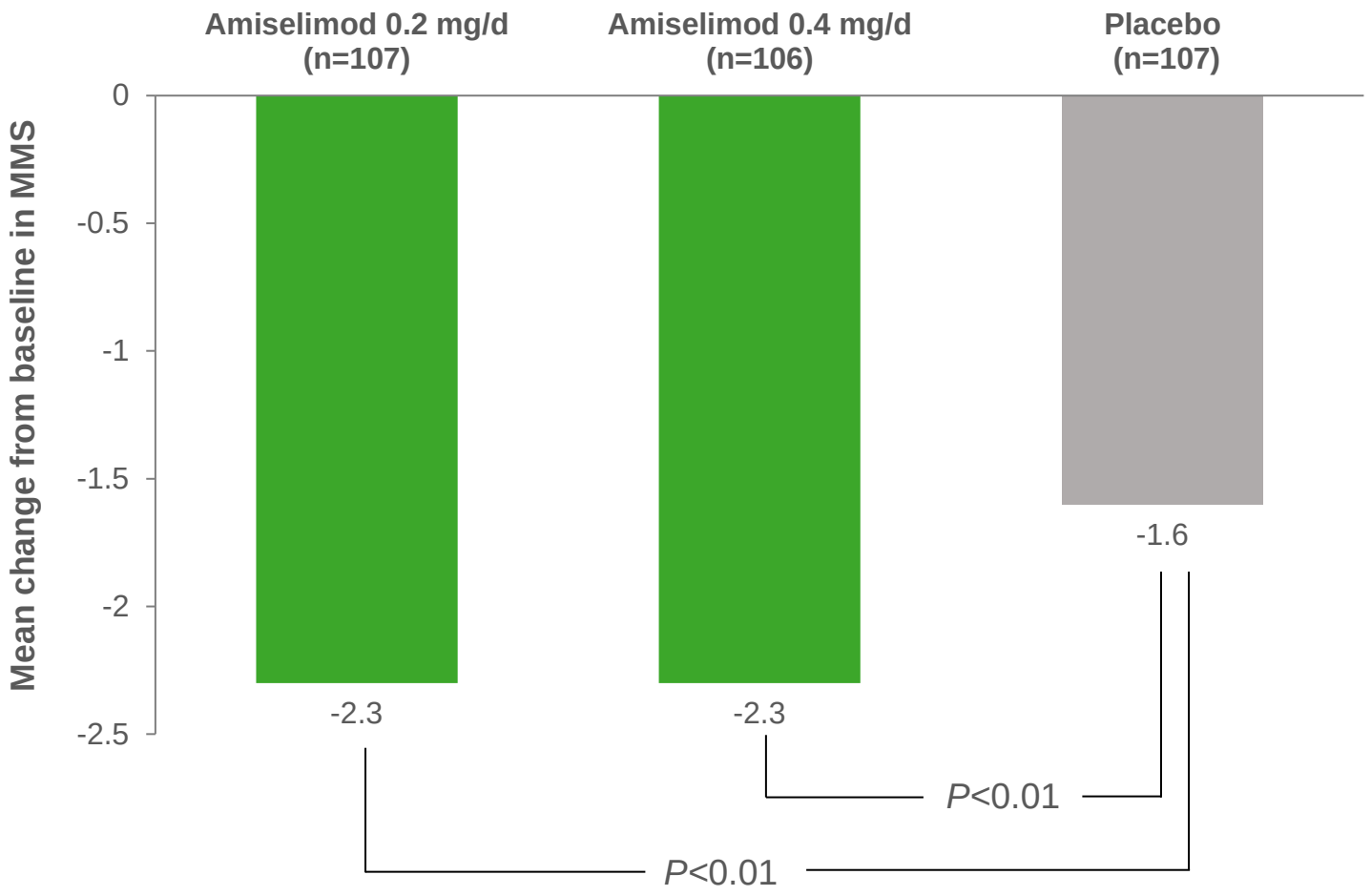
Patient Demographics and Baseline Characteristics

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.

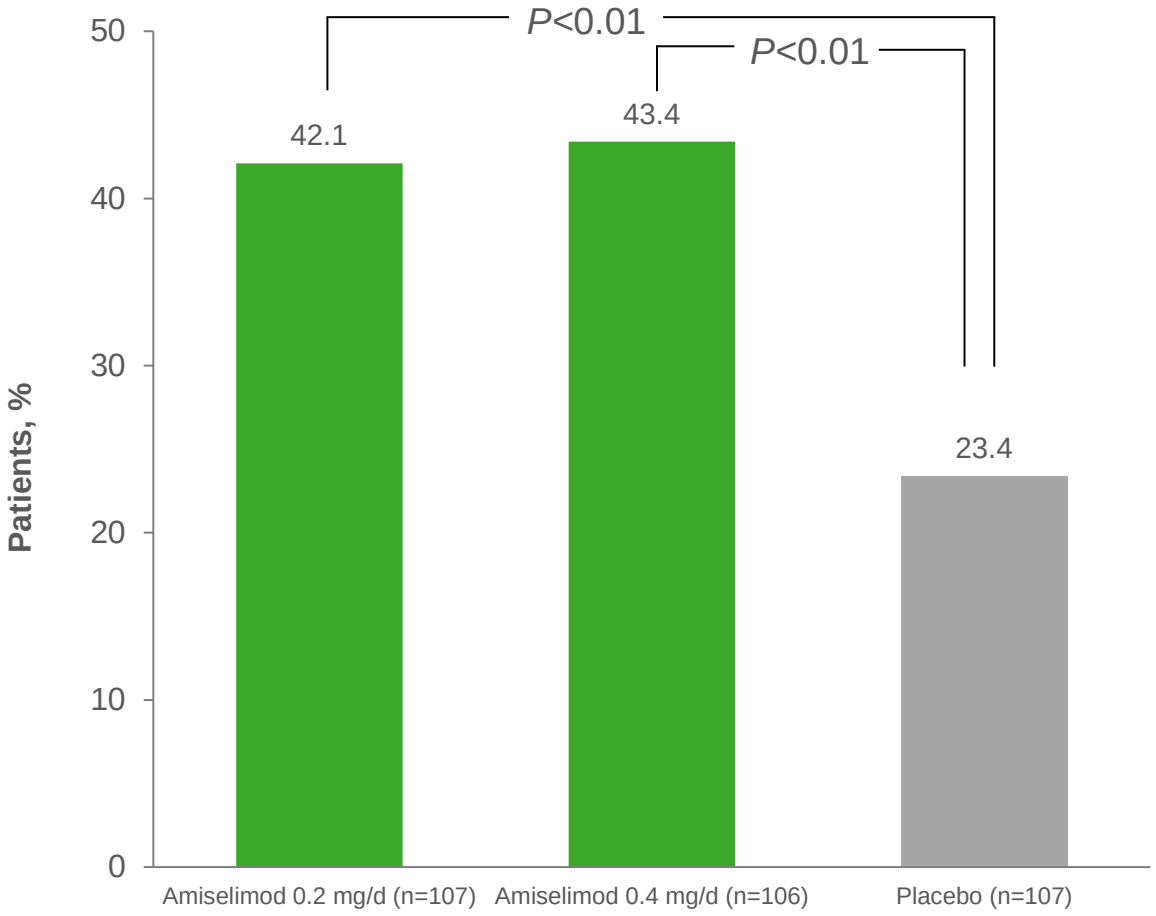
Primary Endpoint: Change From Baseline in MMS (Week 12)



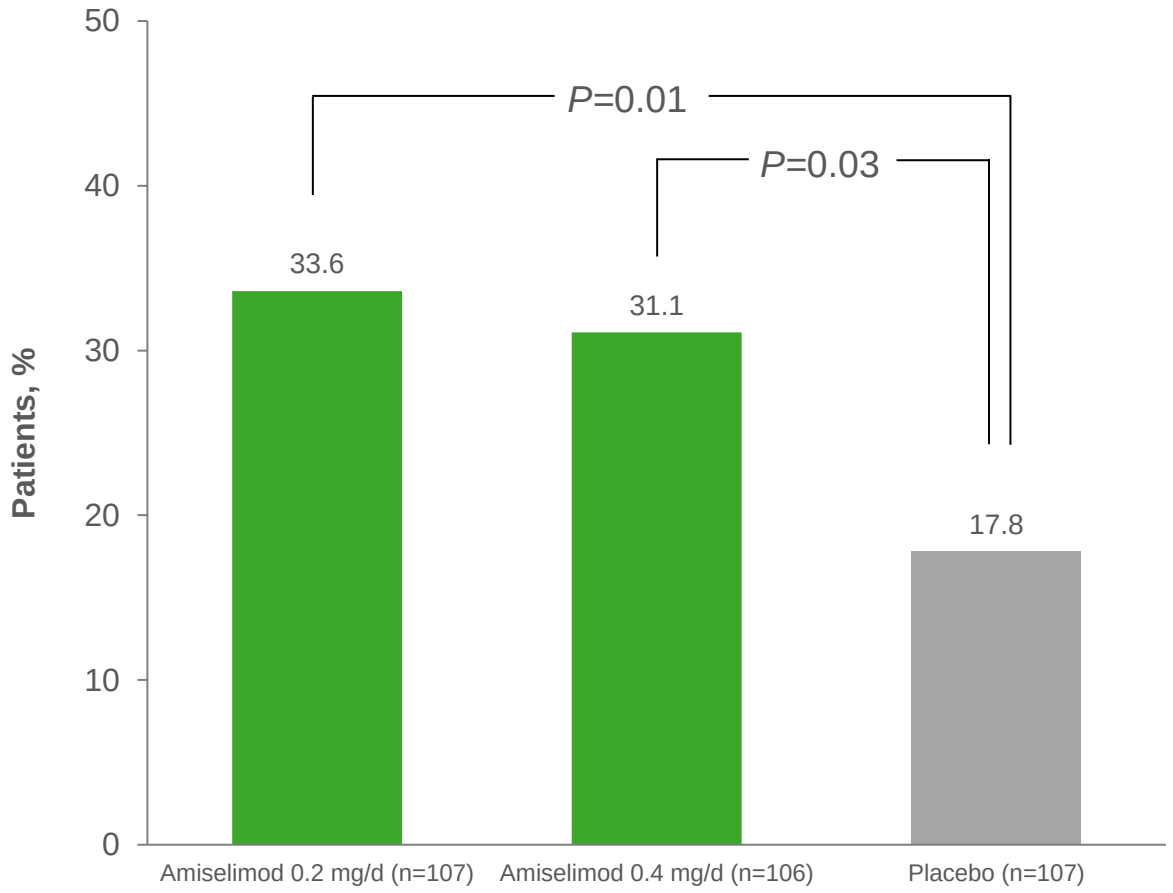
MMS = modified Mayo score.

Secondary Endpoints (Week 12)

Endoscopic improvement*

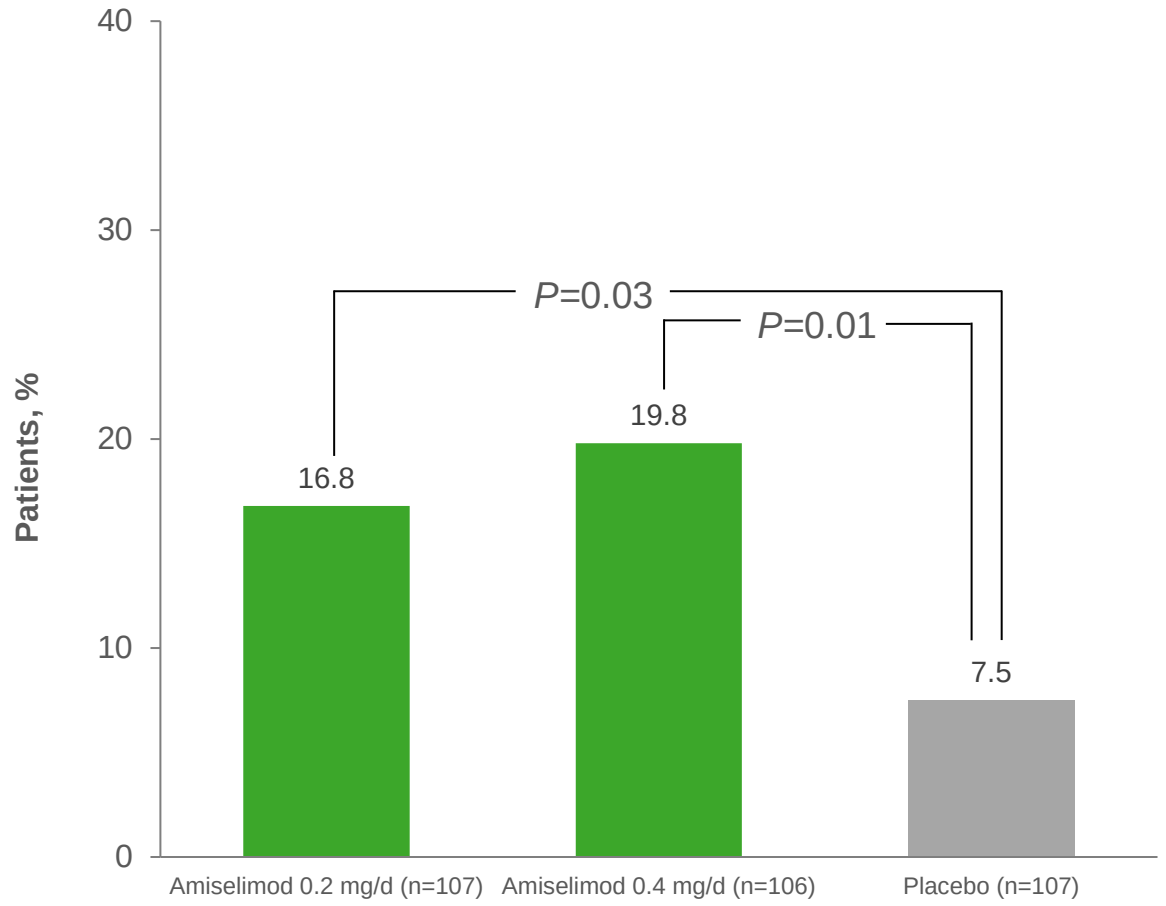


Clinical remission†



*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