# TUSCANY-2: A Dose-Ranging Phase IIb Study Evaluating Efficacy and Safety of RO7790121, an Antibody Against Tumor Necrosis Factor-like Ligand 1A (Anti-TL1A) in Adults with Moderately to Severely Active Ulcerative Colitis

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# Introduction

- There is a need for continued evolution and novel therapeutic approaches in IBD[1–3]
- TL1A and its receptor DR3 are implicated in immune pathways involved in **IBD pathogenesis and intestinal fibrosis**[1,4,5]
- **RO7790121 is a fully human monoclonal antibody against TL1A**, preventing the binding and subsequent signaling of TL1A to DR3 on immune cells

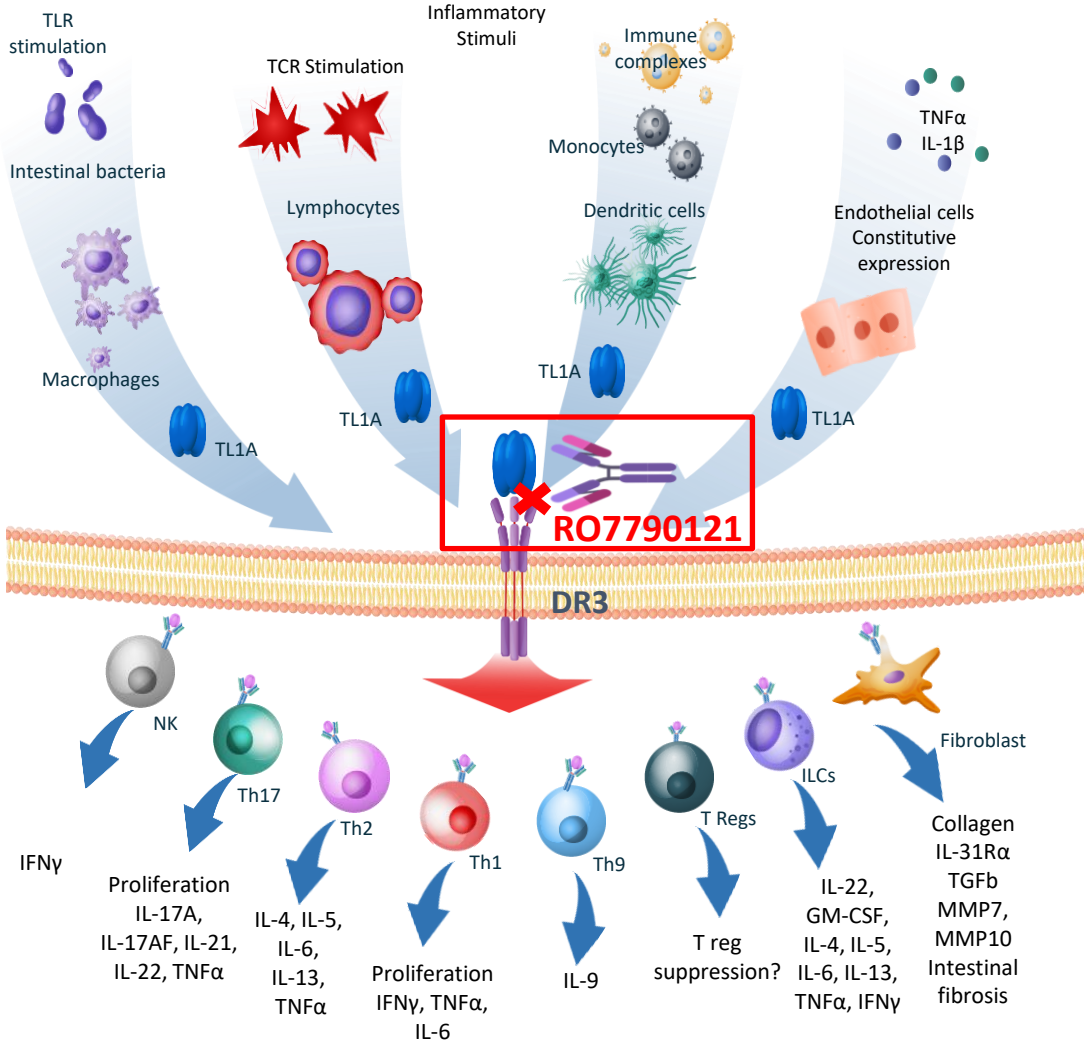



Figure developed with information from: Nakase H, et al. *Autoimmun Rev* 2022;21:103017. Bamias, et al. *Clin Immunol* 2010;137:242–9. Xu et al. *Front Immunol* 2022;13:891328. Solitano V, et al. *Med* 2024;5:386–400. Hassan-Zahraee M, et al. *Inflamm Bowel Dis* 2022;28:434–46.

DR3, death receptor 3; GM-CSF, granulocyte-macrophage colony-stimulating factor; IBD, inflammatory bowel disease; IFN-γ, interferon gamma; IL, interleukin; ILC, innate lymphoid cell; MMP, matrix metalloproteinase; NK, natural killer cell; TCR, T-cell receptor; TGF-β, transforming growth factor beta; Th, T helper; TL1A, TNF-like ligand 1A; TLR, toll-like receptor; TNF, tumour necrosis factor; T reg, regulatory T cell; UC, ulcerative colitis.

1. Furfaro F, et al. *Curr Drug Targets* 2021;22:760–9; 2. Revés J, et al. *Curr Res Pharmacol Drug Discov* 2021;2:100070; 3. Raine T, Danese S. *Gastroenterol* 2022;162:1507–11; 4. Kokkotis G, Bamias G. *Expert Rev Clin Immunol* 2022;18:551–5; 5. Solitano V, et al. *Med* 2024;5:386–400.

# The phase 2b TUSCANY-2 study aimed to evaluate the efficacy and safety of RO7790121 in adult patients with moderately to severely active UC

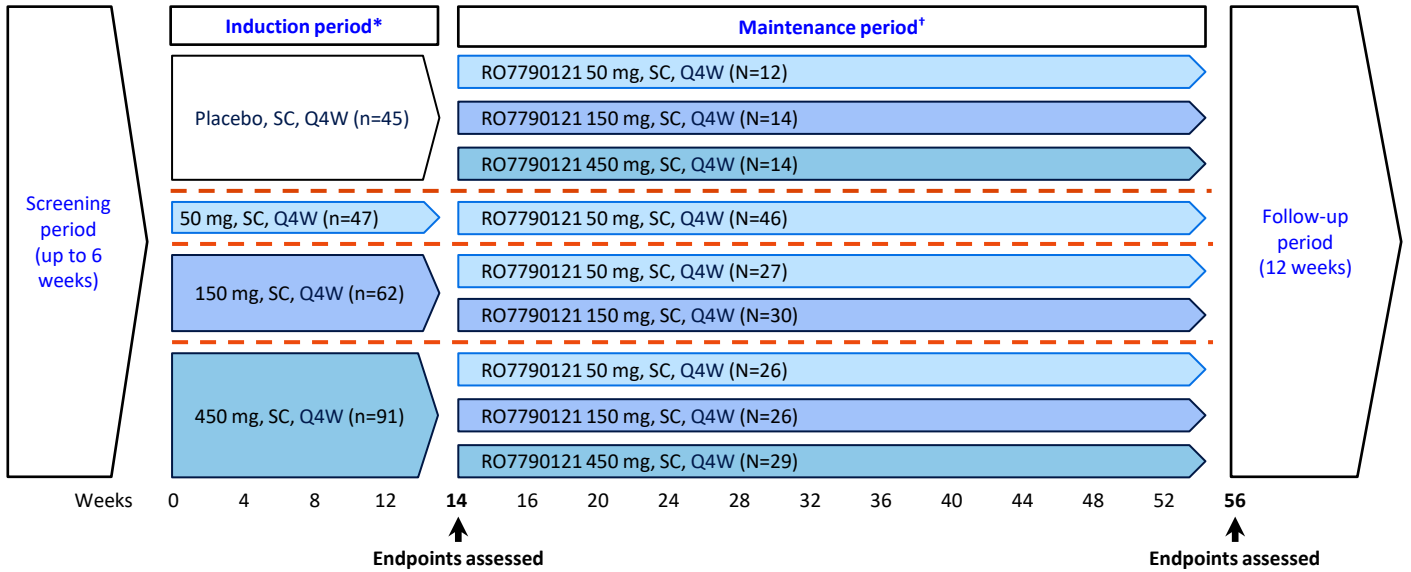


UC, ulcerative colitis.

# TUSCANY-2: a randomized, double-blind, placebo-controlled, treat-through, dose-ranging, phase 2b study

**Key eligibility criteria**

- Patients aged 18–75 years with moderate to severely active UC (total Mayo Score [tMS] ≥6, endoscopic subscore ≥2)
- Previously failed conventional or advanced therapy




**Primary endpoint**

- Clinical remission by tMS at Week 14
- Safety

**Secondary endpoints**

- Clinical remission by modified Mayo Score (mMS) at Week 14
- Clinical remission by tMS, mMS at Week 56
- Endoscopic improvement at Weeks 14 and 56
- Change from baseline in fecal calprotectin through Week 14

*Clinical remission by tMS: tMS ≤2, with no individual subscore >1*
*Clinical remission by mMS: endoscopic subscore =0 or 1, ≥1-point decrease from baseline to achieve a stool frequency subscore =0 or 1, and rectal bleeding subscore =0*
*Endoscopic improvement: endoscopic subscore =0 or 1*

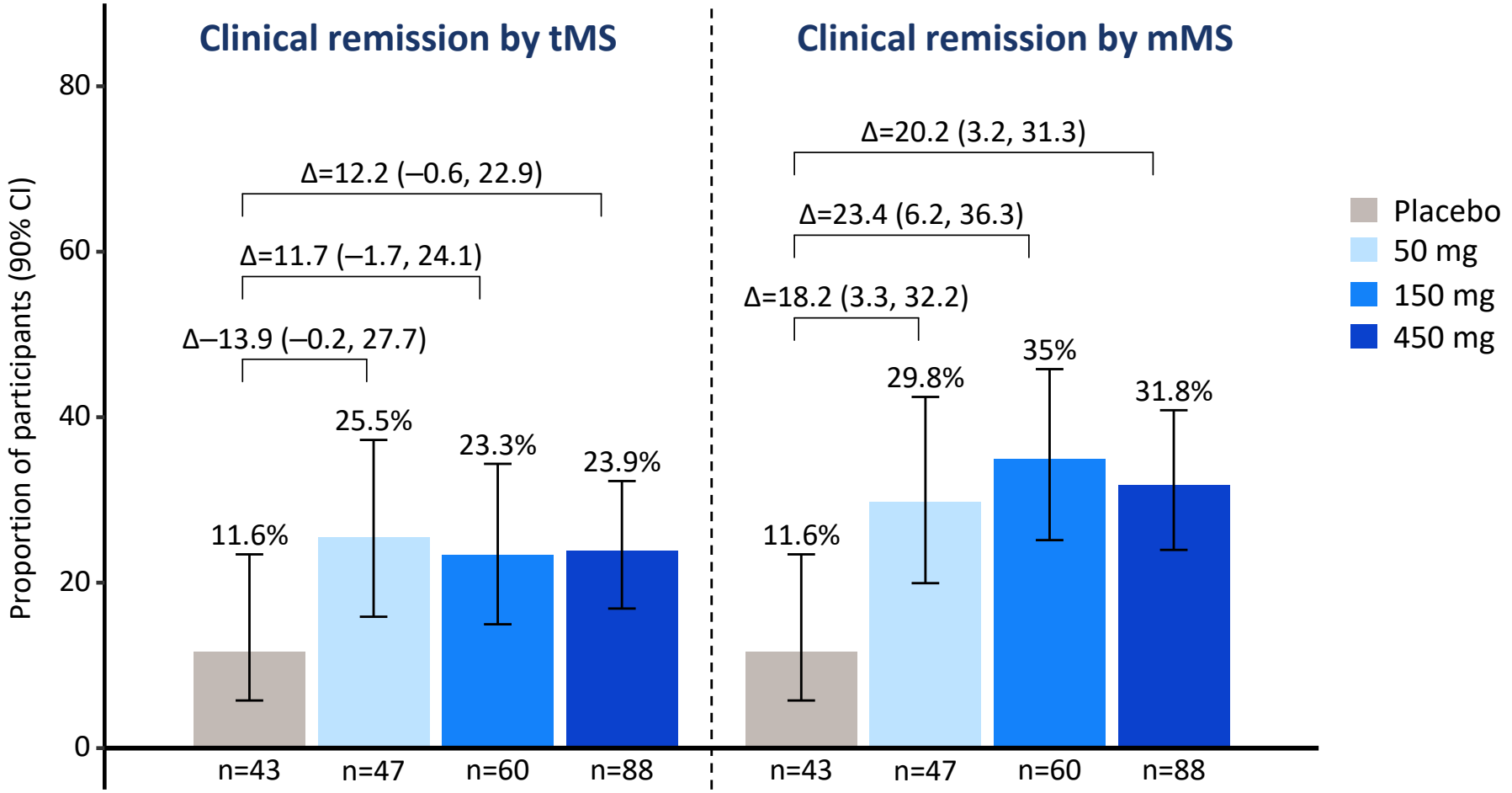
*N=245 received at least one induction dose; †N=224 received at least one maintenance dose.
Clinical trial identification: NCT04090411.
mMS, modified Mayo Score; SC, subcutaneous; tMS, total Mayo Score; Q4W, every 4 weeks.

# Baseline characteristics were generally similar between induction treatment arms

| | Placebo (n=45) | 50 mg (n=47) | 150 mg (n=62) | 450 mg (n=91) | Overall (N=245) |
|---|---|---|---|---|---|
| **Age (yr), mean (SD)** | 39.9 (12.9) | 37.8 (13.9) | 42.2 (13.0) | 41.6 (13.8) | 40.7 (13.5) |
| **Sex, female, n (%)** | 21 (46.7) | 19 (40.4) | 23 (37.1) | 36 (39.6) | 99 (40.4) |
| **BMI (kg/m$^2$), mean (SD)** | 24.4 (5.0) | 23.6 (5.4) | 24.7 (5.2) | 24.6 (5.1) | 24.4 (5.1) |
| **Disease duration (yr), mean (SD)** | 7.6 (7.3) | 6.8 (7.7) | 7.3 (7.4) | 7.5 (6.8) | 7.3 (7.2) |
| **Pancolitis, n (%)** | 19 (42.2) | 16 (34.0) | 23 (37.1) | 38 (41.8) | 96 (39.2) |
| **mMS, median (IQR)*** | 7.0 (6.0–8.0) | 6.0 (5.0–7.0) | 7.0 (6.0–8.0) | 7.0 (6.0–8.0) | 7.0 (6.0–8.0) |
| **Endoscopy subscore, n (%)** | | | | | |
| 2 | 22 (48.9) | 28 (59.6) | 23 (37.1) | 44 (48.4) | 117 (47.8) |
| 3 | 23 (51.1) | 19 (40.4) | 39 (62.9) | 47 (51.6) | 128 (52.2) |
| **Fecal calprotectin (µg/g), median (IQR)** | 1560.0 (927.0– 4,497.0) | 1354.0 (488.0–2,299.0) | 2112.0 (922.0–3,972.0) | 1349.5 (702.0–2,730.0) | 1511.0 (738.0–3,152.0) |
| **Steroid use at baseline, n (%)** | 11 (24.4) | 19 (40.4) | 32 (51.6) | 41 (45.1) | 103 (42.0) |
| **Number of prior advanced therapy failures†, n (%)** | | | | | |
| 0 | 28 (62.2) | 28 (59.6) | 41 (66.1) | 52 (57.1) | 149 (60.8) |
| 1 | 6 (13.3) | 7 (14.9) | 10 (16.1) | 14 (15.4) | 37 (15.1) |
| 2 | 4 (8.9) | 5 (10.6) | 4 (6.5) | 15 (16.5) | 28 (11.4) |
| ≥3 | 7 (15.5) | 7 (14.9) | 7 (11.3) | 10 (11.0) | 31 (12.6) |

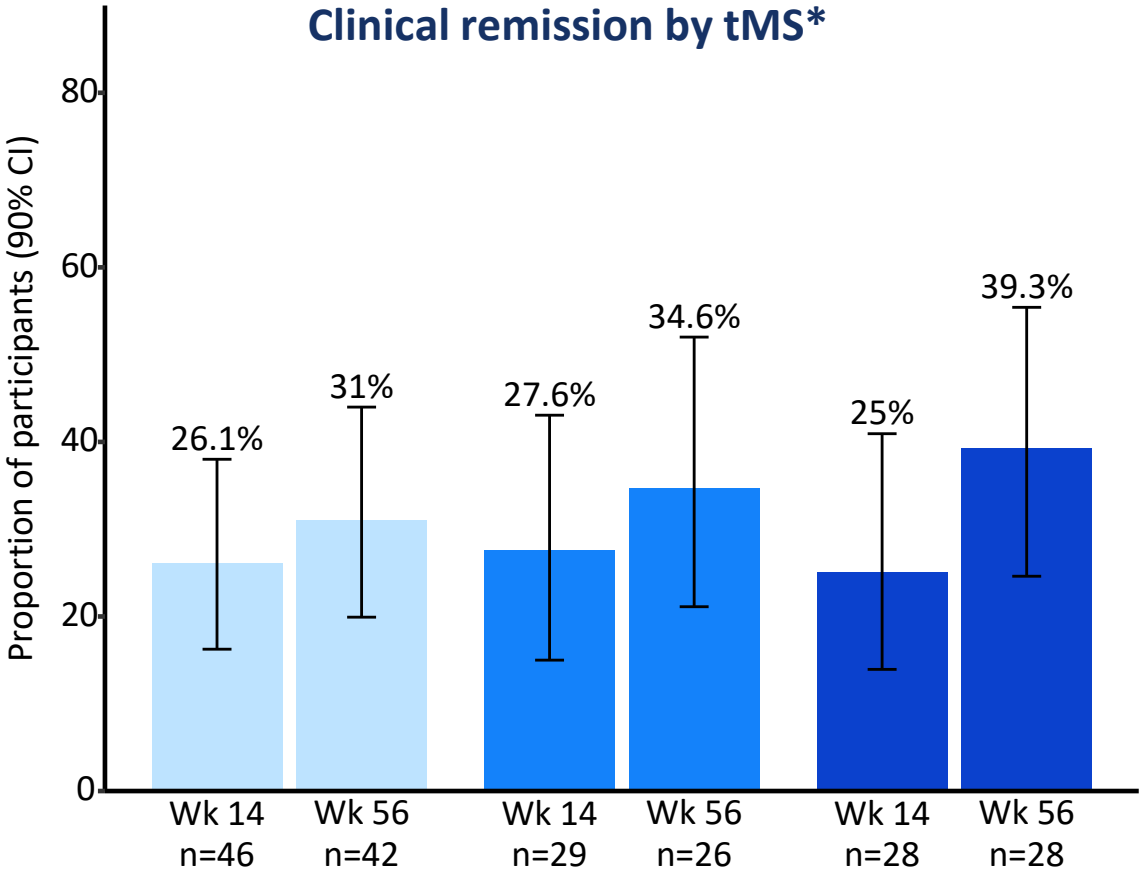
*Data were available for n=61 participants in the RO7790121 150mg group.
†Number of prior failures to the following classes: anti-IL-12/23, anti-integrin, anti-TNF, JAKi.
BMI, Body Mass Index; IQR, interquartile range; JAKi, Janus kinase inhibitor; mMS, modified Mayo Score; SD, standard deviation; TNF, tumor necrosis factor ; yr, year

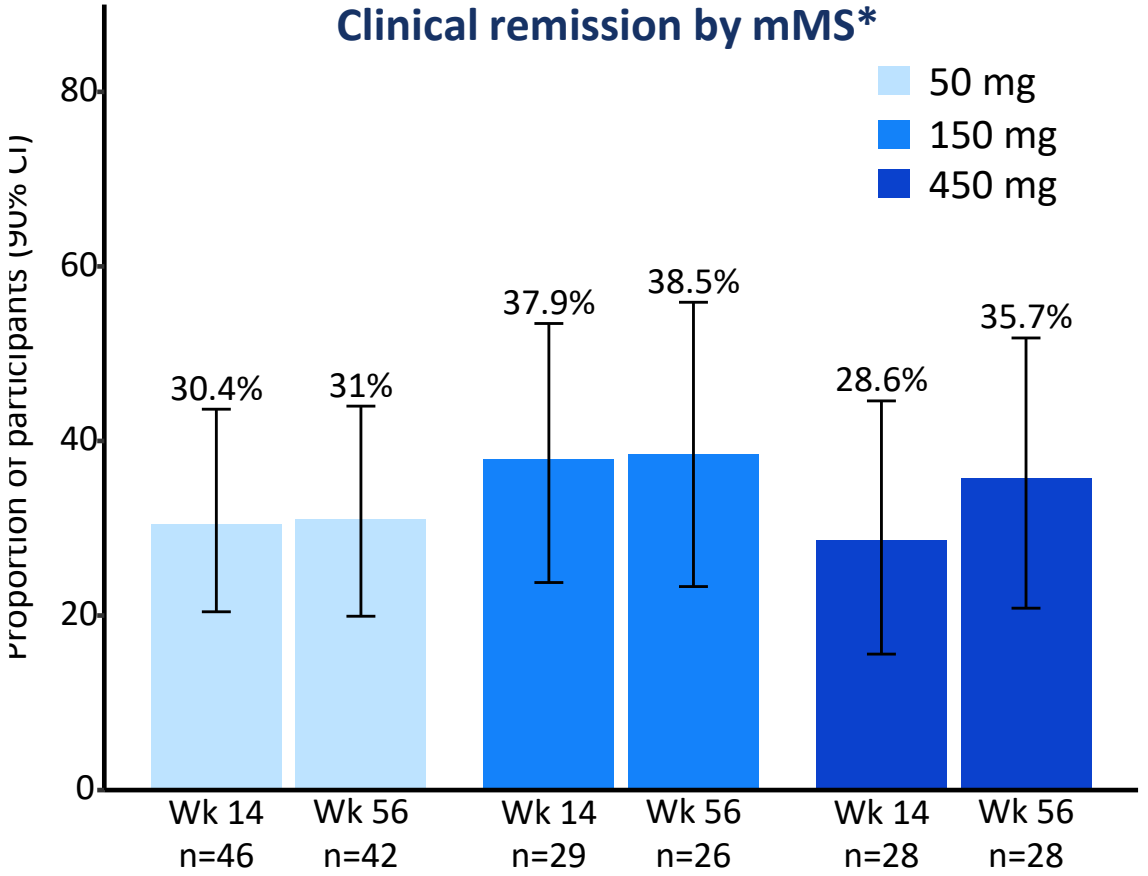
# Higher proportions of patient across all RO7790121 doses experienced clinical remission vs placebo at Week 14




Clinical remission by tMS defined as tMS ≤2, with no individual subscore >1.
Clinical remission by mMS defined as endoscopic subscore =0 or 1, ≥1-point decrease from baseline to achieve a stool frequency subscore =0 or 1, and rectal bleeding subscore =0.
Excluding 7 participants with missing data due to medical or operational complications resulting from COVID-19.
CI, confidence interval; COVID-19, coronavirus disease 2019; mMS, modified Mayo Score; tMS, total Mayo Score.

# Remission rates at Week 14 were sustained through Week 56 in participants treated with RO7790121



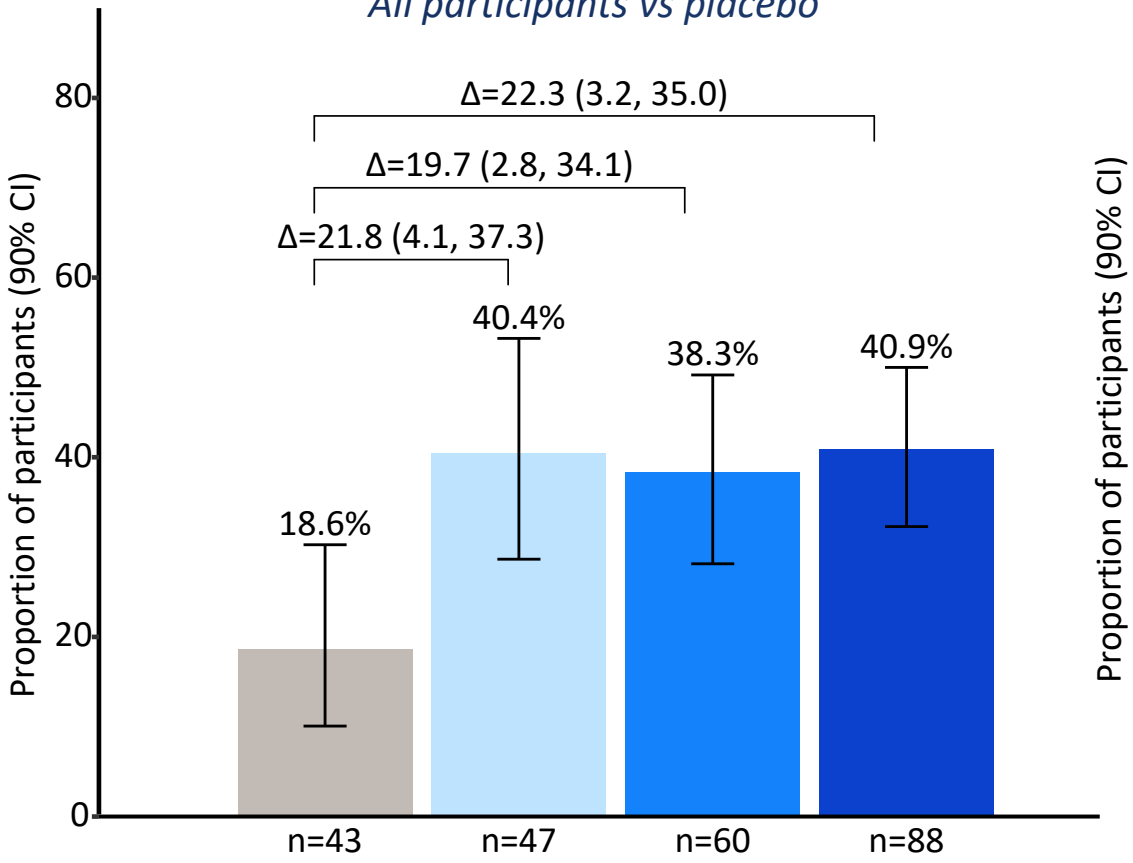




Clinical remission by tMS defined as tMS ≤2, with no individual subscore >1.
or 1, ≥1-point decrease from baseline to achieve a stool frequency subscore =0 or 1, and rectal bleeding subscore =0.
Excluding participants with missing data due to medical or operational complications resulting from COVID-19.
*Data shown for participants receiving the same RO7790121 dose during both the induction and maintenance period of the study (50 mg → 50 mg; 150 mg → 150 mg; 450 mg → 450 mg).
The maintenance period of the study did not include a placebo arm.
CI, confidence interval; COVID-19, coronavirus disease 2019; mMS, modified Mayo Score; tMS, total Mayo Score; wk, Week.

# Rates of endoscopic improvement at Week 14 were greater in participants receiving RO7790121 vs placebo, sustained up to Week 56

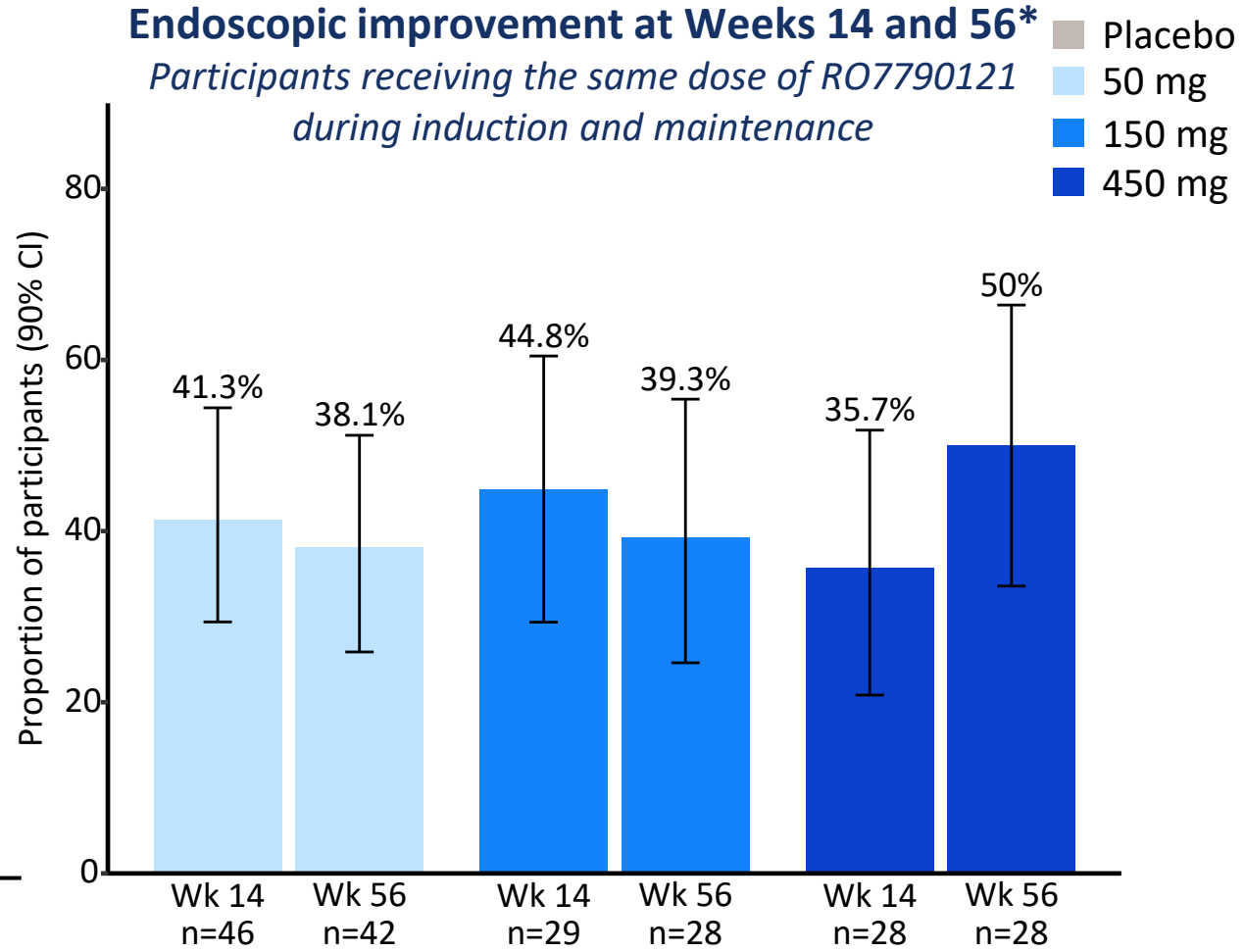
## Endoscopic improvement at Week 14

*All participants vs placebo*




## Endoscopic improvement at Weeks 14 and 56*

*Participants receiving the same dose of RO7790121 during induction and maintenance*



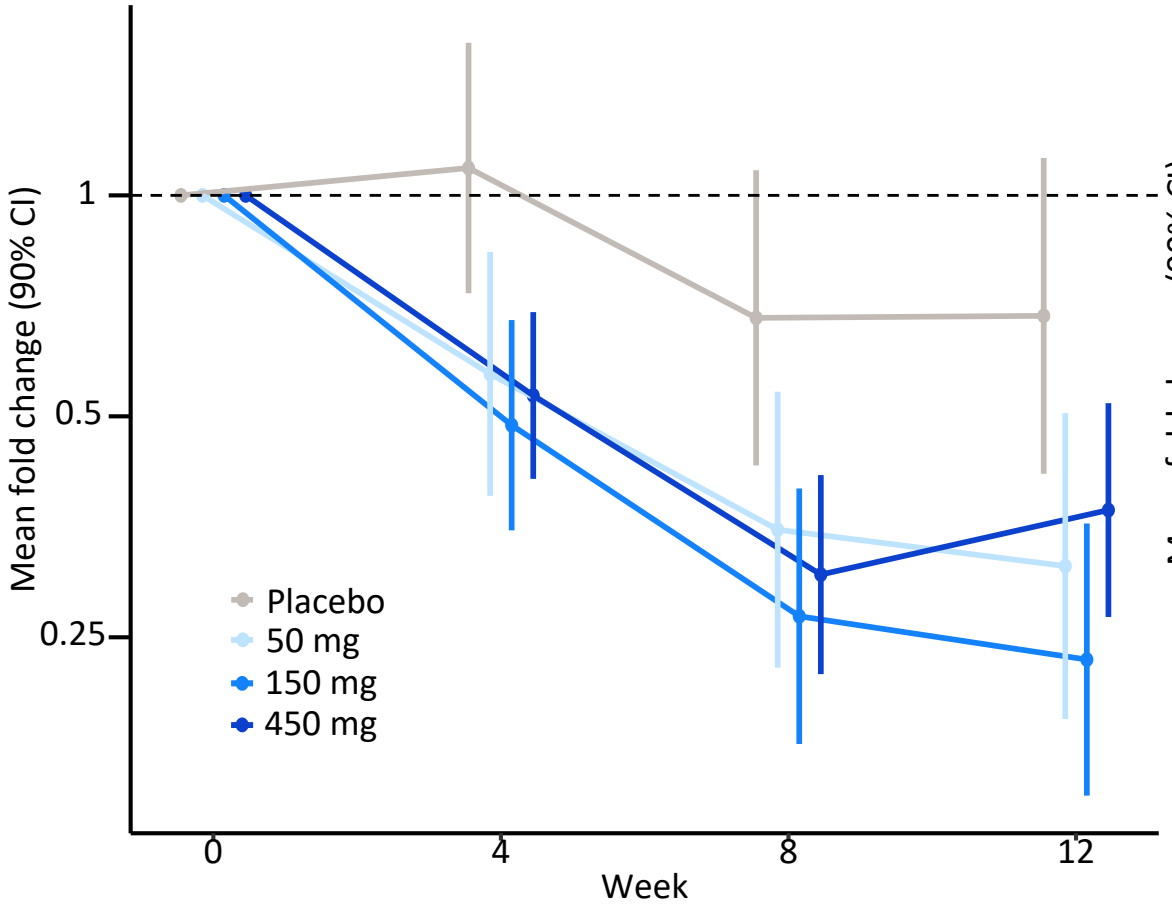

Endoscopic improvement defined as endoscopic subscore =0 or 1.

*Data shown for participants receiving the same RO7790121 dose during both the induction and maintenance period of the study (50 mg → 50 mg; 150 mg → 150 mg; 450 mg → 450 mg). Excluding participants with missing data due to medical or operational complications resulting from COVID-19. The maintenance period of the study did not include a placebo arm.

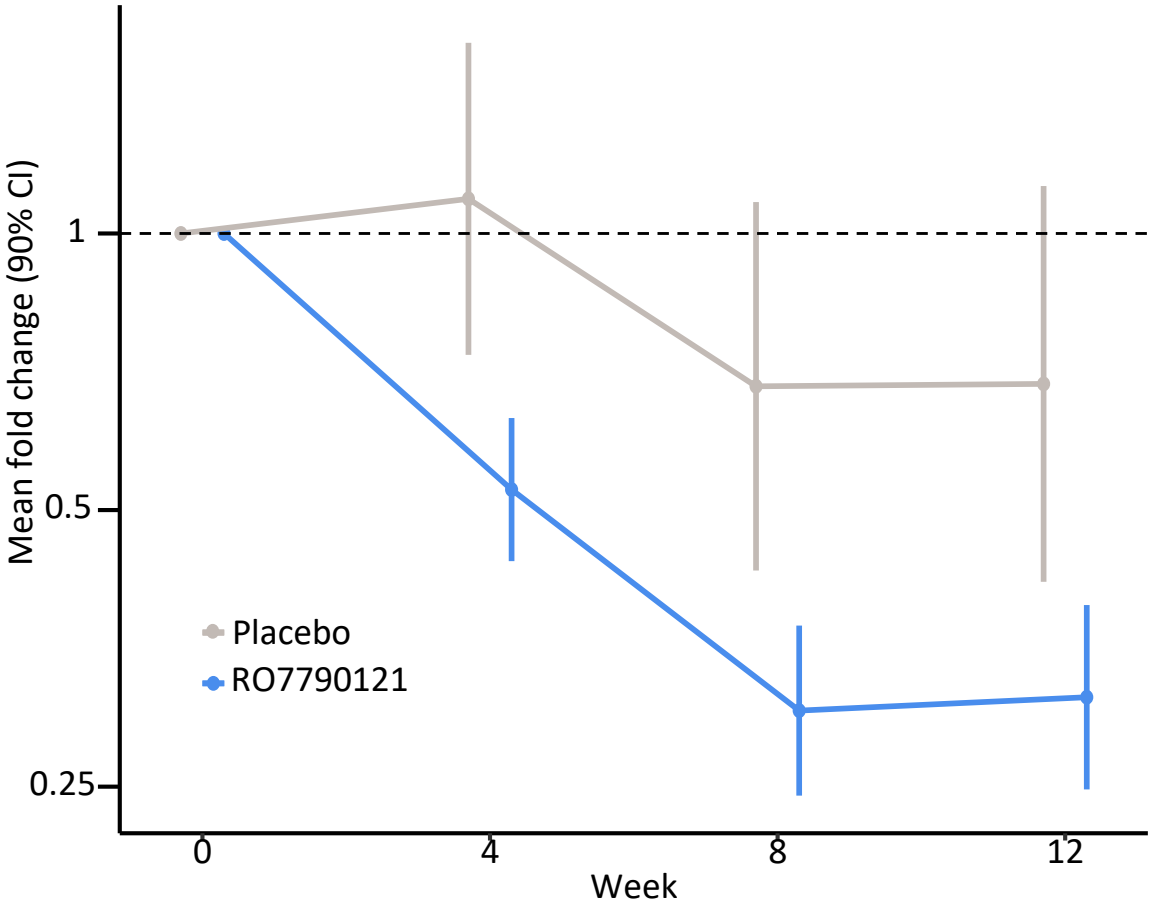
CI, confidence interval; COVID-19, coronavirus disease 2019; wk, week.

# Substantial decreases in fecal calprotectin were observed between baseline and Week 12 across all RO7790121 doses vs placebo

## Mean fecal calprotectin fold change (µg/g) at weeks 0, 4, 8 and 12




## Mean fecal calprotectin fold change (µg/g) at weeks 0, 4, 8, and 12 (combined RO7790121 doses)






CI, confidence interval.

# Safety results

## Induction period*

| | Placebo (N=45) | 50 mg (N=47) | 150 mg (N=62) | 450 mg (N=91) | Total (N=245) |
|---|---|---|---|---|---|
| **Participants with any adverse event, n (%)** | 25 (55.6) | 16 (34.0) | 28 (45.2) | 48 (52.7) | 117 (47.8) |
| Participants with serious adverse events | 4 (8.9) | 3 (6.4) | 0 (0.0) | 3 (3.3) | 10 (4.1) |
| Participants discontinued study drug due to adverse events | 3 (6.7) | 1 (2.1) | 1 (1.6) | 1 (1.1) | 6 (2.4) |
| **Participants with treatment-related adverse events, n (%)** | 4 (8.9) | 6 (12.8) | 9 (14.5) | 13 (14.3) | 32 (13.1) |
| Participants with serious treatment-related adverse events | 1 (2.2) | 0 (0.0) | 0 (0.0) | 1 (1.1) | 2 (0.8) |

## Maintenance period†

| | N/A | 50 mg → 50 mg (N=46) | 150 mg → 150 mg (N=30) | 450 mg→ 450mg (N=29) | Total maintenance population (N=224) |
|---|---|---|---|---|---|
| **Participants with any adverse event, n (%)** | | 28 (60.9) | 15 (50.0) | 19 (65.5) | 132 (58.9) |
| Participants with serious adverse events | | 4 (8.7) | 0 (0.0) | 4 (13.8) | 12 (5.4) |
| Participants discontinued study drug due to adverse events | | 3 (6.5) | 0 (0.0) | 1 (3.4) | 11 (4.9) |
| **With treatment-related adverse events, n (%)** | | 5 (10.9) | 2 (6.7) | 2 (6.9) | 30 (13.4) |
| Participants with serious treatment-related adverse events | | 0 (0.0) | 0 (0.0) | 1 (3.4) | 1 (0.4) |

The denominator for percentage calculation was the number of participants evaluable for adverse events in the given treatment group.
Results based on Final CSR (primary completion date) Version 1.0 16-June-2023.
*Included all adverse events starting during induction period only.
†Included all adverse events starting during maintenance period or follow-up period up to Week 56. Data shown for participants receiving the same RO7790121 dose during both the induction and maintenance period of the study. These data are consistent with the overall mITT safety population.
mITT population was defined as all participants randomly assigned to investigational product and who took at least one dose of investigational product in maintenance period.
mITT, modified Intention-To-Treat; N/A, non-applicable.

# Conclusions

- **Treatment with RO7790121 resulted in notable improvements in efficacy endpoints**
  - Clinically meaningful improvements in clinical remission by tMS, mMS, as well as endoscopic improvements were seen across all RO7790121 doses versus placebo at week 14, and these were sustained up to week 56
- **Substantial decreases in fecal calprotectin were observed between baseline and Week 12 across all RO7790121 doses compared with placebo**
- **RO7790121 was well tolerated, with a favorable safety profile**

Results from the phase 2b TUSCANY-2 dose-ranging study suggest that RO7790121 has a favorable benefit/risk profile with clinically meaningful improvements in participants with moderately to severely active UC



mMS, modifed Mayo Score; tMS, total Mayo Score; UC, ulcerative colitis.

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