ueg week

# Efficacy and safety of tamuzimod in moderately to severely active ulcerative colitis through 52 weeks: phase 2 long-term extension data

Silvio Danese[1], Remo Panaccione[2], Geert D'Haens[3], Stefan Schreiber[4], Vipul Jairath[5], Aaron DuVall[6], Jaroslaw Kierkus[7], Snehal Naik[8], Kye Gilder[8], Beatriz Lindstrom[8], William J. Sandborn[9], Severine Vermeire[10], David T. Rubin[11], Laurent Peyrin-Biroulet[12], and Bruce E. Sands[13]

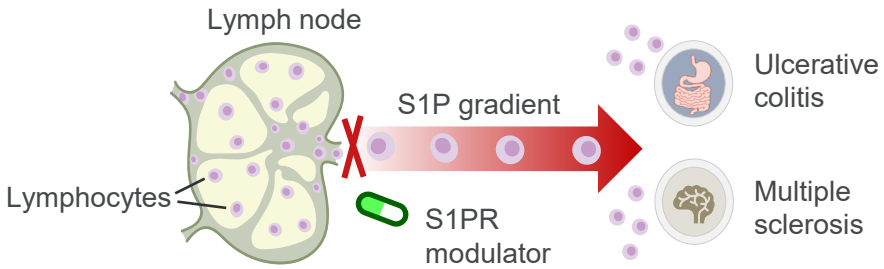
[1]Department of Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy; [2]Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, AB, Canada; [3]Department of Gastroenterology and Hepatology, Amsterdam University Medical Centres, Amsterdam, Netherlands; [4]Hospital Schleswig-Holstein, Department Internal Medicine I, Kiel University, Kiel, Germany; [5]Division of Gastroenterology, Department of Medicine, Western University, London, ON, Canada; [6]Tyler Research Institute, Tyler, TX, USA; [7]Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, The Children's Memorial Health Institute, Warsaw, Poland; [8]Ventyx Biosciences, Inc., San Diego, CA, USA; [9]Division of Gastroenterology, University of California, San Diego, La Jolla, CA, USA; [10]Department of Gastroenterology & Hepatology, University Hospitals Leuven, Leuven, Belgium; [11]Inflammatory Bowel Disease Centre, University of Chicago Medicine, Chicago, IL, USA; [12]Department of Gastroenterology, University of Lorraine, Inserm, NGERE, F-54000 Nancy, France; [13]Dr Henry D Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

# Disclosure

Silvio Danese reports consulting fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Enthera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, Vifor; lecture fees from Abbvie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer, Takeda.

# Background

- S1PR modulators bind S1P receptors on lymphocyte surfaces, leading to receptor internalisation and sequestration of lymphocytes within lymph nodes
- Several S1PR modulators with varying receptor selectivity are approved for the treatment of multiple sclerosis (MS) and/or ulcerative colitis (UC)

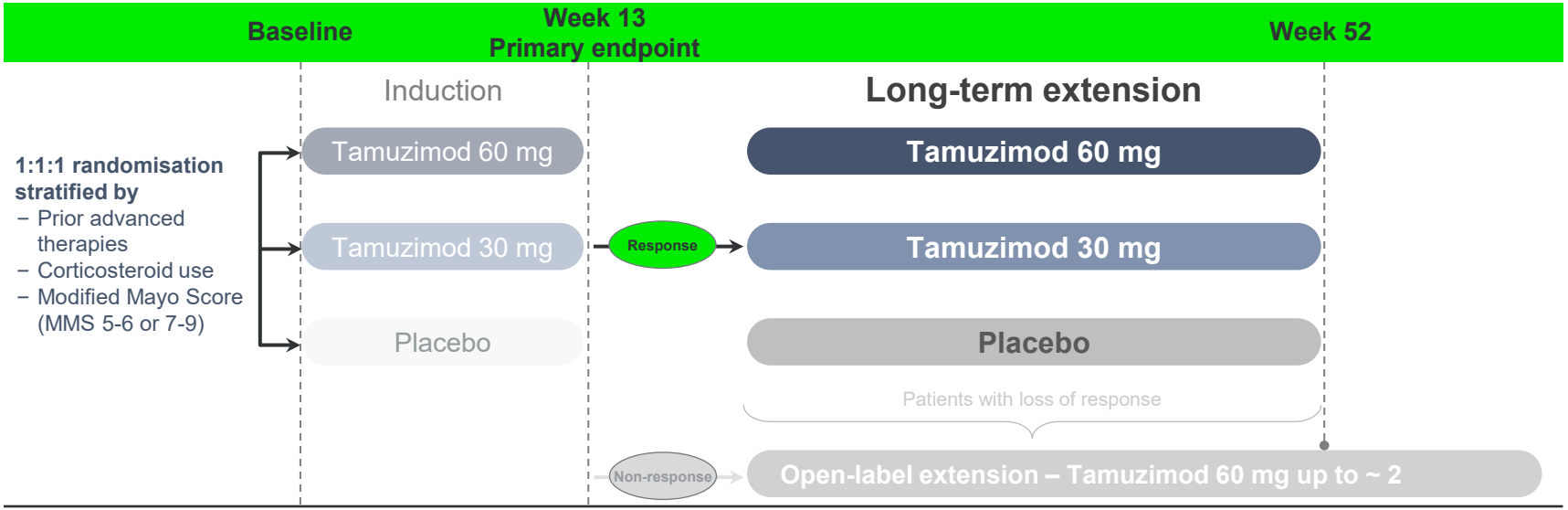



| S1PR modulator | Receptor selectivity | Indication |
|---|---|---|
| Fingolimod | S1PR1, S1PR3, S1PR4, S1PR5 | MS |
| Siponimod | S1PR1 and S1PR5 | MS |
| Ponesimod | S1PR1 | MS |
| Ozanimod | S1PR1 and S1PR5 | MS, UC |
| Etrasimod | S1PR1, S1PR4, S1PR5 | UC |
| Tamuzimod | S1PR1 | UC |

- Tamuzimod (formerly VTX002) is a novel oral selective S1PR1 modulator in development for the treatment of UC
- The efficacy and safety of tamuzimod as induction therapy was previously demonstrated in a phase 2, multicentre, randomised, double-blind, placebo-controlled trial (NCT05156125)[1]

1.Sands BE et al. *Gastroenterology* 2024;166:S-240.

# Study Design



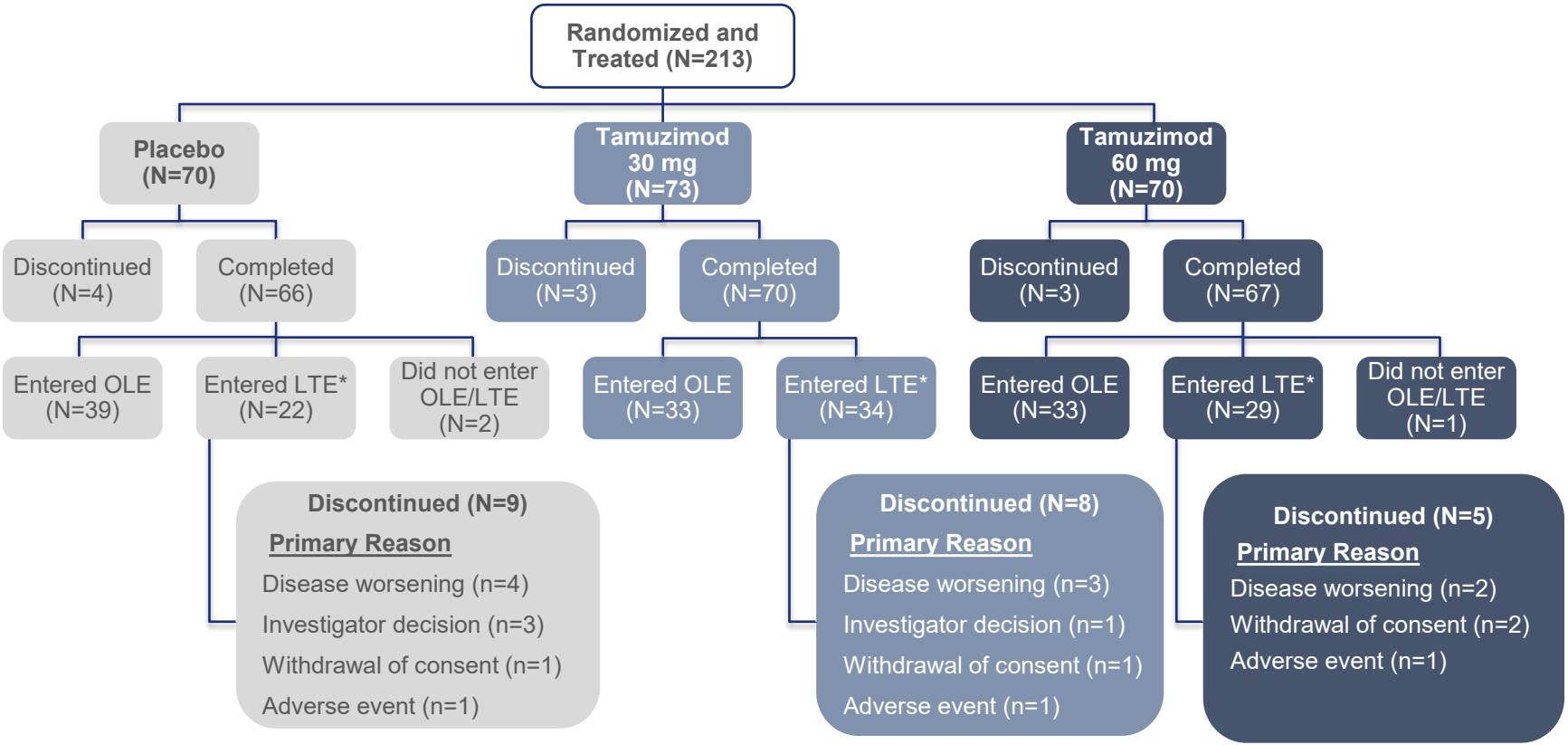

**Key eligibility criteria:**

- Moderately to severely active UC
- No/insufficient response, loss of response, and/or intolerance to conventional or advanced therapies (≤ 2 biologics with different mechanisms of action or 1 biologic + a Janus kinase inhibitor)

**Primary endpoint:** clinical remission (MMS stool frequency (SF) subscore ≤ 1, rectal bleeding (RB) = 0, endoscopic subscore (ES) ≤ 1) at Week 13 in patients with baseline MMS 5-9

**Long-term extension:** clinical responders (≥ 2-point and ≥ 30% decrease from baseline in MMS, and ≥ 1-point decrease from baseline in RB or an absolute RB ≤ 1) at Week 13 were eligible for maintenance therapy with previously assigned treatment for up to 39 weeks

# Patient Disposition




Abbreviations: LTE, long-term extension; OLE, open-label extension.
*Excludes 10 patients (placebo n=3; tamuzimod 30 mg n=3; tamuzimod 60 mg n=4) who incorrectly entered LTE and were moved to OLE. These patients were included in the safety analysis population. Four patients (tamuzimod 30 mg n=2; tamuzimod 60 mg n=2) with baseline modified MMS=4 were excluded from the efficacy analysis population due to a protocol amendment limiting eligibility to patients with a baseline MMS of 5-9. These patients were included in the safety analysis population.

# Disease Characteristics

| | Placebo (N=25) | Tamuzimod 30 mg (N=37) | Tamuzimod 60 mg (N=33) |
|---|---|---|---|
| Duration of UC, years, mean (SD) | 6.1 (5.0) | 7.3 (6.8) | 6.0 (5.3) |
| Extent of UC, n (%) | | | |
| Proctitis | 3 (12%) | 3 (8%) | 2 (6%) |
| Proctosigmoiditis | 10 (40%) | 14 (38%) | 16 (49%) |
| Pancolitis | 11 (44%) | 17 (46%) | 15 (46%) |
| Other | 1 (4%) | 3 (8%) | 0 |
| Modified Mayo score, mean (SD) | 6.8 (1.0) | 6.5 (1.1) | 6.5 (1.0) |
| Mayo endoscopic subscore, n (%) | | | |
| 2 | 13 (52%) | 22 (60%) | 15 (46%) |
| 3 | 12 (48%) | 15 (41%) | 18 (55%) |
| Corticosteroid use at baseline[a], n (%) | 7 (28%) | 11 (30%) | 10 (30%) |
| Prior use of advanced therapies[b], n (%) | 4 (16%) | 8 (22%) | 7 (21%) |
| Prior failure of anti-TNFα | 1 (4%) | 5 (14%) | 2 (6%) |
| Prior failure of vedolizumab | 2 (8%) | 2 (5%) | 1 (3%) |
| Prior failure of JAK inhibitor | 1 (4%) | 1 (3%) | 0 |

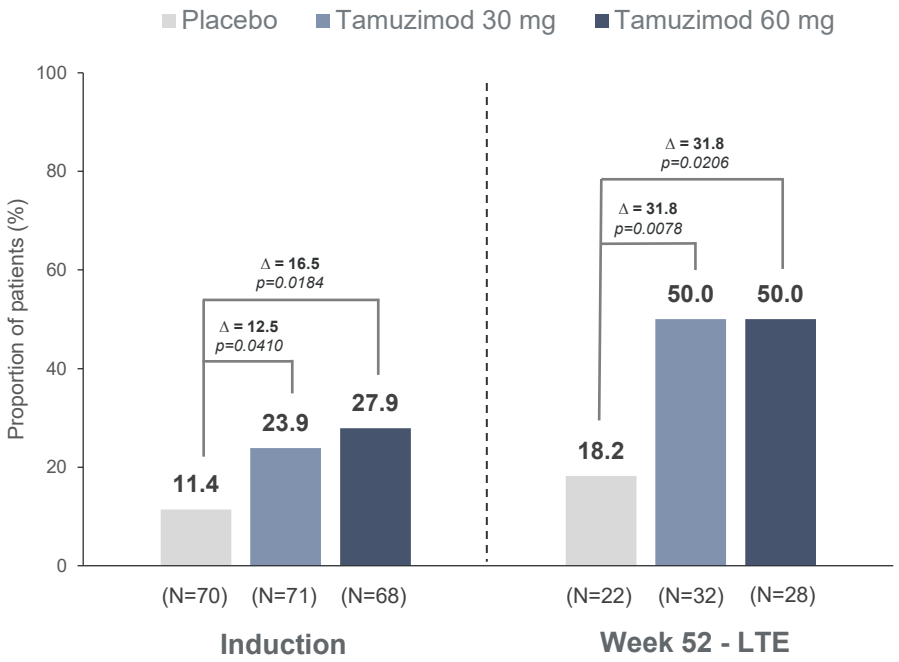
Abbreviations: JAK, Janus kinase; SD, standard deviation; TNF, tumor necrosis factor; UC, ulcerative colitis.

[a] At stable doses (prednisone ≤ 20 mg/day, budesonide ≤ 9 mg/day, or equivalent)

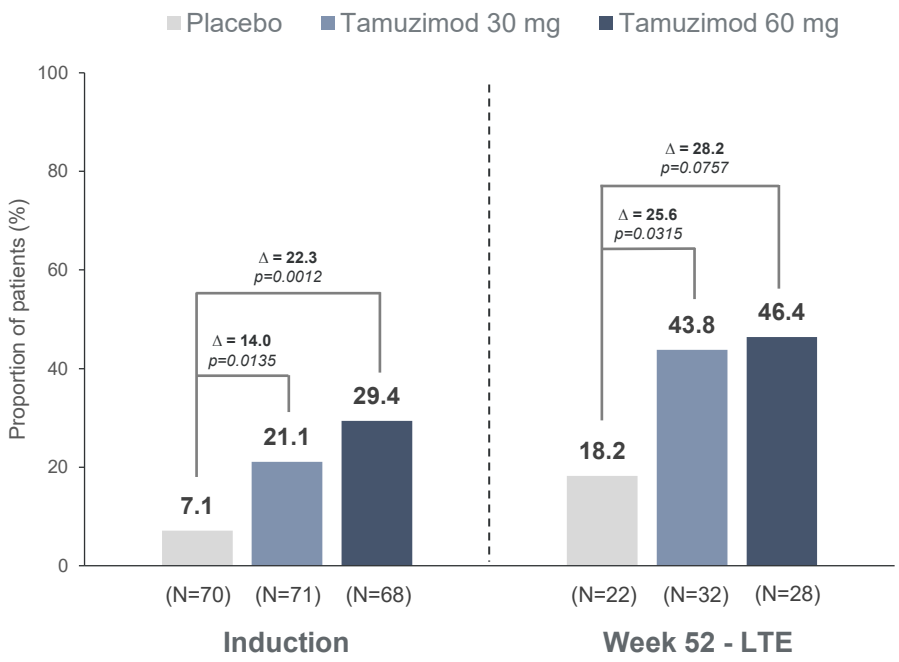
[b] ≤ 2 biologics with different mechanisms of action or 1 biologic + a JAK inhibitor

# Clinical and Endoscopic Remission[1]

## Clinical Remission[a]




## Endoscopic Remission[b]



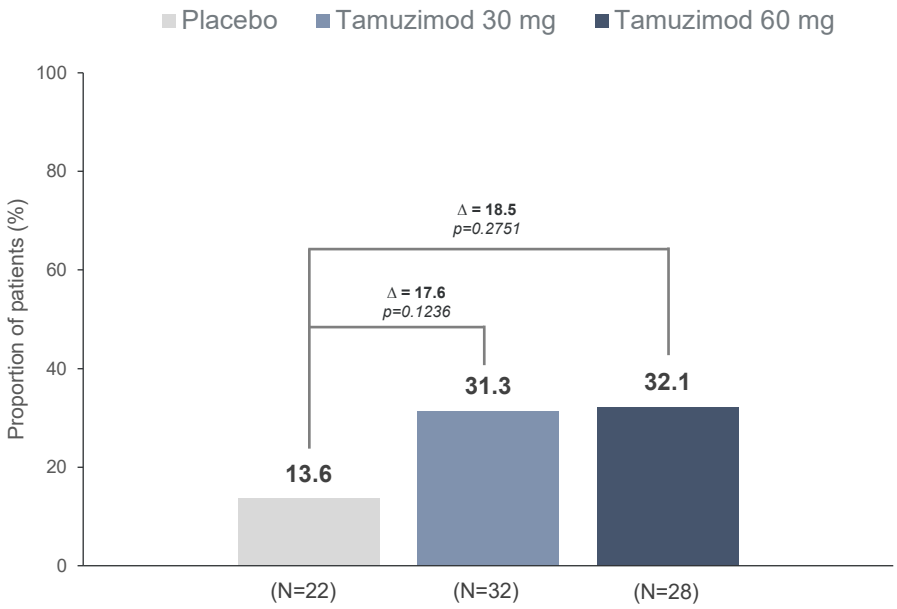

[1]All efficacy outcomes based on non-responder imputation

[a] Modified Mayo stool frequency (SF) subscore ≤ 1, rectal bleeding (RB) subscore = 0, and endoscopic subscore (ES) ≤ 1 (excluding friability)

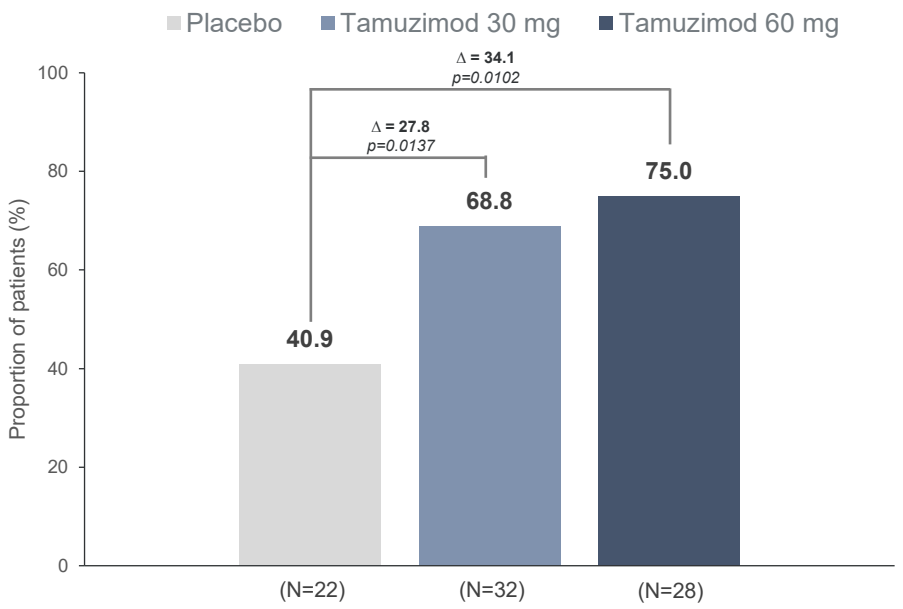
[b] Modified Mayo ES = 0

# Additional Clinical Outcomes at Week 52

## Sustained Clinical Remission[a]




## Symptomatic Remission[b]

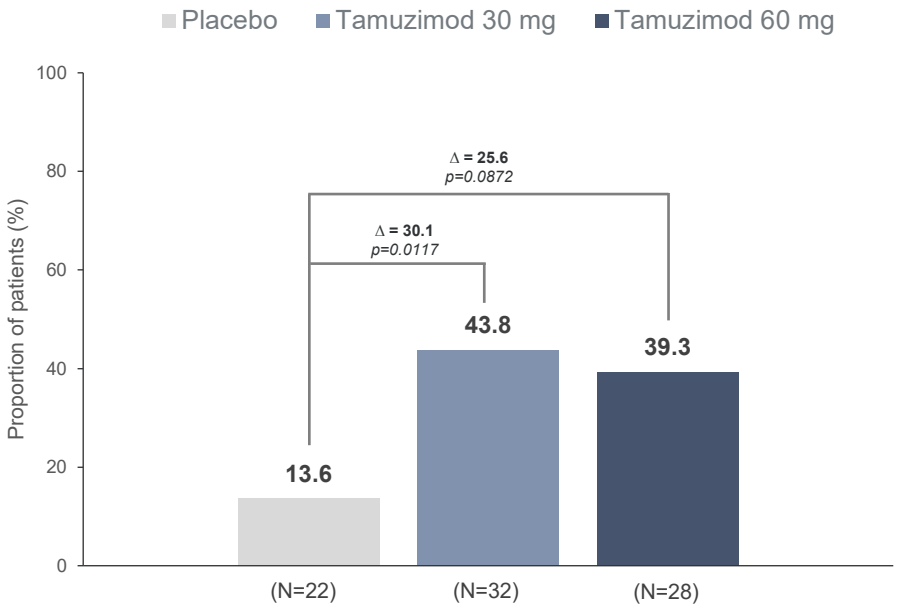



[a] Clinical remission at week 13 and 52

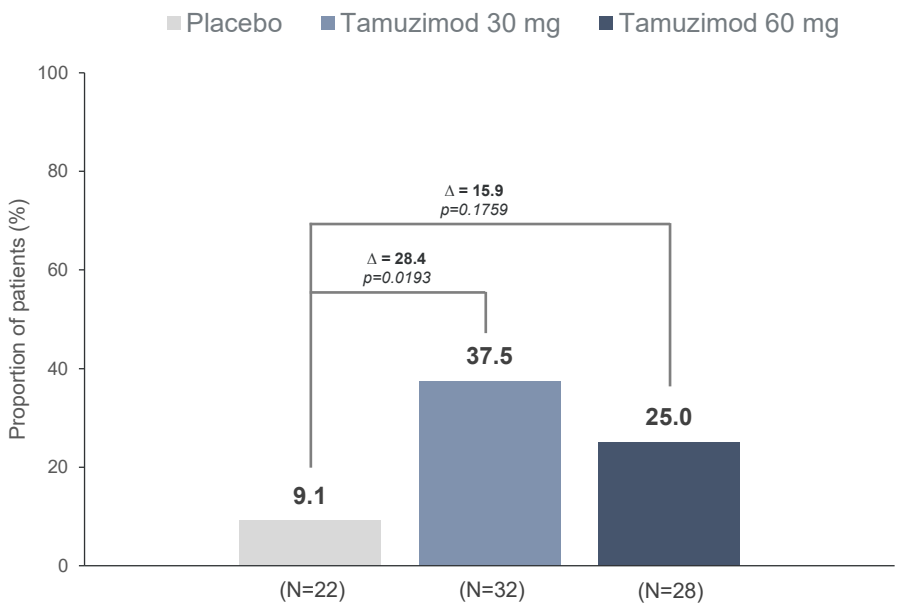
[b] Modified Mayo SF subscore ≤ 1 and RB subscore = 0

# Combined Endoscopic and Clinical or Histologic Remission at Week 52

## Endoscopic and Clinical Remission[a]




## Endoscopic and Histologic Remission[b]

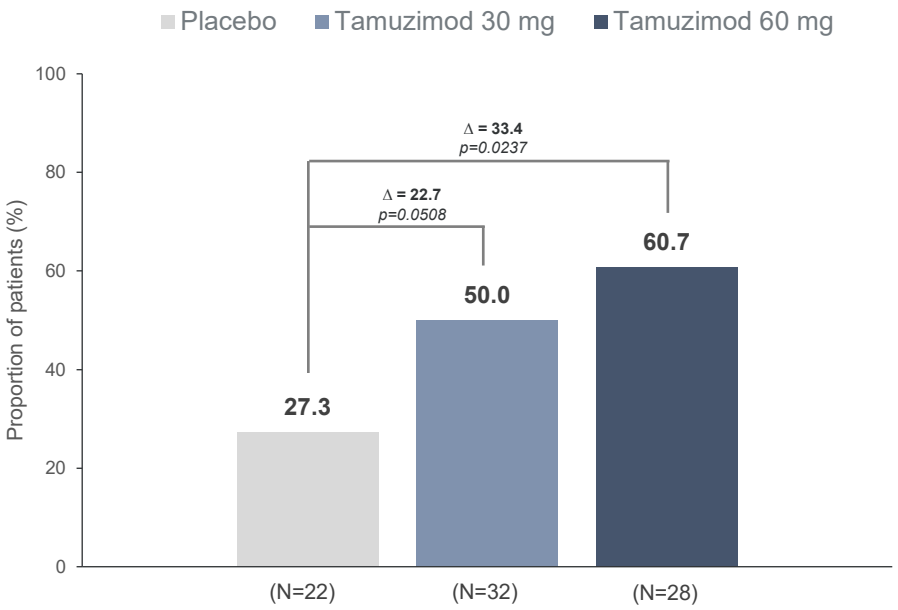



[a] Modified Mayo SF subscore ≤ 1, RB subscore = 0, and ES = 0

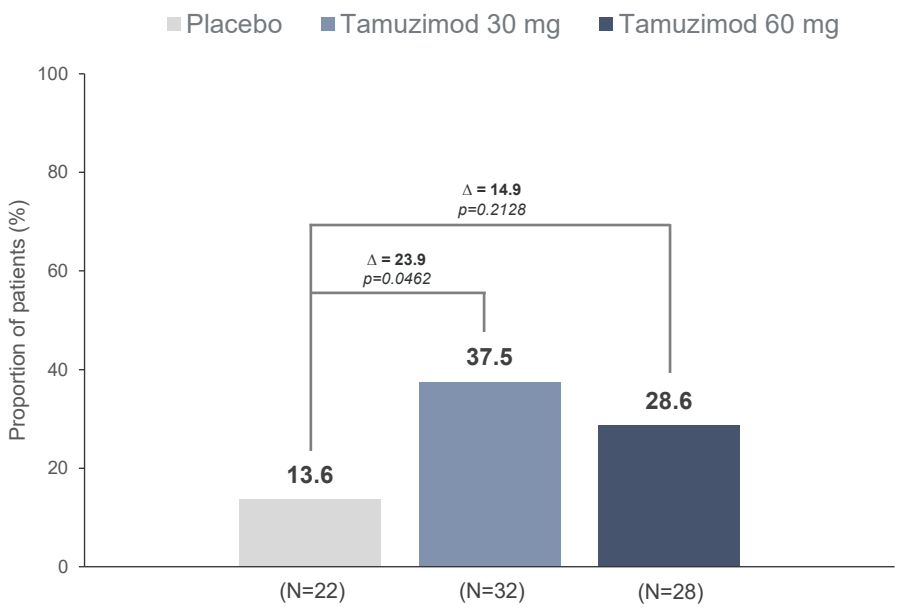
[b] Modified Mayo ES = 0 and Geboes Index score < 2.0

# Endoscopic Improvement and Endoscopic Improvement-Histologic Remission at Week 52

## Endoscopic Improvement[a]




## Endoscopic Improvement-Histologic Remission[b]




[a] Modified Mayo ES ≤ 1 (excluding friability)
[b] Modified Mayo ES ≤ 1 (excluding friability) and Geboes Index score < 2.0

# Safety through Week 52

| | Placebo (N=25) | Tamuzimod 30 mg (N=37) | Tamuzimod 60 mg (N=33) |
|---|---|---|---|
| Any adverse event (AE), n (%) | 13 (52) | 25 (68) | 22 (67) |
| AE related to study drug, n (%) | 2 (8) | 4 (11) | 5 (15) |
| AE leading to study drug discontinuation[a], n (%) | 1 (4) | 1 (3) | 1 (3) |
| Any serious adverse event (SAE), n (%) | 2 (8) | 3 (8) | 0 |
| Gastrointestinal disorders, n (%) | 2 (8) | 2 (5) | 0 |
| Haemorrhagic diarrhoea, n (%) | 0 | 1 (3) | 0 |
| Rectal haemorrhage, n (%) | 0 | 1 (3) | 0 |
| Anal fistula, n (%) | 1 (4) | 0 | 0 |
| Colitis ulcerative, n (%) | 1 (4) | 0 | 0 |
| Hepatobiliary disorders, n (%) | 0 | 1 (3) | 0 |
| Cholecystitis acute, n (%) | 0 | 1 (3) | 0 |
| Infections and infestations, n (%) | 0 | 1 (3) | 0 |
| Peritonitis, n (%) | 0 | 1 (3) | 0 |
| SAE related to study drug, n (%) | 0 | 0 | 0 |
| Death, n (%) | 0 | 0 | 0 |

[a] Oral thrush (Grade 2, placebo, related to study drug); joint pain (Grade 2, 30 mg, related to study drug); alanine aminotransferase increased (Grade 2, 60 mg, related to study drug).

# Conclusion

- Maintenance treatment with both 30 mg and 60 mg tamuzimod was efficacious and well-tolerated for up to 52 weeks
- High rates of both clinical and endoscopic remission observed during tamuzimod induction and maintenance therapy potentially a result of rapid and sustained absolute lymphocyte count (ALC) reductions
  - 58.9% (tamuzimod 30 mg) and 71.5% (tamuzimod 60 mg) ALC decrease from baseline at Week 52
- Efficacy and safety data from this LTE treatment period support the continued clinical development in UC and the use of tamuzimod 60 mg in phase 3