# TREMFYA® (guselkumab)
# TREMFYA - Treatment of ulcerative colitis - QUASAR program

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## Phase 3 studies: overview

- A randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial program that evaluated the efficacy and safety of TREMFYA during induction and maintenance studies in adults with moderately to severely active UC.[1]
- The primary endpoints were clinical remission at week 12 during induction, and clinical remission at week 44 during maintenance.[1]

## Phase 3 studies: efficacy

**Induction study**

Outcomes at week 12 with TREMFYA 200 mg IV Q4W (N=421) vs placebo (N=280)[1]:

- Clinical remission (primary endpoint): 23% vs 8% (*P*<0.0001).
- Clinical response: 62% vs 28% (*P*<0.0001).
- Endoscopic improvement: 27% vs 11% (*P*<0.0001).

**Maintenance study**

Outcomes at week 44 with TREMFYA 100 mg SC Q8W (N=188) and TREMFYA 200 mg SC Q4W (N=190) vs placebo (N=190)[1]:

- Clinical remission (primary endpoint): 45% and 50% vs 19% (*P*<0.0001 for both).
- Corticosteroid-free clinical remission: 45% and 49% vs 18% (*P*<0.0001 for both).
- Maintenance of clinical remission:
  - TREMFYA 100 mg SC Q8W (61%) vs placebo (34%); *P*=0.0036
  - TREMFYA 200 mg SC Q4W (72%) vs placebo (34%); *P*<0.0001
- Endoscopic remission (normalization): 35% and 34% vs 15% (*P*<0.0001 for both).
- HEMI: 44% and 48% vs 17% (*P*<0.0001 for both).

## Phase 3 studies: safety

**Induction study**

Outcomes with TREMFYA 200 mg IV Q4W (N=421) vs placebo (N=280), respectively, at week 12[1,2]:

- AEs: 208 (49%) vs 138 (49%).
- SAEs: 12 (3%) vs 20 (7%).
- Serious infections: 3 (1%) vs 1 (0.4%).
- Most frequent AEs ≥5%: worsening of UC, anemia, COVID-19, headache, arthralgia, and upper RTI.

**Maintenance study**

Outcomes with TREMFYA 100 mg Q8W (N=186) and TREMFYA 200 mg Q4W (N=190) vs placebo (N=192), respectively, at week 44[1,2]

- AEs: 120 (65%) and 133 (70)% vs 131 (68%).
- Most frequent AEs: worsening of UC, anemia, COVID-19, headache, arthralgia, upper RTI.
- No cases of death, serious hepatic AEs, active tuberculosis, opportunistic infection, anaphylaxis, or serum sickness were reported among TREMFYA-treated patients in the primary safety population.

## Phase 2b study: overview

- A randomized, double-blind, placebo -controlled, dose-ranging study evaluated the efficacy and safety of TREMFYA as an induction therapy in adults with moderately to severely active UC.[3]
- The primary endpoint was clinical response at week 12.[3]

## Phase 2b study: efficacy

**Induction study**

Outcomes among patients receiving TREMFYA 200 mg vs TREMFYA 400 mg vs placebo at week 12[3,4]:

- Clinical response at week 12: 61.4% vs 60.7% vs 27.6% (*P*<0.001).

## Phase 2b study: safety

**Induction study**

Outcomes among patients receiving TREMFYA vs placebo at week 32[5]:

- AEs: 45 (44.6%) vs 53 (49.5%) vs 59 (56.2%).
- SAEs: 1 (1.0%) vs 3 (2.8%) vs 7 (6.7%).
- Infections: 14 (13.9%) vs 10 (9.3%) vs 13 (12.4%).
- Serious infections: 0 vs 0 vs 2 (1.9%).
- Most frequent AEs: anemia, headache, worsening of UC, COVID-19, arthralgia, and abdominal pain.

AE, adverse event; COVID-19, coronavirus disease 2019; HEMI, histo-endoscopic mucosal improvement; IV, intravenous; Q4W, every 4 weeks; Q8W, every 8 weeks; RTI, respiratory tract infection; SAE, serious adverse event; SC, subcutaneous; UC, ulcerative colitis.

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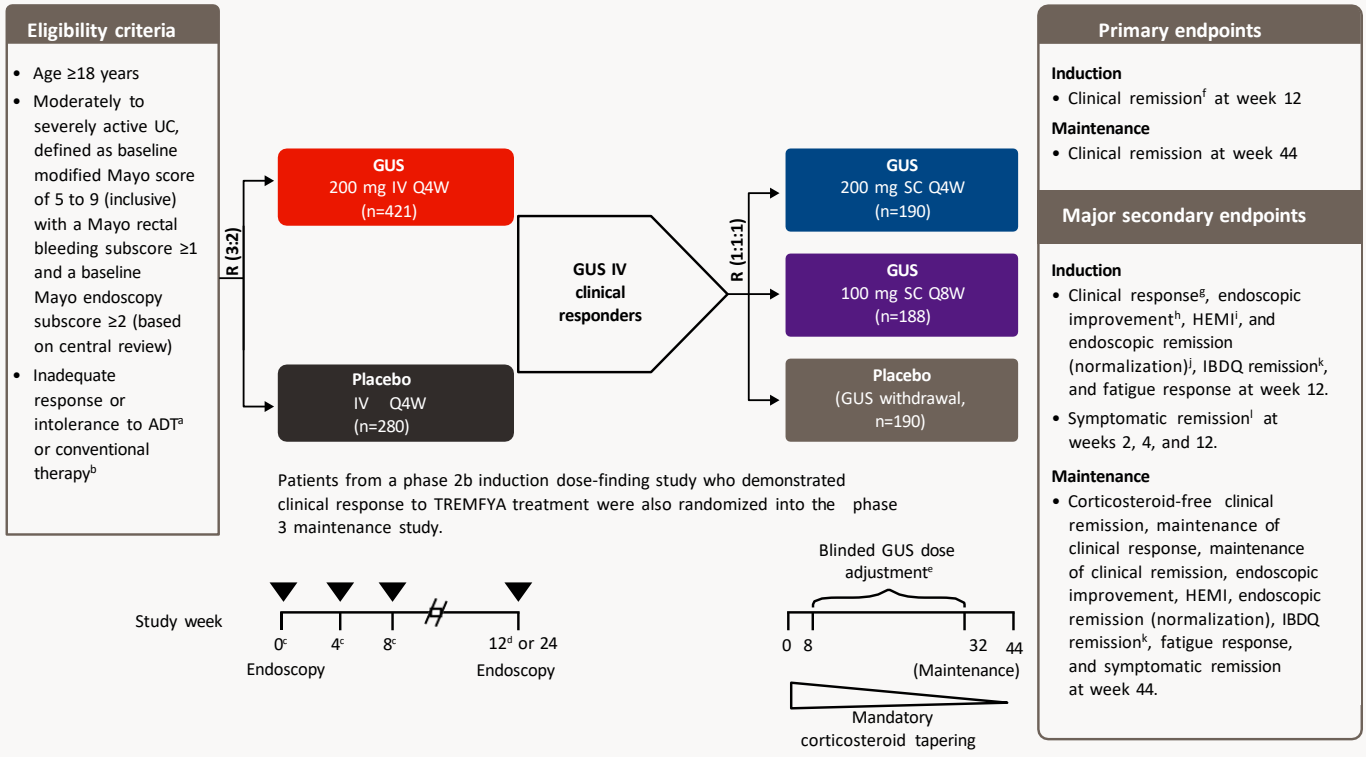
## Phase 3 study design[1,2,6,7,8]




[a]TNF alpha antagonists, vedolizumab, or tofacitinib.

[b]Corticosteroids or thiopurines.

[c]Study treatment administered.

[d]Study treatment administered to week 12 clinical nonresponders.

[e]Between week 8 and week 32, randomized patients meeting loss of clinical response criteria (based on the modified Mayo score and requiring an endoscopic assessment) were eligible for blinded dose adjustment as follows: Placebo SC→GUS 200 mg SC Q4W (rescue treatment), GUS 100 mg SC Q8W→GUS 200 mg SC Q4W, GUS 200 mg SC Q4W→GUS 200 mg SC Q4W (sham adjustment).

[f]Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 that had not increased from baseline; a rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[g]Clinical response was defined as a decrease from baseline in modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.

[h]Endoscopic improvement was defined as a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[i]HEMI was defined as achievement of histologic (neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue based on the Geboes grading system [ie, Geboes score of ≤3.1]) and endoscopic improvement.

[j]Endoscopic remission (normalization) was defined as an endoscopy subscore of 0.

[k]IBDQ remission was defined as a total IBDQ score of ≥170.

[l]Symptomatic remission was defined as a Mayo stool frequency subscore of 0 or 1 that had not increased from baseline and a Mayo rectal bleeding subscore of 0.

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- **Eligibility:** patients who had an inadequate response or intolerance to conventional (thiopurines or corticosteroids) and/or advanced (TNF alpha antagonists, vedolizumab, or tofacitinib) therapies and had a baseline modified Mayo score of 5-9 (inclusive), with a rectal bleeding subscore of ≥1, and an endoscopy subscore of ≥2 were included in the primary analysis population.[6]
- **Primary endpoint:** clinical remission at week 12 (during induction) and clinical remission at week 44 (during maintenance).[6]
  - Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 and did not increase from baseline; a rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.
- **Secondary endpoints:** symptomatic remission, clinical response, endoscopic improvement, HEMI, and endoscopic remission (normalization); corticosteroid-free clinical remission, maintenance of clinical remission, clinical response, symptomatic remission, endoscopic improvement, HEMI, endoscopic remission (normalization), IBDQ remission, and fatigue response (during maintenance).[6]
  - Symptomatic remission was defined as a Mayo stool frequency subscore of 0 or 1 that has not increased from baseline and a Mayo rectal bleeding subscore of 0.
  - Clinical response was defined as a decrease from baseline in modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.
  - Endoscopic improvement was defined as a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.
  - HEMI was defined as achievement of histologic (neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue based on the Geboes grading system [ie, Geboes score of ≤3.1]) and endoscopic improvement.
  - Endoscopic remission (normalization) was defined as a Mayo endoscopy subscore of 0.
  - Corticosteroid-free clinical remission was defined as i.e. not requiring any treatment with corticosteroids for ≥8 weeks prior to week 44, and also meeting the criteria for clinical remission.
  - IBDQ remission was defined as a total IBDQ score ≥170.
  - Fatigue response was defined as a ≥7-point improvement from induction baseline in the PROMIS-Fatigue SF-7a.

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### Induction study

- A total of 701 patients underwent randomization and were included in the primary analysis population. The mean age was 40.5 years, and the mean duration of UC was 7.5 years. The mean modified Mayo score was 6.9, and 67.9% of patients had a Mayo endoscopy subscore of 3, indicating severe disease.[6]
- About 50% of patients had failed prior ADTs for UC. Among these patients, 47.4% had failed ≥2 ADTs.[6]
- The 2 treatment groups were comparable with respect to baseline demographic and disease characteristics.[6]

### Maintenance study

- A total of 568 patients were included in the primary analysis population, which included patients with a modified Mayo score of 5-9 at induction baseline who received ≥1 dose of TREMFYA maintenance therapy. The mean age was 40.7 years, and the mean duration of UC was 7.8 years. The mean modified Mayo score was 6.9 (63.9% with severe disease), and 66.4% of patients had a Mayo endoscopy subscore of 3, indicating severe disease.[7]
- About 42% of patients had prior inadequate response or intolerance to ADT (TNF antagonists, vedolizumab, or tofacitinib), and 42.5% of these patients had failed ≥2 ADT classes.[7]
- Baseline demographic and disease characteristics were similar across treatment groups.[7]

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### Primary endpoint

- At week 12, a significantly greater proportion of patients in the TREMFYA 200 mg IV Q4W group achieved clinical remission compared with those in the placebo group (23% vs 8%, respectively; adjusted treatment difference, 15%; 95% CI, 10-20; *P*<0.0001).[1,6]

### Key secondary endpoints

- Secondary efficacy outcomes are summarized in the table below.[6]

**Secondary efficacy endpoints**

### Early symptomatic improvement through week 12

- At baseline, in the TREMFYA vs placebo group, the mean absolute number of stools per day was 7.10 vs 6.96, stool frequency subscore of 0 or 1 was observed in 10.0% vs 9.6% of patients, and the mean rectal bleeding subscore was 1.7 vs 1.8, respectively.[9]
- Symptomatic remission assessments at weeks 2, 4 and 12 were major secondary endpoints and multiplicity controlled. All other analyses were prespecified, but not controlled for multiple comparisons. Therefore, *P*-values for these analyses are nominal and statistical significance has not been established.[9]
- Stool frequency and rectal bleeding outcomes through week 12 are summarized in the tab below.

**Stool frequency and rectal bleeding outcomes through week 12**

- Treatment differences for TREMFYA vs placebo at week 12 were evident across the symptomatic outcomes and are summarized in the tab below.[2,9]

**Differences in symptomatic outcomes at week 12 for TREMFYA vs placebo**

**Secondary efficacy endpoints**[1]

| Outcomes | TREMFYA 200 mg IV (N=421) | Placebo IV (N=280) | Adjusted treatment difference, %[a] (95% CI) | *P*-value |
|---|---|---|---|---|
| **Symptomatic outcomes, %** | | | | |
| Symptomatic remission at week 1 | 09 | 06 | 03 (-1 to 7) | NS |
| Symptomatic remission at week 2 | 12 | 09 | 03 (-2 to 8) | 0.21 |
| Symptomatic remission at week 4 | 23 | 13 | 10 (4 to 15) | <0.0009 |
| Symptomatic remission at week 8 | 40 | 21 | 19 (13 to 26) | NS |
| Symptomatic remission at week 12 | 50 | 21 | 29 (23 to 36) | <0.0001 |
| Symptomatic response at week 1 | 28 | 19 | 10 (3 to 16) | NS |
| Symptomatic response at week 2 | 34 | 24 | 11 (4 to 17) | NS |
| Symptomatic response at week 4 | 53 | 30 | 23 (16 to 30) | NS |
| Symptomatic response at week 8 | 66 | 40 | 27 (20 to 34) | NS |
| Symptomatic response at week 12 | 72 | 35 | 37 (30 to 44) | NS |
| **Major secondary outcomes, n (%)** | | | | |
| Clinical response at week 12 | 259 (62) | 78 (28) | 34 (27 to 41) | <0.0001 |
| Endoscopic improvement at week 12 | 113 (27) | 31 (11) | 16 (11 to 21) | <0.0001 |
| Histo-endoscopic mucosal improvement at week 12 | 99 (24) | 21 (8) | 16 (11 to 21) | <0.0001 |
| Endoscopic remission (normalization) at week 12 | 63 (15) | 14 (5) | 10 (6 to 14) | NS |
| **IBDQ remission** | 216 (51) | 83 (30) | 22 (15 to 29) | <0.0001 |
| **Fatigue response** | 173 (41) | 60 (21) | 20 (13 to 26) | <0.0001 |

CI, confidence interval; CMH, Cochran-Mantel-Haenszel; IBDQ, Inflammatory Bowel Disease Questionnaire; IV, intravenous; NS, nonsignificant. **Note:** Symptomatic response up to induction week 12 and symptomatic remission at induction week 1 were post hoc. Symptomatic remission assessments at weeks 2, 4, and 12 were major secondary endpoints and multiplicity controlled. **Therefore, *P*-values for these analyses are nominal, and statistical significance has not been established.**

[a]Based on the Wald statistic with CMH weight.

## Stool frequency and rectal bleeding outcomes through week 12[1,2]

| Outcomes | TREMFYA 200 mg IV (N=421) | | | | Placebo IV (N=280) | | | |
|---|---|---|---|---|---|---|---|---|
| | Week 2 | Week 4 | Week 8 | Week 12 | Week 2 | Week 4 | Week 8 | Week 12 |
| Stool frequency subscore of 0 or 1, % | 26 | 41 | 53 | 60 | 18 | 25 | 30 | 32 |
| Rectal bleeding subscore of 0, % | 24 | 37 | 56 | 65 | 19 | 23 | 33 | 29 |

IV, intravenous.

**Note:** Symptomatic remission assessments at weeks 2, 4, and 12 were major secondary endpoints and multiplicity controlled. Analyses listed above were prespecified, but not controlled for multiple comparisons.

**Therefore, *P*-values for these analyses are nominal, and statistical significance has not been established.**

## Differences in symptomatic outcomes at week 12 for TREMFYA vs placebo[1,2,9,a]

| Outcomes | TREMFYA 200 mg IV (N=421) | Placebo IV (N=280) | Treatment difference[b] | *P*-value |
|---|---|---|---|---|
| Deep symptomatic remission, (%)[c] | 21 | 8 | 14 | NS |
| n | 420 | 274 | - | - |
| Mean change from baseline in absolute number of stools per day (95% CI) | -3.2 (-3.5 to -2.8) | -1.4 (-1.7 to 1.0) | -1.8 (-2.20 to -1.37) | NS |
| Mean change from baseline in RBS (95% CI) | -1.2 (-1.3 to -1.1) | -0.6 (-0.7 to -0.5) | -0.7 (-0.8 to -0.5) | NS |
| Mean change from baseline in SFS (95% CI) | -1.1 | -0.5 | -0.6 | NS |

ADT-IR, intolerance to advanced therapy; AE, adverse event; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; IV, intravenous; NS, nonsignificant; RBS, rectal bleeding subscore; SFS, stool frequency subscore; UC, ulcerative colitis.

**Note: All *P*-values are nominal for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the statistical significance has not been established.**

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC prior to the designated time point were considered not to have achieved the endpoint for binary endpoints and had baseline observation carried forward for continuous endpoints. Data after discontinuation of the study agent due to COVID-19-related reasons (excluding COVID-19 infection) were considered missing. Patients who were missing 1 or more components pertaining to a specified endpoint were considered not to have achieved the endpoint for binary endpoints and had baseline observation carried forward for continuous endpoints. The *P*-values for binary endpoints were based on the CMH chi-square test. The *P*-values for continuous endpoints were based on Mixed-Effect Model Repeated Measures.

[b]Treatment differences in proportions were adjusted for strata (ADT-IR status and concomitant use of corticosteroids at baseline) based on CMH weight.

[c]Deep symptomatic remission is defined as a Mayo RBS of 0 and a Mayo SFS of 0.

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- Histologic parameters were similar in both groups at baseline (N=701).[10]
- In the TREMFYA vs placebo groups, the mean Geboes total score was 11.8 vs 11.9, mean NHI score was 2.7 and 2.8, and the mean RHI score was 16.6 vs 16.6, respectively.[10]
- At week 12, a significantly greater proportion of patients treated with TREMFYA 200 mg IV achieved HEMI vs those in the placebo group (23.5% vs 7.5%, respectively; adjusted difference, 16.2%; 95% CI, 11.1-21.2; *P*<0.001).[10]

**Histologic and combined histologic and endoscopic outcomes at week 12[1,10,a]**

| Outcomes, n (%) | TREMFYA 200 mg IV (N=421) | Placebo (N=280) | Treatment differences (95% CI) |
|---|---|---|---|
| Histologic improvement[b] | 189 (45) | 60 (21) | 24 (17-30)[c] |
| Histologic remission[d] | 168 (40) | 52 (19) | 22 (15-28)[c] |
| Histologic remission by alternate definition (NHI≤1) | 168 (39.9) | 52 (18.6) | 21.5 (15.1-27.9)[c] |
| Histologic remission and endoscopic remission (normalization)[e] | 57 (13.5) | 11 (3.9) | 9.8 (5.8-13.7)[c] |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of therapeutic effect or due to an AE of worsening of UC, or due to other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to week 12 were considered not to have achieved the endpoint. Patients who had an unevaluable biopsy (ie, a biopsy that was collected but could not be assessed due to sample preparation or technical errors) or were missing the endoscopy subscore (if applicable) or any of the histology components pertaining to this endpoint (ie, assessment of neutrophils in epithelium, crypt destruction, or erosions or ulcerations or granulations) at week 12 were considered not to have achieved the endpoint.

[b]Neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes histologic score of ≤3.1).

[c]**Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

[d]Absence of neutrophils from the mucosa (both lamina propria and epithelium); no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system, (ie, Geboes histologic score of ≤2 B.0).This definition is equivalent to histologic remission by alternative definition using the RHI (≤3, with subscores of 0 for lamina propria neutrophils and neutrophils in the epithelium and without ulcers or erosion).

[e]Absence of neutrophils from the mucosa (both lamina propria and epithelium); no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes histologic score of ≤2 B.0) and Mayo endoscopy subscore of 0.

- Of 701 patients included, 339 (48%) had no history of ADT-IR (other biologics or JAKis) and 344 (49%) had a history of ADT-IR.[11]
- For treatment outcomes of TREMFYA vs placebo among patients with and without a history of ADT-IR, see the tab below.

**Clinical and histologic-endoscopic outcomes at week 12 by prior advance therapy history**

## Clinical and histologic-endoscopic outcomes at week 12 by prior advance therapy history[1,2,a]

| | No history of ADT-IR | | | History of ADT-IR | | |
|---|---|---|---|---|---|---|
| | TREMFYA 200 mg IV (n=202), n (%) | Placebo IV (n=137), n (%) | Adjusted treatment differences, (%)[b] | TREMFYA 200 mg IV (n=208), n (%) | Placebo IV (n=136), n (%) | Adjusted treatment differences, (%)[b] |
| Clinical remission[c] | 64 (32) | 16 (12) | 20 | 26 (12) | 5 (4) | 09 |
| Symptomatic response[d] | 165 (82) | 56 (41) | 41 | 127 (61) | 38 (28) | 33 |
| Symptomatic remission[e] | 122 (60) | 36 (26) | 34 | 80 (38) | 19 (14) | 24 |
| Clinical response[f] | 144 (71) | 48 (35) | 36 | 107 (51) | 27 (20) | 32 |
| Endoscopic improvement[g] | 77 (38) | 23 (17) | 21 | 31 (15) | 7 (5) | 10 |
| HEMI[h] | 66 (33) | 15 (11) | 22 | 28 (13) | 6 (4) | 09 |
| Endoscopic remission (normalization)[i] | 42 (21) | 10 (7) | 14 | 18 (9) | 3 (2) | 06 |
| IBDQ remission[j] | 126 (62) | 47 (34) | 28 | 82 (39) | 33 (24) | 15 |
| Fatigue response[k] | 84 (42) | 40 (29) | 12 | 80 (38) | 18 (13) | 25 |

ADT-IR, intolerance to advanced therapy; AE, adverse event; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; HEMI, histo-endoscopic mucosal improvement; IBDQ, Inflammatory Bowel Disease Questionnaire; IV, intravenous; JAKi, Janus kinase inhibitor; PROMIS-Fatigue SF-7a, Patient-Reported Outcomes Measurement Information System Fatigue Short Form 7a; UC, ulcerative colitis.

**Note: All *P*-values are nominal for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.** All patients had a modified Mayo score ranging from 5 to 9 at induction baseline. Eighteen patients (7 in the placebo group and 11 in the TREMFYA group) were biologic or JAKi experienced without a documented inadequate response or intolerance to biologics or JAKis.

[a]Patients who had a prohibited change in UC medication, had an ostomy or colectomy, or for whom the study agent was discontinued due to lack of efficacy or an AE of worsening of UC or other reasons (except for COVID-19-related reasons [excluding COVID-19 infection]) or regional crisis in Russia and Ukraine prior to the week 12 visit were considered not to have achieved the endpoint. Patients who were missing 1 or more components pertaining to a specified endpoint at week 12 were considered not to have achieved the endpoint.

[b]The adjusted treatment difference and confidence intervals were based on the Wald statistic with CMH weight.

[c]Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 that had not increased from baseline; a Mayo rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[d]Symptomatic response was defined as a decrease of ≥30% and ≥1 point from baseline in the symptomatic Mayo score, with either a ≥1-point decrease from baseline in the Mayo rectal bleeding score or a Mayo rectal bleeding score of 0 or 1.

[e]Symptomatic remission was defined as a Mayo stool frequency subscore of 0 or 1 that had not increased from baseline and a Mayo rectal bleeding subscore of 0.

[f]Clinical response was defined as a decrease of ≥30% and ≥2 points from baseline in the modified Mayo score, with either a ≥1-point decrease from baseline in the Mayo rectal bleeding subscore or a Mayo rectal bleeding subscore of 0 or 1.

[g]Endoscopic improvement was defined as an Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[h]HEMI was defined as achieving a combination of histologic improvement (neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system) and endoscopic improvement.

[i]Endoscopic remission (normalization) was defined as an Mayo endoscopy subscore of 0.

[j]IBDQ remission was defined as a total IBDQ score of ≥170.

[k]Fatigue response was defined as a ≥7-point improvement from baseline in PROMIS-Fatigue SF-7a score.

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### Improvement in CRP and FCP levels

- At baseline, the median CRP and FCP values between TREMFYA vs placebo were 4.34 mg/L vs 3.83 mg/L and 1651 mg/kg vs 1606 mg/kg, respectively.[2,11]

### CRP and FCP levels at baseline and week 12[2,11,a]

| | TREMFYA 200 mg IV | Placebo IV |
|---|---|---|
| At baseline | | |
| Elevated CRP (>3 mg/L), n (%) | 248 (58.9) | 160 (57.1) |
| Elevated FCP (>250 mg/kg), n (%) | 333 (79.1) | 225 (80.4) |
| N | 248 | 160 |
| CRP ≤3 mg/L, n (%) | | |
| At week 4 | 85 (34)[b] | 35 (22) |
| At week 8 | 97 (39)[b] | 40 (25) |
| At week 12 | 100 (40)[b] | 26 (16) |
| N | 333 | 225 |
| FCP ≤250 mg/kg, n (%) | | |
| At week 4 | 47 (14)[b] | 20 (9) |
| At week 12 | 98 (29)[b] | 39 (17) |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to the designated timepoint had their baseline value carried forward from the time of the event onward. The *P*-values of treatment comparison were based on mixed-effect model repeated measures, with CRP and FCP values being log-transformed.
**[b]Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

### Change from baseline in CRP and FCP through week 12 among patients with elevated CRP or FCP at baseline[11,a]

| | TREMFYA 200 mg IV, n; median (IQR) | Placebo IV, n; median (IQR) |
|---|---|---|
| CRP, mg/L | | |
| Baseline | 248; 9.26 (5.31 to 18.05) | 160; 8.02 (5.40 to 16.85) |
| Median change from baseline at week 4 | 245; -3.35 (-8.60 to -0.23)[b] | 158; -2.06 (-5.70 to 1.58) |
| Median change from baseline at week 8 | 239; -3.80 (-10.77 to -0.19)[b] | 156; -1.75 (-5.68 to 1.46) |
| Median change from baseline at week 12 | 239; -3.99 (-11.46 to -0.85)[b] | 153; -0.51 (-4.64 to 2.72) |
| FCP, mg/kg | | |
| Baseline | 333; 1787 (920 to 4009) | 225; 1743 (1120 to 3395) |
| Median change from baseline at week 4 | 308; -603 (-1866 to 230)[b] | 213; -227 (-1041 to 658) |
| Median change from baseline at week 12 | 293; -800 (-2532 to 0)[b] | 201; -86 (-1254 to 504) |

[a]Patients who had a prohibited change in UC medication, had an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to the designated timepoint had their baseline value carried forward from the time of the event onward.
**[b]Nominal *P*-value ≤0.001. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established.**

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## Effects on serum proteins and colonic epithelial cells

- Overall, serum proteins from 302 patients, who had at least one paired sample at weeks 0 and 4 or week 12, were evaluated.[12]
- Matched colonic biopsies from 255 patients were available for evaluation at weeks 0 and 12 using transcriptional profiling based on bulk RNAseq.[12]
- Transcriptional modules derived from public UC scRNAseq were evaluated with differential expression in the bulk RNAseq dataset.[12]
- Serum IL-22, IFNγ, and IL-17A significantly decreased ($P$<0.00001) as early as week 4 with TREMFYA treatment, which further decreased through week 12.[12]
- Unsupervised analysis of tissue transcriptomic modules (n=69) demonstrated significant changes in 57 modules with TREMFYA at week 12.[12]
  - Top 6 downregulated modules were: Th17 cell (IL-23 pathway), neutrophil, IFNγ signaling, plasma cell, and inflammatory epithelial and fibroblast cell states.
  - Upregulated modules were: Epithelial cell populations and metabolism (all FDR<0.05).
- Fc-γ receptor (CD64) expression was increased at baseline in all patients and reduced at week 12.[12]
- Module analysis revealed an increase in goblet cells (FDR<0.05), contributing to barrier integrity.[12]
- Flow cytometry and scRNAseq were performed on a subset of matched week 0 and week 12 cryopreserved biopsies from 60 patients.[12]
  - Flow cytometry demonstrated reductions of CD45+ lymphocyte and CD66+ granulocyte populations ($P$<0.01).
- Parallel scRNAseq revealed a reduction of inflammatory monocytes and fibroblasts in TREMFYA responders at week 12, while pro-healing indicators observed at week 12, which included increased EpCam+, BEST4+ enterocytes, and ADAMDEC1+ fibroblasts ($P$<0.01).[12]

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## Effects on serum proteins and colonic epithelial cells

- A molecular analysis of the randomized population was performed, comparing induction week 12 to baseline.[13]
- Transcriptional profiling of colonic biopsies from 593 patients was performed, with bulk RNAseq; gene modules were evaluated for differential expression.[13]
- Serum proteomic profiling of 648 patients was conducted using a targeted O-link inflammation panel, and differential protein abundance was evaluated.[13]
- At week 12, patients who underwent TREMFYA IV induction exhibited significant downregulation of inflammatory transcriptional modules in the colon tissue, representing Th17, plasma cell, neutrophil, and inflammatory fibroblast biology, and upregulation of healthy epithelium-related gene modules including goblet cells and healthy epithelium (all FDR<0.05).[13]
  - This response was correlated with changes observed in the TREMFYA 200 mg IV group of a phase 2b induction study (r=0.97; *P*<0.0001).
- Patients treated with TREMFYA who achieved HEMI at week 12 demonstrated the most robust changes in gene module expression at week 12 (*P*<0.0001).[13]
- Inflammatory serum proteins (IFNγ, IL-17A, OSM, and IL-6; FDR<0.05) were reduced as early as week 4 and continued to decline through week 12.[13]
- Changes in serum proteins were consistent with those observed in the TREMFYA 200 mg group of the phase 2b induction study (r=0.96; *P*<0.0001).[13]

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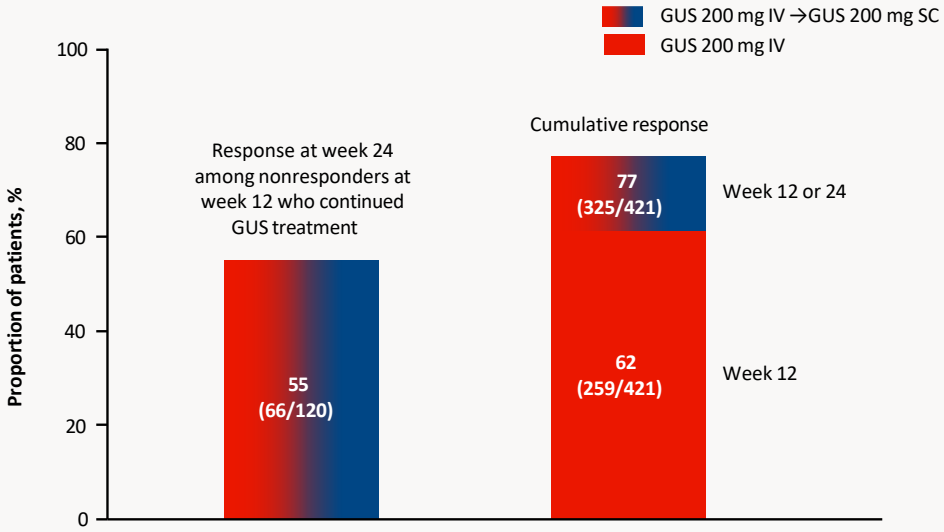
### Cumulative clinical response through week 24[14,a]

- An analysis was conducted to evaluate cumulative efficacy through week 24 among patients who did not achieve clinical response at week 12 and continued treatment with TREMFYA.[14]
  - Patients who did not respond to TREMFYA 200 mg IV at week 12 received TREMFYA SC Q4W (weeks 12, 16, and 20). Patients who did not respond to placebo treatment at week 12 received TREMFYA 200 mg IV Q4W.
- Clinical response rates at week 24 by prior advance therapy status in patients who were nonresponders at week 12 were as follows[14]:
  - Patients without a history of ADT-IR: 28/46 (60.9%)
  - Patients with ADT-IR: 38/74 (51.4%)
- Cumulative clinical response rates at week 12 or 24 by prior advance therapy status were as follows[14]:
  - Patients without a history of ADT-IR: 180/213 (84.5%)
  - Patients with ADT-IR: 145/208 (69.7%)
- Among placebo-treated patients who did not show a clinical response at week 12 and were switched to TREMFYA IV, the clinical response rate at week 24 (69.7%) was similar to that at week 12 for patients initially randomized to TREMFYA at baseline (61.5%).[14]

### Cumulative clinical response through week 24[2,14,a]




[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to the designated timepoint were considered not to have achieved clinical response at the designated timepoint. Patients who were missing 1 or more Mayo subscore(s) pertaining to clinical response at the designated timepoint were considered not to have achieved clinical response.

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### Improvement in PROs at week 12

- This section provides data on PROs pertaining to:
  - Improvement in HRQoL at week 12.
    - IBDQ
    - PROMIS-29
  - Improvement in abdominal pain and bowel urgency symptoms at week 12.
  - Improvement in fatigue symptoms at week 12.

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### Improvement in HRQoL at week 12 IBDQ

- The IBDQ (score range, 32-224) was assessed at baseline and week 12.[15]
  - Higher scores signify better HRQoL and a score ≥170 indicates IBDQ Remission.
  - Clinically meaningful improvements were defined as a decrease of ≥16 or >20 points from the baseline in IBDQ Total score.
- These HRQoL analyses were prespecified, but only IBDQ Remission at week 12 was controlled for multiple comparisons.[15]
- The mean baseline IBDQ Total scores in the TREMFYA (n=405) and placebo (n=261) groups were 125.8 and 126.3, respectively.[15]

### IBDQ scores and remission rates at week 12[15,a]

| Proportion of patients | TREMFYA 200 mg IV | Placebo IV | Treatment differences, (95% CI) | *P*-value |
|---|---|---|---|---|
| Patients in IBDQ remission (total score ≥170) at W12, %, [n/N] | 51.3 [216/421] | 29.6 [83/280] | 21.9[b] (14.9-29.0) | <0.001 |
| Patients with prior ADT-IR in IBDQ remission at W12, % [n/N] | 39.4 [82/208] | 24.3 [33/136] | 15.2[c] (5.4-24.9) | Nominal[d] |
| Patients without prior ADT-IR in IBDQ remission at W12, % [n/N] | 62.9 [134/213] | 34.7 [50/144] | 28.2[c] (18.1-38.3) | Nominal[e] |
| IBDQ total score change from baseline, mean | 39.0 (n=405) | 18.6 (n=261) | 20.5[f] (15.4-25.5) | Nominal[e] |
| IBDQ bowel symptoms score change, mean | 14.9 | 7.5 | 7.3[f] (5.6-9.0) | Nominal[e] |
| IBDQ emotional function score change, mean | 11.6 | 5.4 | 6.5[f] (4.6-8.4) | Nominal[e] |
| IBDQ systemic symptoms score change, mean | 5.7 | 2.6 | 3.1[f] (2.3-3.9) | Nominal[e] |
| IBDQ social function score change, mean | 6.7 | 3.1 | 3.6[f] (2.6-4.6) | Nominal[e] |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine had their baseline value carried forward and were considered not in IBDQ Remission. Patients missing an IBDQ total score at week 12 were considered not in IBDQ remission.
[b]The adjusted treatment difference was based on the Wald statistic with CMH weight. The *P*-value was based on the CMH chi-square test, stratified by ADT-failure status (Yes/No) and concomitant use of corticosteroids at baseline (Yes/No).
[c]The adjusted treatment difference was based on the Wald statistic with CMH weight. The *P*-value was based on the CMH chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No).
[d]**Nominal *P*-value <0.05 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**
[e]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**
[f]Treatment difference was estimated by the difference in LSM (ANCOVA). The *P*-value was based on ANCOVA.

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**PROMIS-29**

- PROMIS-29, consists of 7 domains (anxiety, depression, fatigue, pain interference, sleep disturbance, physical function, and social participation) and a pain intensity NRS (range, 0-10), was evaluated at week 12.[16]
  - PROMIS-29 raw scores were converted to standardized T-scores based on a general population mean of 50 and a SD of 10. Higher scores signify better outcomes for physical function and social participation, and worse outcomes for all other domains.
  - PCS and MCS scores were calculated from domain T-scores for physical and mental HRQoL, with higher scores reflecting better outcomes.
- At week 12, treatment with TREMFYA resulted in a numerically greater mean change from baseline as well as the percentage of patients achieving minimal clinically meaningful improvement compared to placebo in each domain T-score, the pain intensity NRS score and the PCS/MCS.[16]

**Mean change from baseline and clinically meaningful improvements in PROMIS-29 anxiety and depression scores at week 12[16,a,b,c]**

| Proportion of patients | TREMFYA 200 mg IV (N=421) | Placebo IV (N=280) | LSM differences (95% CI) | Treatment differences[d] |
|---|---|---|---|---|
| Anxiety | | | | |
| Baseline T-score, mean (SD) | 57.11 (8.714) n=407 | 56.94 (9.443) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | -4.83 (8.933) n=405 | -1.52 (8.784) n=261 | -3.3 (-4.5 to -2.0) | - |
| Clinically meaningful improvements, % | 44.9 | 25.4 | - | 19.6 |
| Depression | | | | |
| Baseline T-score, mean (SD) | 53.85 (8.663) n=407 | 54.39 (9.375) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | -3.64 (8.470) n=405 | -1.26 (7.989) n=261 | -2.6 (-3.8 to -15) | - |
| Clinically meaningful improvements, % | 39.0 | 21.8 | - | 17.3 |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine had their baseline value carried forward from the time of the event onward. [b]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.** [c]Minimum clinically meaningful improvement was defined as a ≥3-point improvement in the pain intensity NRS score, ≥5-point improvement in each domain (one-half SD of the population), and ≥5-point improvement in PCS/MCS scores. [d]The treatment differences were based on the Wald statistic with CMH weight. The *P*-value was based on the CMH chi-square test, stratified by ADT-failure status (Yes/No) and concomitant use of corticosteroids at baseline (Yes/No).

**Mean change from baseline and minimum clinically meaningful improvements in PROMIS-29 fatigue, pain interference, sleep disturbance, physical function scores at week 12**

**Mean change from baseline and minimum clinically meaningful improvements in PROMIS-29 social participation, pain intensity, and PCS/MCS scores at week 12**

**Mean change from baseline and minimum clinically meaningful improvements in PROMIS-29 fatigue, pain interference, sleep disturbance, physical function scores at week 12[16,a,b,c]**

| Proportion of patients | TREMFYA 200 mg IV (N=421) | Placebo IV (N=280) | LSM differences (95% CI) | Treatment differences[c] |
|---|---|---|---|---|
| Fatigue | | | | |
| Baseline T-score, mean (SD) | 55.78 (9.405) n=407 | 56.18 (9.317) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | -5.60 (9.027) n=405 | -2.65 (8.057) n=261 | -3.1 (-4.3 to -1.8) | - |
| Clinically meaningful improvements, % | 51.5 | 30.0 | - | 21.7 |
| Pain interference | | | | |
| Baseline T-score, mean (SD) | 56.36 (8.856) n=407 | 56.74 (8.406) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | -5.65 (9.272) n=405 | -3.03 (8.152) n=261 | -2.9 (-4.1 to -1.7) | - |
| Clinically meaningful improvements, % | 44.2 | 28.2 | - | 16.1 |
| Sleep disturbance | | | | |
| Baseline T-score, mean (SD) | 53.68 (7.793) n=407 | 53.09 (7.045) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | -3.82 (7.550) n=405 | -0.93 (6.299) n=261 | -2.7 (-3.8 to -1.7) | - |
| Clinically meaningful improvements, % | 38.5 | 20.4 | - | 18.2 |
| Physical function | | | | |
| Baseline T-score, mean (SD) | 45.89 (8.104) n=407 | 45.31 (8.159) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | 3.58 (7.473) n=405 | 1.59 (6.061) n=261 | 2.2 (1.2-3.2) | - |
| Clinically meaningful improvements, % | 30.9 | 19.3 | - | 11.7 |

AE, adverse event; CI, confidence interval; COVID-19, coronavirus disease 2019; IV, intravenous; LSM, least squares means; MCS, mental component summary; NRS, numeric rating scale; PCS, physical component summary; PROMIS, Patient-Reported Outcomes Measurement Information System; SD, standard deviation; UC, ulcerative colitis.

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine had their baseline value carried forward from the time of the event onward.

[b]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

[c]Minimum clinically meaningful improvement was defined as a ≥3-point improvement in the pain intensity NRS score, ≥5-point improvement in each domain (one-half SD of the population), and ≥5-point improvement in PCS/MCS scores.

**Mean change from baseline and minimum clinically meaningful improvements in PROMIS-29 social participation, pain intensity, and PCS/MCS scores at week 12[16,a,b,c]**

| Proportion of patients | TREMFYA 200 mg IV (N=421) | Placebo IV (N=280) | LSM differences (95% CI) | Treatment differences[c] |
|---|---|---|---|---|
| Ability to participate in social roles and activities T-score | | | | |
| Baseline T-score, mean (SD) | 46.33 (8.637) n=407 | 46.42 (8.652) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | 5.88 (8.811) n=405 | 2.90 (7.981) n=261 | 3.0 (1.8-4.2) | - |
| Clinically meaningful improvements, % | 50.4 | 31.1 | - | 19.4 |
| Pain intensity NRS score | | | | |
| Baseline T-score, mean (SD) | 4.21 (2.466) n=407 | 4.30 (2.499) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | -1.69 (2.466) n=405 | -0.95 (2.340) n=261 | -0.8 (-1.1 to -0.5) | - |
| Clinically meaningful improvements,[d] % | 45.4 n=295 | 29.8 n=198 | - | 15.9 |
| PCS scores | | | | |
| Baseline T-score, mean (SD) | 45.29 (8.193) n=407 | 44.76 (8.431) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | 4.42 (7.601) n=405 | 2.07 (6.302) n=261 | 2.6 (1.5-3.6) | - |
| Clinically meaningful improvements, % | 34.7 | 21.8 | - | 13.0 |
| MCS scores | | | | |
| Baseline T-score, mean (SD) | 44.07 (7.996) n=407 | 43.94 (8.099) n=271 | - | - |
| Change from baseline in T-score, mean (SD) | 6.00 (7.696) n=405 | 2.67 (7.155) n=261 | 3.4 (2.3-4.5) | - |
| Clinically meaningful improvements, % | 50.8 | 29.3 | - | 21.7 |

ADT, advanced therapy; AE, adverse event; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; IV, intravenous; LSM, least squares means; MCS, mental component summary; NRS, numeric rating scale; PCS, physical component summary; PROMIS, Patient-Reported Outcomes Measurement Information System; SD, standard deviation; UC, ulcerative colitis.

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine had their baseline value carried forward from the time of the event onward.

[b]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

[c]Minimum clinically meaningful improvement was defined as a ≥3-point improvement in the pain intensity NRS score, ≥5-point improvement in each domain (one-half SD of the population), and ≥5-point improvement in PCS/MCS scores.

[d]The treatment differences were based on the Wald statistic with CMH weight. The *P*-value was based on the CMH chi-square test, stratified by ADT-failure status (Yes/No) and concomitant use of corticosteroids at baseline (Yes/No).

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## Improvement in abdominal pain and bowel urgency symptoms at week 12

- Abdominal pain and bowel urgency were assessed at baseline and week 12 using items from IBDQ.[17]
  - Patients rated abdominal pain, symptoms of bowel urgency, and impact of bowel urgency over the past 2 weeks on 7-point scales (from "all of the time" [1] to "none of the time" [7]). An increase of ≥2 points from baseline was considered clinically meaningful improvement.
- These analyses were prespecified but not multiplicity controlled; therefore, all *P*-values were nominal.[17]
- At baseline, in the TREMFYA vs placebo group, the proportions of patients with abdominal pain, symptoms of bowel urgency, and impact of bowel urgency with at least "a little of the time" (score ≤5) were similar between the 2 groups.[17]
  - Abdominal pain: 77.7% vs 77.9%
  - Symptoms of bowel urgency: 86.0% vs 83.2%
  - Impact of bowel urgency: 70.8% vs 70.4%

### Change from baseline to week 12 in abdominal pain, bowel urgency symptoms, and impact of bowel urgency[2,17,a]

| Outcomes | TREMFYA 200 mg IV (n=405) | Placebo IV (n=261) |
|---|---|---|
| Abdominal pain, n (%) | | |
| Improved | 267 (66)[b] | 123 (47) |
| No change | 103 (25)[b] | 102 (39) |
| Worsened | 35 (9)[b] | 36 (14) |
| Bowel urgency symptoms, n (%) | | |
| Improved | 288 (71)[b] | 125 (48) |
| No change | 89 (22)[b] | 93 (36) |
| Worsened | 28 (7)[b] | 43 (16) |
| Social impact of bowel urgency, n (%) | | |
| Improved | 246 (61)[b] | 110 (42) |
| No change | 115 (28)[b] | 101 (39) |
| Worsened | 44 (11)[b] | 50 (19) |

**Note: All *P*-values are nominal for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

[a]Change from baseline was evaluated at week 12 among all evaluable patients regardless of baseline score.

**Proportion of patients with clinically meaningful improvement (≥2-point change) in abdominal pain, bowel urgency symptoms, and impact of bowel urgency at week 12**

**Proportion of patients with clinically meaningful improvement (≥2-point change) in abdominal pain, bowel urgency symptoms, and impact of bowel urgency at week 12[2,17]**

| Outcomes | TREMFYA 200 mg IV | Placebo IV | Adjusted treatment difference, % (95% CI) |
|---|---|---|---|
| Abdominal pain[a], % (n/N) | | | |
| Clinically meaningful improvement from baseline[b] | 52 (170/327) | 33 (72/218) | 19 (11-27) |
| Resolution of symptoms from baseline[c] | 21 (80/379) | 12 (31/252) | 9 (3-14) |
| Bowel urgency symptoms[d], % (n/N) | | | |
| Clinically meaningful improvement from baseline[b] | 59 (212/362) | 33 (77/233) | 25 (18-33) |
| Resolution of symptoms from baseline[c] | 24 (95/396) | 10 (26/265) | 14 (9-20) |
| Impact of bowel urgency[e], % (n/N) | | | |
| Clinically meaningful improvement from baseline[b] | 58 (172/298) | 33 (65/197) | 25 (16-33) |
| Resolution of symptoms from baseline[c] | 32 (115/355) | 13 (13/237) | 20 (13-26) |
| Resolution of bowel urgency (symptoms or impact scores ≤6) from baseline[f,g], % (n/N) | 20 (79/402) | 8 (22/268) | 12 (7-17) |

CI, confidence interval; IBDQ, Inflammatory Bowel Disease Questionnaire; IV, intravenous; mMayo, modified Mayo.

**Note: All *P*-values are nominal for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.** All patients had an mMayo score ranging from 5 to 9 at induction baseline. Responses for all IBDQ items ranged from 1 (all of the time) to 7 (none of the time), with a higher score indicating a better health status. A score of ≤5 indicated notable presence of symptoms.

[a]Abdominal pain symptoms were assessed using the IBDQ item 13 question, "How often during the last 2 weeks have you been troubled by pain in the abdomen?"

[b]Clinically meaningful change was defined as a ≥2-point improvement from induction baseline at week 12 among patients with a baseline score of ≤5.

[c]Resolution was defined as a score of 7 at week 12 among patients with a baseline score of ≤6.

[d]Bowel urgency symptoms were assessed using the IBDQ item 24 question, "How much of the time during the last 2 weeks have you been troubled by a feeling of having to go to the bathroom even though your bowels were empty?"

[e]Social impact of bowel urgency symptoms was assessed using the IBDQ item 16 question, "How often during the last 2 weeks have you had to avoid attending events where there was no washroom close at hand?"

[f]IBDQ were assessed in combination for a bowel urgency score.

[g]Resolution of the combined bowel urgency outcome was defined as a score of 7 for both items at week 12 among patients with a score of ≤6 at baseline.

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### Improvement in fatigue symptoms at week 12

- Patient-reported fatigue outcomes were assessed at baseline and week 12 using 7 items from the PROMIS-Fatigue SF-7a which includes symptoms of fatigue (ie, tiredness, exhaustion, mental tiredness, and lack of energy) and associated impacts on daily activities (ie, activity limitations related to work, self-care, and exercise).[18]
  - PROMIS-Fatigue-SF7a raw scores were converted to standard T-scores based on a general population mean of 50 and a SD of 10. Higher T-scores signify more severe fatigue symptoms. Outcomes were assessed by improvements of ≥3, ≥5, and ≥7 points from baseline in PROMIS-Fatigue SF7a T-score, with a ≥7-point improvement defined as fatigue response (multiplicity-controlled secondary endpoint).
- At baseline, in the TREMFYA vs placebo group, the mean (SD) PROMIS-Fatigue SF7a T-scores were 56.0 (8.77) and 56.4 (8.90), respectively.[18]
- Clinically meaningful ≥3 and ≥5 improvement in PROMIS-Fatigue SF7a T-scores in the TREMFYA vs placebo group were[18]:
  - ≥3-point: 56.8% vs 34.6% (nominal *P*-values)
  - ≥5-point: 49.4% vs 26.4% (nominal *P*-values)
- Fatigue response was achieved by greater proportion of patients receiving TREMFYA vs placebo, as summarized in the table below.[18]

**Proportion of patients with fatigue response at week 12 by history of ADT-IR[18]**

| Outcomes | Overall | | No history of ADT-IR | | History of ADT-IR | |
|---|---|---|---|---|---|---|
| | TREMFYA 200 mg IV (n=421) | Placebo IV (n=280) | TREMFYA 200 mg IV (n=213) | Placebo IV (n=144) | TREMFYA 200 mg IV (n=208) | Placebo IV n=136) |
| Fatigue response,[a] n (%) | 173 (41.1) | 60 (21.4) | 93 (43.7) | 42 (29.2) | 80 (38.5) | 18 (13.2) |
| Adjusted treatment difference, % (95% CI)[b] | 19.8 (13.1-26.4) *P*<0.001 | | 14.5 (4.5-24.5)[c] | | 25.2 (16.6-33.9)[d] | |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to the week 12 visit were considered not to have achieved fatigue response.
[b]The adjusted treatment difference and CI were based on the Wald statistic with CMH weight.
[c]**Nominal *P*-value <0.05 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**
[d]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

## Model prediction long-term sustained remission

### Objectives and methods

- A hybrid decision tree/Markov disease model was developed to predict optimal treatment sequencing with TREMFYA in patients with moderate to severe UC.[19]
- The model projected rates of clinical remission, response, and active disease over 5 years. Projection was based on the rates of clinical remission and response reported in the induction phases of phase 2 and phase 3 trials, patients were first distributed into the following 3 health states[19]:
  - Clinical remission
  - Response without remission
  - Active UC
- Over time, loss of response and transition to subsequent lines of therapy were derived from loss of response rates in the clinical trial data.[19]
- Patients failing third-line treatment were categorized as having active disease, where they can receive surgery.[19]
- Age- and sex-adjusted mortality rates from the US population life table were incorporated in the model.[12]
- The following 3 treatment sequences were assessed: TREMFYA as first-, second-, and third-line therapy.[12]
- Other treatment lines were modeled using a treatment basket informed by 2024 MarketScan market share data.[12]

### Results

- Over 5 years, the predicted average proportion of time patients spent in active disease is consistently lower for patients treated with TREMFYA as a first-line therapy vs those receiving TREMFYA treatment in later lines.[12]
- In the first year, the proportion of time spent in active disease was 28% for patients treated with TREMFYA as first-line therapy vs 33% for patients treated with TREMFYA as second- or third-line therapy.[19]

**Projected average proportion of time spent in each health state over a 5-year period**[19]

| | Remission | Response without remission | Active UC | Surgery |
|---|---|---|---|---|
| **First-line TREMFYA** | 52.1% | 10.8% | 36.4% | 0.7% |
| **Second-line TREMFYA** | 39.5% | 11.9% | 47.7% | 0.9% |
| **Third-line TREMFYA** | 38.1% | 9.9% | 51.0% | 1.0% |

# TREMFYA® (guselkumab)
# TREMFYA - Treatment of ulcerative colitis - QUASAR program

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### Analysis of the QUASAR phase 3 induction study

- This analysis evaluated the rate of UC-related medical encounters (including ED visits, hospitalizations and/or surgeries [ostomy, colectomy]) among participants in the QUASAR Phase 3 induction study.[20]
- Through week 12, UC-related ED visits were reported in 2 (0.5%) patients in the TREMFYA group and 7 (2.5%) patients in the placebo group (nominal *P*-values), whereas UC-related hospitalizations occurred in 8 (1.9%) patients in the TREMFYA group and 15 (5.4%) patients in the placebo group (*P*=0.016).[20]
- UC-related surgeries (include ostomy or colectomy) were observed in 2 (0.5%) patients and 2 (0.7%) patients in the TREMFYA and placebo groups, respectively (*P*=0.653).[20]
- Overall, either a UC-related hospitalization or surgery was experienced in 9 (2.1%) patients in the TREMFYA group and 15 (5.4%) patients in the placebo group through week 12 (*P*=0.032).[20]

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### Primary endpoint

- At week 44, a significantly greater proportion of patients treated with TREMFYA achieved the primary endpoint (for both dosing regimens) compared with the placebo group.[7]
- For results on all maintenance therapy endpoints, see tab below:

**Primary, major secondary, and histologic endpoints at week 44**

**Primary, major secondary and histological endpoints at week 44[1,7]**

| Outcomes | TREMFYA 100 mg SC Q8W (N=188), n (%) | TREMFYA 200 mg SC Q4W (N=190), n (%) | Placebo (N=190), n (%) | Adjusted treatment difference (95% CI) (TREMFYA 100 mg vs placebo), %[a] | Adjusted treatment difference (95% CI) (TREMFYA 200 mg vs placebo), %[a] |
|---|---|---|---|---|---|
| **Primary endpoint** | | | | | |
| Clinical remission[b] | 85 (45) | 95 (50) | 36 (19) | 25; *P*<0.0001 | 30; *P*<0.0001 |
| **Major secondary endpoints** | | | | | |
| Corticosteroid-free clinical remission[c] | 85 (45) | 93 (49) | 35 (18) | 26; *P*<0.0001 | 29; *P*<0.0001 |
| Maintenance of clinical remission[b] | 40/66 (61) | 50/60 (72) | 20/59 (34) | 26; *P*=0.0036 | 38; *P*<0.0001 |
| Clinical response[d] | 146 (78) | 142 (75) | 82 (43) | 34; *P*<0.0001 | 31; *P*<0.0001 |
| Symptomatic remission[e] | 70 | 69 | 37 | 32; *P*<0.0001 | 30; *P*<0.0001 |
| Endoscopic improvement[f] | 93 (49) | 98 (52) | 36 (19) | 30; *P*<0.0001 | 31; *P*<0.0001 |
| HEMI[g] | 82 (44) | 91 (48) | 32 (17) | 26; *P*<0.0001 | 30; *P*<0.0001 |
| Endoscopic remission (normalization)[h] | 65 (35) | 64 (34) | 29 (15) | 18; *P*<0.0001 | 17; *P*<0.0001 |
| IBDQ remission[i] | 121 (64) | 122 (64) | 71 (37) | 26; *P*<0.0001 | 26; *P*<0.0001 |
| Fatigue response[j] | 95 (51) | 82 (43) | 56 (29) | 20; *P*<0.0001 | 13; *P*=0.0092 |
| Histological endpoints | | | | | |
| Histological improvement[k] | 122 (65) | 122 (64) | 58 (31) | 34[l] | 33 |
| Histological remission[m] | 111 (59) | 115 (61) | 51 (27) | 31[l] | 33 |

CI, confidence interval; CMH, Cochran-Mantel-Haenszel; HEMI, histo-endoscopic mucosal improvement; IBDQ, Inflammatory Bowel Disease Questionnaire; PROMIS-Fatigue SF-7a, Patient-Reported Outcomes Measurement Information System Fatigue Short Form 7a; Q4W, every 4 weeks; Q8W, every 8 weeks; RHI, Robarts Histopathology Index; SC, subcutaneous.

[a]Based on the Wald statistic with CMH weight.

[b]Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 that did not increase from baseline; a rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[c]Corticosteroid-free clinical remission was defined as not requiring any treatment with corticosteroids for ≥8 weeks prior to week 44 and also meeting the criteria for clinical remission.

[d]Clinical response was defined as a decrease from baseline in modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.

[e]Symptomatic remission was defined as a stool frequency subscore of 0 or 1 that had not increased from baseline and a rectal bleeding subscore of 0.

[f]Endoscopic improvement was defined as an endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[g]HEMI was defined as achievement of histologic (neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue based on the Geboes grading system [ie, Geboes score of ≤3.1]) and endoscopic improvement.

[h]Endoscopic normalization was defined as an endoscopy subscore of 0.

[i]IBDQ remission was defined as a total IBDQ score ≥170.

[j]Fatigue response was defined as a ≥7-point improvement from induction baseline in the PROMIS-Fatigue SF7a.

[k]Histological improvement was defined as neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes score ≤3·1).

**[l]Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

[m]Histological remission was defined as an absence of neutrophils in the mucosa (both lamina propria and epithelium); no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes score ≤2B·0); this was equivalent to the RHI-based definition of histological remission (RHI of ≤3 with subscores of 0 for lamina propria neutrophils and neutrophils in the epithelium and without ulcers or erosion).

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### Corticosteroid-sparing outcomes at week 44

- Among 568 patients from the primary analysis population, 38.9% (221/568) received oral corticosteroids.[21]
- Patients already taking oral corticosteroids at the time of entry into the maintenance study had their daily corticosteroid dose tapered at week 0, unless medically not feasible.[21]
- At week 44, corticosteroid use and corticosteroid-free clinical remission were assessed.[21]
- At week 44, the mean decrease from maintenance baseline in the average daily prednisone-equivalent corticosteroid dose was higher in the TREMFYA 100 mg SC Q8W and TREMFYA 200 mg SC Q4W groups vs the withdrawal (placebo) group (-10.22 and -10.25, respectively, vs -7.35 mg/day; both nominal *P*-value).[21]
- As early as week 8, the elimination of oral corticosteroid use was higher in TREMFYA 100 mg SC Q8W and TREMFYA 200 mg SC Q4W groups vs the withdrawal (placebo) group through week 44 (65.8% [48/73] and 64.4% [47/73], respectively, vs 32.0% [24/75]; both nominal *P*-value).[21]
- At week 44, the oral corticosteroid use elimination and the patients with clinical remission were higher in both TREMFYA treatment groups compared to TREMFYA withdrawal (placebo) group.[21]
- For corticosteroid use and corticosteroid-free clinical remission at week 44, see the tab below.

**Corticosteroid use and corticosteroid-free clinical remission at week 44: primary analysis population**

**Corticosteroid use and corticosteroid-free clinical remission at week 44: primary analysis population[21,a]**

| Outcome | TREMFYA 100 mg SC Q8W (n=188) | TREMFYA 200 mg SC Q4W (n=190) | TREMFYA withdrawal placebo (n=190) |
|---|---|---|---|
| Clinical remission at week 44 (multiplicity-controlled),[b,c] n (%) | 85 (45.2) | 95 (50.0) | 36 (18.9) |
| *P*-value | <0.001 | <0.001 | - |
| Clinical remission at week 44 and not receiving corticosteroids for ≥8 weeks prior to week 44 (multiplicity-controlled),[b,c] n (%) | 85 (45.2) | 93 (48.9) | 35 (18.4) |
| Adjusted treatment difference, % (95% CI)[d] | 25.7 (17.0-34.5) | 29.0 (20.5-37.6) | - |
| *P*-value | <0.001 | <0.001 | - |
| Clinical remission at week 44 and not receiving corticosteroids for ≥12 weeks prior to week 44,[b,c] n (%) | 85 (45.2) | 93 (48.9) | 35 (18.4) |
| Adjusted treatment difference, % (95% CI)[d] | 25.7 (17.0-34.5)[e] | 29.0 (20.5-37.6)[e] | - |
| Receiving oral corticosteroids at maintenance baseline, n (%) | 73 (38.8) | 73 (38.4) | 75 (39.5) |
| Steroid use prednisone equivalent at maintenance baseline, mg/day | 15.0 | 14.9 | 17.3 |
| Eliminating oral corticosteroids for ≥12 weeks prior to week 44,[f,c] n (%) | 51 (69.9) | 48 (65.8) | 27 (36.0) |
| Adjusted treatment difference, % (95% CI)[d] | 33.5 (19.0-48.0)[e] | 29.2 (14.4-44.0)[e] | - |
| Eliminating oral corticosteroids for ≥8 weeks prior to week 44 and in clinical remission at week 44,[f,c] n (%) | 35 (47.9) | 29 (39.7) | 10 (13.3) |
| Adjusted treatment difference, % (95% CI)[d] | 34.2 (21.4-47.1)[e] | 25.8 (13.1-38.6)[e] | - |

AE, adverse event; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; UC, ulcerative colitis.

[a]Randomized treated patients with a modified Mayo score of 5-9 at induction baseline.

[b]Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 that did not increase from induction baseline; a rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[c]Patients who had an ostomy or colectomy, a dose adjustment, a prohibited change in UC medications, or discontinued study agent due to lack of efficacy or an AE of worsening of UC or other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to week 44 were considered not to have achieved the endpoint.

[d]The adjusted treatment difference and CI were based on the Wald statistic with CMH weight.

[e]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established.**

[f]Eliminating oral corticosteroids by a designated time point was defined as not requiring any oral corticosteroid treatment from that time point until maintenance week 44.

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### Histologic and combined histologic-endoscopic outcomes

- At maintenance baseline, the histologic activity evaluated by mean continuous Geboes total score was 6.7, 6.8, and 6.9 for TREMFYA 200 mg SC Q4W, TREMFYA 100 mg SC Q8W, and placebo groups, respectively.[22]
- At week 44, the histologic activity improved in both TREMFYA groups, whereas the histologic activity worsened in the placebo group.[22]
  - The mean change from maintenance baseline in continuous Geboes total score was -1.0, -1.2, and 2.2 for TREMFYA 200 mg SC Q4W, TREMFYA 100 mg SC Q8W, and placebo groups, respectively; both nominal *P*-value).[22]
- At week 44, HEMI was achieved by significantly greater proportion of patients treated with TREMFYA 200 mg SC Q4W and those treated with TREMFYA 100 mg SC Q8W vs placebo (47.9% and 43.6%, respectively, vs 16.8%; both *P*<0.001).[22]
- Among subpopulations with a biologic/JAKi therapy history, a greater proportion of patients in the TREMFYA treatment groups achieved the assessed endpoints when compared with the placebo group.[22]
- For a summary of the histologic and combined histologic and endoscopic outcomes at week 44, see the tab below.

**Summary of histologic and combined histologic and endoscopic outcomes at week 44**

## Summary of histologic and combined histologic and endoscopic outcomes at week 44[22]

| Outcomes | TREMFYA 100 mg SC Q8W (n=188) | TREMFYA 200 mg SC Q4W (n=190) | TREMFYA withdrawal (placebo) (n=190) |
|---|---|---|---|
| Histologic improvement, n (%)[a] | 122 (64.9) | 122 (64.2) | 58 (30.5) |
| Adjusted treatment difference, % (95% CI) | 33.6 (24.3-42.9)[b] | 32.6 (23.3-41.9)[b] | - |
| Histologic remission, n (%)[c,d] | 111 (59.0) | 115 (60.5) | 51 (26.8) |
| Adjusted treatment difference, % (95% CI) | 31.2 (21.9-40.5)[b] | 32.6 (23.5-41.8)[b] | - |
| HEMI, n (%)[e] | 82 (43.6) | 91 (47.9) | 32 (16.8) |
| Adjusted treatment difference, % (95% CI) | 25.7 (17.1-34.3) | 29.6 (21.1-38.0) | - |
| Multiplicity-controlled *P*-value | <0.001 | <0.001 | - |
| Histologic remission and endoscopic improvement, n (%)[f] | 78 (41.5) | 89 (46.8) | 30 (15.8) |
| Adjusted treatment difference, % (95% CI) | 24.7 (16.2-33.2)[b] | 29.6 (21.3-38.0)[b] | - |
| Histologic remission and endoscopic normalization (remission), n (%)[g] | 59 (31.4) | 62 (32.6) | 27 (14.2) |
| Adjusted treatment difference, % (95% CI) | 16.2 (8.2-24.3)[b] | 16.9 (9.2-24.7)[b] | - |

AE, adverse event; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; COVID-19, coronavirus disease 2019; HEMI, histologic endoscopic mucosal improvement; IV, intravenous; NHI, Nancy Histological Index; Q4W, every 4 weeks; Q8W, every 8 weeks; RHI, Robarts Histopathology Index; SC, subcutaneous; UC, ulcerative colitis; Y/N, yes or no.

**Note:** Patients who, prior to week 44, had a prohibited change in UC medication, an ostomy or colectomy, a dose adjustment (including sham dose adjustment) or had discontinued study agent due to lack of therapeutic effect, an AE of worsening of UC, or other reasons (except for COVID-19 infections or regional crisis in Russia and Ukraine) were considered not to have achieved the endpoint. Patients who had an unevaluable biopsy (ie, a biopsy that was collected but could not be assessed due to sample preparation or technical errors) or for whom the endoscopy subscore (if applicable) or data on any of the histology components pertaining to an endpoint at week 44 were missing were considered not to have achieved the endpoint. The adjusted treatment difference and CI were based on the Wald statistic with CMH weight.

The *P*-values were based on the CMH chi-square test, stratified by the clinical remission status at maintenance baseline (Y/N), and induction treatment (TREMFYA 400 mg IV, TREMFYA 200 mg IV, and placebo IV crossover to TREMFYA 200 mg IV).

[a]Neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes histologic score ≤3.1).

[b]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established.**

[c]Absence of neutrophils in the mucosa (both lamina propria and epithelium); no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes histologic score ≤2 B.0).

[d]Results for histologic remission by alternative definitions using RHI ≤3 (with subscore of 0 for lamina propria neutrophils and neutrophils in the epithelium and without ulcers or erosion) and NHI ≤1 were identical.

[e]Achieving a combination of histologic and endoscopic improvement (Mayo endoscopy subscore of 0 or 1 with no friability).

[f]Geboes histologic score ≤2 B.0 and endoscopic improvement.

[g]Geboes histologic score ≤2 B.0 and Mayo endoscopy subscore of 0.

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### Outcomes by week 24 responders

- At week 24, 123/203 (60.6%) week 12 TREMFYA IV nonresponders achieved clinical response and entered the maintenance study phase.[23]
- The patient characteristics included,[23]
  - 78% patients with severe disease (modified Mayo score 7-9).
  - 77.2% patients with Mayo endoscopy subscore of 3.
  - 59.3% patients with a history of inadequate response or intolerance to biologic or JAKi therapy for UC.
- The proportion of TREMFYA week 24 responders in symptomatic remission at maintenance baseline (58.5%) was sustained through maintenance week 44 (56.9%).[23]
- AEs were reported for 78.0% of week 24 reponders, 5.7% patients had SAEs and 1.6% patients had serious infections. There were no incidence of OIs, deaths or any new safety concerns.[23]
- For efficacy outcomes at week 44 for TREMFYA induction week 24 responders, see the tab below.

**Efficacy outcomes at maintenance week 44 for TREMFYA induction week 12 nonresponders who achieved clinical response at induction week 24**

**Efficacy outcomes at maintenance week 44 for TREMFYA induction week 12 nonresponders who achieved clinical response[a] at induction week 24[23]**

| Outcomes, n (%) | TREMFYA 200 mg SC Q4W (n=123) |
|---|---|
| Clinical remission[b] | 37 (30.1) |
| Endoscopic improvement[c] | 44 (35.8) |
| Endoscopic normalization (remission)[d] | 21 (17.1) |
| Corticosteroid-free clinical remission[e] | 37 (30.1) |
| Maintenance of clinical response[f] | 83 (67.5) |
| HEMI[g] | 34 (27.6) |
| Fatigue response[h] | 49 (39.8) |
| Maintenance of clinical remission,[i] n=20 | 10 (50.0) |

HEMI, histologic endoscopic mucosal improvement; PROMIS, Patient-Reported Outcomes Measurement Information System; Q4W, every 4 weeks; SC, subcutaneous.

[a]Clinical response was defined as a decrease from induction baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from induction baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.

[b]Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 that did not increase from induction baseline; a Mayo rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[c]Endoscopic improvement was defined as an endoscopy subscore of 0 or 1, with no friability observed on endoscopy.

[d]Endoscopic normalization (remission) was defined as an endoscopy subscore of 0.

[e]Corticosteroid-free clinical remission was defined as clinical remission at maintenance week 44 without any use of corticosteroids for ≥8 weeks prior to maintenance week 44.

[f]Maintenance of clinical response was defined as clinical response at maintenance week 44 among patients with clinical response at maintenance baseline.

[g]HEMI was defined as achieving a combination of histologic improvement (defined as neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue according to the Geboes grading system [ie, Geboes score of ≤3.1]) and endoscopic improvement.

[h]Fatigue response was defined as a ≥7-point improvement from induction baseline in the PROMIS Fatigue Short Form 7a.

[i]Maintenance of clinical remission was defined as clinical remission at maintenance week 44 among patients in clinical remission at maintenance baseline.

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### Efficacy by extent of disease and inflammatory burden

- In the QUASAR study, efficacy endpoints assessed at week 44 in the primary analysis population consisted of patients randomized and treated in the maintenance study who had a modified Mayo score of 5 to 9 at induction baseline (I-0).[24]
- A subgroup analysis was conducted to evaluate the efficacy of TREMFYA 100 mg Q8W and 200 mg Q4W SC maintenance regimens in subgroups of patients with and without extensive UC or elevated inflammatory burden.[24]
  - Extent of disease was categorized as disease limited to left side of colon or extensive, based on screening endoscopy and/or medical history at I-0
  - Inflammatory burden was defined by serum CRP levels (≤3 vs >3 mg/L) at maintenance baseline (M-0)
- Efficacy endpoints evaluated were:
  - Clinical remission was defined as a stool frequency subscore of 0 or 1 without increase from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability.[24]
  - Maintenance of clinical remission was defined as clinical remission at week 44 among patients who achieved clinical remission at maintenance baseline.[24]
  - Endoscopic improvement was defined as an endoscopy subscore of 0 or 1 with no friability.[24]
  - HEMI was defined as the combined achievement of histologic improvement and endoscopic improvement.[24]
- Of the 568 patients in the primary analysis population, 257 (45.2%) had extensive UC at I-0 and 182 (32.0%) had serum CRP >3 mg/L at M-0.[24]

**Key efficacy endpoints at week 44 in subgroups by the extent of UC (limited to the left side of the colon vs extensive) at induction baseline**

**Key efficacy endpoints at week 44 in subgroups by the inflammatory burden (serum CRP ≤3 vs >3 mg/L) at maintenance baseline**

**Key efficacy endpoints at week 44 in subgroups by the extent of UC (limited to the left side of the colon vs extensive) at induction baseline**[24]

| Endpoint at week 44 | Limited to the left side of the colon | | | Extensive | | |
|---|---|---|---|---|---|---|
| | TREMFYA 100 mg SC Q8W (n=109) | TREMFYA 200 mg SC Q4W (n=107) | TREMFYA Withdrawal (PBO) (n=95) | TREMFYA 100 mg SC Q8W (n=79) | TREMFYA 200 mg SC Q4W (n=83) | TREMFYA withdrawal (PBO) (n=95) |
| Clinical remission[a] | 42.2%[b] | 40.2%[b] | 26.3% | 49.4%[b] | 62.7%[b] | 11.6% |
| Maintenance of clinical remission[c,d] | 56.1% (23/41) | 64.1% (25/39) | 45.2% (14/31) | 68.0%[b] (17/25) | 83.3%[b] (25/30) | 21.4% (6/28) |
| Endoscopic improvement[e] | 47.7%[b] | 42.1%[b] | 26.3% | 51.9%[b] | 63.9%[b] | 11.6% |
| HEMI[f] | 43.1%[b] | 40.2%[b] | 24.2% | 44.3%[b] | 57.8%[b] | 9.5% |
| Endoscopic remission[g] | 31.2% | 25.2% | 22.1% | 39.2%[b] | 44.6%[b] | 8.4% |

**Note:** Includes patients with a modified Mayo score of 5 to 9 at induction baseline who achieved clinical response to GUS induction and were rerandomized at maintenance study entry. Patients who had an ostomy or colectomy, dose adjustment, or prohibited change in UC medication or who discontinued the study agent due to lack of efficacy or an AE of worsening of UC prior to week 44 were considered not to have achieved the efficacy endpoints. For patients who discontinued the study agent due to COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to week 44, observed values were used if available. Patients who discontinued the study agent for other reasons prior to week 44 were considered not to have achieved the endpoint. Nonresponder imputation for missing data: patients who were missing 1 or more of the components pertaining to an endpoint at week 44 were considered not to have achieved the endpoint. Patients who had an unevaluable biopsy were considered not to have achieved the histologic endpoints.

[a]Clinical remission was defined as a stool frequency subscore of 0 or 1 without increase from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability.

[b]***P*-value vs PBO. The endpoints were not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established**.

[c]Maintenance of clinical remission was defined as clinical remission at week 44 among patients who achieved clinical remission at maintenance baseline.

[d]Denominator includes only patients with clinical remission at maintenance baseline.

[e]Endoscopic improvement was defined as an endoscopy subscore of 0 or 1 with no friability.

[f]HEMI was defined as achieving a combination of histologic improvement and endoscopic improvement.

[g]Endoscopic remission was defined as an endoscopy subscore of 0.

AE, adverse event; COVID-19, coronavirus disease 2019; GUS, guselkumab; HEMI, histologic-endoscopic mucosal improvement; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; UC, ulcerative colitis.

**Key efficacy endpoints at week 44 in subgroups by the inflammatory burden (serum CRP ≤3 vs >3 mg/L) at maintenance baseline[24]**

| Endpoint at week 44 | ≤3 mg/L | | | >3 mg/L | | |
|---|---|---|---|---|---|---|
| | TREMFYA 100 mg SC Q8W (n=125) | TREMFYA 200 mg SC Q4W (n=134) | TREMFYA withdrawal (PBO) (n=127) | TREMFYA 100 mg SC Q8W (n=63) | TREMFYA 200 mg SC Q4W (n=56) | TREMFYA withdrawal (PBO) (n=63) |
| Clinical remission[a] | 52.8%[b] | 50.7%[b] | 21.3% | 30.2%[b] | 48.2%[b] | 14.3% |
| Maintenance of clinical remission[c,d] | 63.5%[b] (33/52) | 67.3%[b] (35/52) | 41.5% (17/41) | 50.0% (7/14) | 88.2%[b] (15/17) | 16.7% (3/18) |
| Endoscopic improvement[e] | 56.8%[b] | 51.5%[b] | 21.3% | 34.9%[b] | 51.8%[b] | 14.3% |
| HEMI[f] | 51.2%[b] | 48.5%[b] | 18.9% | 28.6%[b] | 46.4%[b] | 12.7% |
| Endoscopic remission[g] | 40.0%[b] | 34.3%[b] | 18.1% | 23.8%[b] | 32.1%[b] | 9.5% |

**Note:** Includes patients with a modified Mayo score of 5 to 9 at induction baseline who achieved clinical response to GUS induction and were rerandomized at maintenance study entry. Patients who had an ostomy or colectomy, dose adjustment, or a prohibited change in UC medication or who discontinued the study agent due to lack of efficacy or an AE of worsening of UC prior to week 44 were considered not to have achieved the efficacy endpoints. For patients who discontinued the study agent due to COVID-19-related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine prior to week 44, observed values were used if available. Patients who discontinued the study agent for other reasons prior to week 44 were considered not to have achieved the endpoint. Nonresponder imputation for missing data: patients who were missing 1 or more of the components pertaining to an endpoint at week 44 were considered not to have achieved the endpoint. Patients who had an unevaluable biopsy were considered not to have achieved the histologic endpoints.

[a]Clinical remission was defined as a stool frequency subscore of 0 or 1 without increase from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability.

[b]***P*-value vs PBO. The endpoints were not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established.** The values are based on the Cochran-Mantel-Haenszel test stratified by the clinical remission status at maintenance baseline and induction treatment, except for maintenance of clinical remission where *P* values were based on a Fisher's exact test.

[c]Maintenance of clinical remission was defined as clinical remission at week 44 among patients who achieved clinical remission at maintenance baseline.

[d]Denominator includes only patients with clinical remission at maintenance baseline.

[e]Endoscopic improvement was defined as an endoscopy subscore of 0 or 1 with no friability.

[f]HEMI was defined as achieving a combination of histologic improvement and endoscopic improvement.

[g]Endoscopic remission was defined as an endoscopy subscore of 0.

AE, adverse event; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; GUS, guselkumab; HEMI, histologic-endoscopic mucosal improvement; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; UC, ulcerative colitis.

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### Endpoint by history of biologics/JAKi therapy

- Of 568 patients, 240 (42.3%) patients had a history of an inadequate response or intolerance to biologics/JAKi, 309 (54.4%) were biologic/JAKi-naïve, and 19 (3.3%) were biologics/JAKi experienced without a documented inadequate response or intolerance.[25]
- Among patients with an inadequate response or intolerance to biologics/JAKi (patients with anti-TNFs [87.9%], vedolizumab [49.2%], or tofacitinib [20.0%]), 48.3% patients had an inadequate response or intolerance to ≥2 biologic/JAKi therapies.[25]
- At week 44, clinical remission was achieved by 40.0% of TREMFYA-treated patients (vs 8.0% of withdrawal patients, nominal *P*-value) who had an inadequate response or intolerance to biologics/JAKi and by 54.2% of biologic/JAKi-naïve patients who were treated with TREMFYA (vs 25.9% of withdrawal patients, nominal *P*-value).[25]
- Through week 44, AEs for both the subpopulations were consistent with those for the overall population, and no new safety concerns were reported.[25]
- For outcomes at maintenance week 44 of patients with a history of biologics/JAKi therapy, see the tab below.

**Outcomes at maintenance week 44 by history of biologics/JAKi therapy: primary analysis population**

## Outcomes at maintenance week 44 by history of biologics/JAKi therapy: primary analysis population[25]

| Outcomes | History of inadequate response/ intolerance to biologics/JAKi | | | Biologic/JAKi naïve | | |
|---|---|---|---|---|---|---|
| | TREMFYA 100 mg SC Q8W (n=77) | TREMFYA 200 mg SC Q4W (n=88) | TREMFYA withdrawal (placebo) (n=75) | TREMFYA 100 mg SC Q8W (n=105) | TREMFYA 200 mg SC Q4W (n=96) | TREMFYA withdrawal (placebo) (n=108) |
| | | | | | | |
| Clinical remission,[a,b] n (%) | 31 (40.3) | 35 (39.8) | 6 (8.0) | 53 (50.5) | 56 (58.3) | 28 (25.9) |
| Adjusted treatment difference, % (95% CI) | 30.4 (18.7 to 42.1)[c] | 32.4 (21.1 to 43.7)[c] | - | 24.3 (12.0 to 36.5)[c] | 28.8 (16.5 to 41.1)[c] | - |
| Maintenance of clinical remission,[d,b] n/N (%) | 12/20 (60) | 10/18 (55.6) | 4/15 (26.7) | 28/43 (65.1) | 38/48 (79.2) | 14/41 (34.1) |
| Treatment difference, % (95% CI) | 33.3 (-0.9 to 62.1)[c] | 28.9 (-5.9 to 59.0)[c] | - | 31.0 (9.3 to 50.6)[c] | 45.0 (24.9 to 62.2%)[c] | - |
| Maintenance of clinical response,[e,b] n (%) | 54 (70.1) | 59 (67.0) | 21 (28.0) | 87 (82.9) | 78 (81.3) | 58 (53.7) |
| Adjusted treatment difference, % (95% CI) | 40.8 (27.4 to 54.2)[c] | 39.4 (25.8 to 53.0)[c] | - | 29.0 (17.2 to 40.8)[c] | 26.3 (14.0 to 38.6)[c] | - |
| Symptomatic remission,[f,b] n (%) | 50 (64.9) | 53 (60.2) | 18 (24.0) | 78 (74.3) | 73 (76.0) | 50 (46.3) |
| Adjusted treatment difference, % (95% CI) | 39.1 (25.9 to 52.2)[c] | 36.8 (23.4 to 50.2)[c] | - | 27.6 (15.1 to 40.1)[c] | 28.2 (15.4 to 41.0)[c] | - |
| Endoscopic improvement,[g,b] n (%) | 35 (45.5) | 37 (42.0) | 6 (8.0) | 56 (53.3) | 57 (59.4) | 28 (25.9) |
| Adjusted treatment difference, % (95% CI) | 35.8 (23.8 to 47.8)[c] | 34.6 (23.1 to 46.0)[c] | - | 27.2 (15.0 to 39.5)[c] | 30.0 (17.6 to 42.4)[c] | - |
| HEMI,[h,b] n (%) | 29 (37.7) | 34 (38.6) | 6 (8.0) | 52 (49.5) | 54 (56.3) | 25 (23.1) |
| Adjusted treatment difference, % (95% CI) | 27.7 (16.0 to 39.5)[c] | 31.2 (19.8 to 42.5)[c] | - | 26.1 (14.0 to 38.2)[c] | 29.5 (17.3 to 41.7)[c] | - |
| Endoscopic normalization (remission),[i,b] n (%) | 24 (31.2) | 21 (23.9) | 6 (8.0) | 40 (38.1) | 40 (41.7) | 22 (20.4) |
| Adjusted treatment difference, % (95% CI) | 21.4 (10.0 to 32.7)[c] | 16.3 (6.4 to 26.1)[c] | - | 17.3 (5.6 to 29.1)[c] | 17.5 (6.0 to 29.0)[c] | - |

AE, adverse event; CI, confidence interval; COVID-19, coronavirus disease 2019; HEMI, histologic endoscopic mucosal improvement; JAK, Janus kinase; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; UC, ulcerative colitis.

Note: Biologic/JAK inhibitor experienced without a documented inadequate response or intolerance to biologic/JAK inhibitors: TREMFYA 100 mg, n=6 and TREMFYA 200 mg, n=6; and placebo, n=7.

[a]Clinical remission: A Mayo stool frequency subscore of 0 or 1 that did not increase from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability.

[b]Patients who, prior to the week 44 visit, had a prohibited change in UC medication, an ostomy or colectomy, a dose adjustment (including a sham dose adjustment) or had discontinued study agent due to lack of efficacy, an AE of worsening of UC or other reasons except for COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine were considered not to have achieved the endpoint. Patients who were missing 1 or more components pertaining to a specified endpoint at week 44 were considered not to have achieved the endpoint.

[c]**Nominal *P*-value <0.001 for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established.**

[d]Maintenance of clinical remission: clinical remission at week 44 among patients in clinical remission at maintenance baseline.

[e]Maintenance of clinical response: clinical response at week 44 among patients in clinical response at maintenance baseline.

[f]Symptomatic remission: A stool frequency subscore of 0 or 1 that did not increase from induction baseline and a rectal bleeding subscore of 0.

[g]Endoscopic improvement: An endoscopy subscore of 0 or 1 with no friability observed on endoscopy.

[h]HEMI: Achieving a combination of histologic improvement (neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue per Geboes grading system) and endoscopic improvement.

[i]Endoscopic normalization: An endoscopy subscore of 0.

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### Summary of HRQOL outcomes

- For HRQOL outcomes, see tab below.[2,26]

**Change from maintenance baseline in PROMIS-29 domain T-scores, pain intensity, and PCS/MCS score at week 44**

**Change from maintenance baseline in PROMIS-29 domain T-scores, pain intensity, and PCS/MCS score at week 44[26]**

| | TREMFYA 100 mg SC Q8W (N=188) | TREMFYA 200 mg SC Q4W (N=190) | TREMFYA withdrawal (placebo SC) (N=190) |
|---|---|---|---|
| **PROMIS-29 domain** | | | |
| **Anxiety T-score** | | | |
| Maintenance baseline, mean (SD) | 50.00 (8.495); n=188 | 50.31 (8.862); n=189 | 49.95 (8.226); n=188 |
| Change from maintenance baseline, mean (SD) | -0.87 (9.000); n=184 | 0.12 (8.432); n=181 | 3.09 (9.011); n=184 |
| Treatment difference (95% CI) | -3.91 (-5.55 to -2.26) | -2.81 (-4.46 to -1.15) | - |
| **Depression T-score** | | | |
| Maintenance baseline, mean (SD) | 48.43 (8.180); n=188 | 48.26 (8.112); n=189 | 48.30 (7.800); n=188 |
| Change from maintenance baseline, mean (SD) | -0.26 (8.618); n=184 | 0.60 (8.055); n=181 | 2.75 (7.506); n=184 |
| Treatment difference (95% CI) | -2.96 (-4.44 to -1.47) | -2.19 (-3.68 to -0.71) | - |
| **Fatigue T-score** | | | |
| Maintenance baseline, mean (SD) | 47.79 (9.232); n=188 | 47.90 (10.342); n=189 | 47.00 (9.184); n=188 |
| Change from maintenance baseline, mean (SD) | -0.37 (10.065); n=184 | 0.64 (9.406); n=181 | 4.20 (8.658); n=184 |
| Treatment difference (95% CI) | -4.18 (-5.95 to -2.40) | -3.20 (-4.98 to -1.42) | - |
| **Pain interference T-score** | | | |
| Maintenance baseline, mean (SD) | 47.84 (7.480); n=188 | 48.53 (8.373); n=189 | 47.71 (7.608); n=188 |
| Change from maintenance baseline, mean (SD) | 0.20 (9.012); n=184 | -0.22 (9.341); n=181 | 3.39 (9.467); n=184 |
| Treatment difference (95% CI) | -3.13 (-4.78 to -1.48) | -3.14 (-4.79 to -1.48) | - |
| **Sleep disturbance T-score** | | | |
| Maintenance baseline, mean (SD) | 48.09 (7.256); n=188 | 49.09 (8.776); n=189 | 47.32 (7.968); n=188 |
| Change from maintenance baseline, mean (SD) | 0.16 (6.965); n=184 | 0.61 (7.626); n=181 | 3.29 (7.247); n=184 |
| Treatment difference (95% CI) | -2.88 (-4.23 to -1.53) | -2.08 (-3.44 to -0.73) | - |
| **Physical function T-score** | | | |
| Maintenance baseline, mean (SD) | 51.56 (6.877); n=188 | 50.73 (7.535); n=189 | 51.40 (6.712); n=188 |
| Change from maintenance baseline, mean (SD) | -0.12 (7.344); n=184 | 0.80 (7.189); n=181 | -1.94 (7.437); n=184 |
| Treatment difference (95% CI) | 1.82 (0.47 to 3.18) | 2.45 (1.09 to 3.81) | - |

## Change from maintenance baseline in PROMIS-29 domain T-scores, pain intensity, and PCS/MCS score at week 44[26]

| | TREMFYA 100 mg SC Q8W (N=188) | TREMFYA 200 mg SC Q4W (N=190) | TREMFYA withdrawal (placebo SC) (N=190) |
|---|---|---|---|
| **PROMIS-29 domain** | | | |
| **Ability to participate in social roles and activities T-score** | | | |
| Maintenance baseline, mean (SD) | 54.57 (8.470); n=188 | 54.92 (9.306); n=189 | 55.65 (8.319); n=188 |
| Change from maintenance baseline, mean (SD) | 1.43 (9.755); n=184 | 0.80 (9.557); n=181 | -4.07 (9.648); n=184 |
| Treatment difference (95% CI) | 4.87 (3.15 to 6.59) | 4.48 (2.75 to 6.20) | - |
| **Pain intensity NRS score** | | | |
| Maintenance baseline, mean (SD) | 1.9 (1.78); n=188 | 1.9 (2.04); n=189 | 1.6 (1.96); n=188 |
| Change from maintenance baseline, mean (SD) | 0.0 (2.10); n=184 | 0.1 (2.39); n=181 | 1.2 (2.46); n=184 |
| Treatment difference (95% CI) | -1.1 (-1.5 to -0.7) | -1.0 (-1.4 to -0.6) | - |
| **PROMIS-29 summary T-scores** | | | |
| **PCS score** | | | |
| Maintenance baseline, mean (SD) | 52.08 (7.022); n=188 | 51.35 (7.846), n=189 | 52.12 (7.041); n=188 |
| Change from maintenance baseline, mean (SD) | 0.06 (7.532); n=184 | 0.77 (7.511), n=181 | -2.58 (7.916); n=184 |
| Treatment difference (95% CI) | 2.54 (1.12 to 3.96) | 3.04 (1.62 to 4.46) | - |
| **MCS score** | | | |
| Maintenance baseline, mean (SD) | 52.68 (7.537); n=188 | 52.52 (8.735); n=189 | 53.46 (7.636); n=188 |
| Change from maintenance baseline, mean (SD) | 0.61 (8.134); n=184 | -0.23 (8.033); n=181 | -4.34 (7.822); n=184 |
| Treatment difference (95% CI) | 4.64 (3.11 to 6.16) | 3.81 (2.28 to 5.34) | - |

AE, adverse event; CI, confidence interval; COVID-19, coronavirus disease 2019; IV, intravenous; LSM, least square mean; MCS, mental component summary; mMayo, modified Mayo; NRS, numeric rating scale; PCS, physical component summary; PROMIS-29, 29-Item Patient-Reported Outcomes Measurement Information System; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SD, standard deviation; UC, ulcerative colitis.
**Note**: Includes only patients with an mMayo score ranging from 5 to 9 at induction baseline who were in clinical response to TREMFYA IV induction and were randomized into the maintenance study. **All *P*-values are nominal for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal and statistical significance has not been established.**
Higher scores indicate better outcomes for physical function, social participation, PCS, and MCS and worse outcomes for all other domains. Patients who had a prohibited change in UC medication, an ostomy or colectomy, or a dose adjustment or for whom the study agent was discontinued due to a lack of efficacy or an AE of worsening of UC prior to the designated timepoint had their induction baseline value carried forward from the time of the event onward. For patients for whom the study agent was discontinued due to COVID-19-related reasons (excluding COVID-19 infection) or the regional crisis in Russia and Ukraine prior to the designated timepoint, observed values were used.
*P*-values are based on mixed-effect model repeated measures, and the treatment difference between the TREMFYA and placebo groups was estimated by the difference in the LSM.

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### Effect on serum proteins and colonic epithelial cells

- Transcriptional profiling of colonic biopsies (n=396) was performed using RNAseq and gene modules for differential expression.[27]
- Serum proteins were evaluated (n=430) using a targeted inflammation panel, and differential protein abundance was assessed.[27]
- Molecular analysis showed significant downregulation of key inflammatory gene modules from maintenance baseline to week 44 (all FDR<0.05).[27]
- Gene modules related to intestinal mesenchymal biology (pericytes, fibroblasts, and endothelium) showed changes in maintenance compared to induction.[27]
  - Upregulation of gene modules representing healthy epithelial biology (crypt, goblet cells, and M-cells) was also observed at maintenance week 44.
- Serum analysis showed continued reductions in inflammatory proteins (IL-17A and IL-8; FDR <0.05) and several chemokines (including CCL11, which has been linked to mesenchymal biology) from maintenance baseline to week 44.[27]
- TREMFYA discontinuation led to a reversal in anti-inflammatory effects (achieved at the end of induction) by maintenance week 44.[27]

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### Study design/methods

- Patients who completed the maintenance study, including the week 44 visit, were eligible to enter the LTE study and continue their current treatment regimen. Following study unblinding, participants in the placebo group were discontinued from treatment.[28]
- The efficacy analysis included patients who were randomized to TREMFYA at maintenance at week 0 and continued to receive treatment in the LTE. Safety analysis included all patients in the maintenance study who continued treatment in the LTE.[28]
- Overall, 87% of patients randomized to TREMFYA entered the LTE, with approximately 95% of those completing treatment through week 92.[28]

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### Efficacy at week 92 in the overall population randomized at week 0 and treated in the LTE (NRI and as observed analyses)[28]

| Outcomes, n/N (%) | NRI | | As observed | |
|---|---|---|---|---|
| | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W |
| Clinical remission[a] | 110/155 (71) | 109/148 (73.6) | 110/147 (74.8) | 109/132 (82.6) |
| Maintenance of clinical remission[b] | 45/58 (77.6) | 49/57 (86) | 45/55 (81.8) | 49/51 (96.1) |
| Symptomatic remission[c] | 136/155 (87.7) | 132/148 (89.2) | 136/148 (91.9) | 132/139 (95) |
| Endoscopic improvement[d] | 116/155 (74.8) | 112/148 (75.7) | 116/147 (78.9) | 112/133 (84.2) |
| Endoscopic remission (normalization)[e] | 65/155 (41.9) | 65/148 (43.9) | 65/147 (44.2) | 65/133 (48.9) |
| HEMI[f] | 101/155 (65.2) | 98/148 (66.2) | 101/145 (69.7) | 98/130 (75.4) |

Note: Includes patients with modified Mayo score of 5-9 at induction baseline who achieved clinical response to TREMFYA IV induction and were randomized to receive TREMFYA maintenance treatment and did not experience a dose adjustment from week 8 through week 32. [a]Clinical remission is defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, a rectal bleeding subscore of 0, and an endoscopic subscore of 0 or 1.
[b]Maintenance of clinical remission is defined as meeting the criteria for clinical remission at week 92 among patients who met the criteria for clinical remission at maintenance baseline.
[c]Symptomatic remission is defined as a stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0, where the stool frequency subscore has not increased from induction baseline.
[d]Endoscopic improvement is defined as an endoscopy subscore of 0 or 1.
[e]Endoscopic remission (normalization) is defined as an endoscopy subscore of 0.
[f]HEMI is defined as achieving a combination of histologic and endoscopic improvement.

### Corticosteroid-sparing outcomes at week 92

- Among the 219 patients in clinical remission at week 92, 99.5% (n=218) were corticosteroid free ≥8 weeks before week 92.[28]

### Histo-endoscopic and endoscopic outcomes at week 92

- Among patients who achieved endoscopic improvement at week 44, 87.2% in the TREMFYA 100 mg group and 80.2% in the TREMFYA 200 mg group maintained this improvement through week 92. Similarly, of those who achieved HEMI at week 44, 73.5% and 75.5% of patients sustained HEMI at week 92 with TREMFYA 100 mg and TREMFYA 200 mg, respectively.[28]

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### Maintenance of endoscopic and histologic endpoints

- Maintenance of endoscopic and histologic efficacy was evaluated in the LTE among patients who continued their assigned TREMFYA regimen from week 0.[32]
- Efficacy data were analyzed using the following 2 methods[32]:
  - Nonresponder imputation (NRI), which accounted for patients with treatment failure or missing data
  - "As observed" analysis
- A total of 303 randomized patients continued TREMFYA treatment in the LTE, with 155 receiving 100 mg Q8W and 148 receiving 200 mg Q4W.[32]
- Endoscopic improvement was defined as an endoscopic subscore of 0 or 1.[32]
- Histologic improvement was defined according to the Geboes grading system as neutrophil infiltration in <5% of crypts; absence of crypt destruction; and no evidence of erosions, ulcerations, or granulation tissue.[32]
- HEMI was defined as the combined achievement of histologic improvement and endoscopic improvement.[32]
- Histologic remission was defined according to the Geboes grading system as the absence of neutrophils in both the lamina propria and epithelium; no crypt destruction; and no erosions, ulcerations, or granulation tissue, consistent with RHI ≤2b. This includes subscores of 0 for lamina propria neutrophils and epithelial neutrophils and an absence of ulcers or erosion.[32]
- Results from the as-observed analysis were consistent with those from the nonresponder analysis, with a low dropout rate among patients treated with TREMFYA.[32]

**Maintenance of endoscopic and histologic endpoints with TREMFYA**

## Maintenance of endoscopic and histologic endpoints with TREMFYA[32]

| % [95% CI], n/m | Endpoint maintenance: week 44 to week 92[a] | | | | Endpoint maintenance: week 0 to week 92[b] | | | |
|---|---|---|---|---|---|---|---|---|
| | NRI analysis | | As-observed analysis | | NRI analysis | | As-observed analysis | |
| | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W |
| **Endoscopic improvement[c]** | 87.2% [80.5, 94.0] (82/94) | 80.2% [72.4, 88.0] (81/101) | 92.1% [86.5, 97.7] (82/89) | 90.0% [83.8, 96.2] (81/90) | 80.3% [70.7, 89.9] (53/66) | 85.9% [77.4, 94.5] (55/64) | 85.5% [76.7, 94.3] (53/62) | 94.8% [89.1, 100] (55/58) |
| **Histologic improvement[d]** | 77.9% [70.5, 85.2] (95/122) | 75.2% [67.6, 82.8] (94/125 | 83.3% [76.5, 90.2] (95/114) | 83.2% [76.3, 90.1] (94/113) | 74.3% [65.7, 82.8] (75/101) | 72.0% [62.9, 81.2] (67/93) | 80.6% [72.6, 88.7] (75/93) | 80.7% [72.2, 89.2] (67/83) |
| **HEMI[e]** | 73.5% [64.0, 83.0] (61/83) | 75.5% [66.8, 84.2] (71/94) | 80.3% [71.3, 89.2] (61/76) | 85.5% [78.0, 93.1] (71/83) | 70.2% [58.3, 82.1] (40/57) | 79.6% [68.9, 90.4] (43/54) | 78.4% [67.1, 89.7] (40/51) | 91.5% [83.5, 99.5] (43/47) |
| **Histologic remission[f]** | 71.2% [62.7, 79.6] (79/111) | 71.2% [63.0, 79.4] (84/118) | 76.7% [68.5, 84.9] (79/103) | 77.8 % [69.9, 85.6] (84/108) | 67.0% [57.4, 76.7] (61/91) | 67.1% [56.9, 77.2] (55/82) | 73.5% [64.0, 83.0] (61/83) | 76.4% [66.6, 86.2] (55/72) |

[a]Percentages represent the proportion of patients achieving the endpoint at week 92 among those who achieved the corresponding endpoint at week 44. CIs in each treatment group are based on the normal approximation confidence limits.
[b]Percentages represent the proportion of patients achieving the endpoint at week 92 among those who achieved the corresponding endpoint at week 0 (baseline of the maintenance study). CIs in each treatment group are based on the normal approximation confidence limits.
Includes patients with a modified Mayo score of 5 to 9 at induction baseline who achieved clinical response to TREMFYA IV induction and were randomized to receive TREMFYA maintenance treatment and did not experience a dose adjustment from week 8 through week 32.
[c]Endoscopic improvement was defined as an endoscopic subscore of 0 or 1.
[d]Histologic improvement was defined according to the Geboes grading system as neutrophil infiltration in <5% of crypts; absence of crypt destruction; and no evidence of erosions, ulcerations, or granulation tissue.
[e]HEMI was defined as the combined achievement of histologic improvement and endoscopic improvement.
[f]Histologic remission was defined according to the Geboes grading system as the absence of neutrophils in both the lamina propria and epithelium; no crypt destruction; and no erosions, ulcerations, or granulation tissue, consistent with RHI ≤2b. This includes subscores of 0 for lamina propria neutrophils and epithelial neutrophils and an absence of ulcers or erosion.
CI, confidence interval; HEMI, histologic-endoscopic mucosal improvement; IV, intravenous; m, number of patients achieving the endpoint at week 0 or week 44; n, number of patients achieving the endpoint at week 92; NRI, nonresponder imputation; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous.

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### Efficacy by history of biologics/JAKi therapy at week 92[28]

| Outcomes at week 92, n/N (%) | History of inadequate response/ intolerance to biologics/JAKi | | Biologic/JAKi naïve | |
|---|---|---|---|---|
| | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W |
| Clinical remission[a] | 42/60 (70) | 41/62 (66.1) | 65/90 (72.2) | 64/81 (79) |
| Maintenance of clinical remission[b] | 13/19 (68.4) | 10/12 (83.3) | 30/37 (81.1) | 37/42 (88.1) |
| Symptomatic remission[c] | 51/60 (85) | 53/62 (85.5) | 80/90 (88.9) | 74/81 (91.4) |
| Endoscopic improvement[d] | 45/60 (75) | 43/62 (69.4) | 68/90 (75.6) | 65/81 (80.2) |
| Endoscopic remission (normalization)[e] | 27/60 (45) | 23/62 (37.1) | 37/90 (41.1) | 41/81 (50.6) |
| HEMI[f] | 37/60 (61.7) | 37/62 (59.7) | 61/90 (67.8) | 57/81 (70.4) |

Note: Includes patients with modified Mayo score of 5-9 at induction baseline who achieved clinical response to TREMFYA IV induction and were randomized to receive TREMFYA maintenance treatment and did not experience a dose adjustment from week 8 through week 32.

[a]Clinical remission is defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, a rectal bleeding subscore of 0, and an endoscopic subscore of 0 or 1.

[b]Maintenance of clinical remission is defined as meeting the criteria for clinical remission at week 92 among patients who met the criteria for clinical remission at maintenance baseline.

[c]Symptomatic remission is defined as a stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0, where the stool frequency subscore has not increased from induction baseline.

[d]Endoscopic improvement is defined as an endoscopy subscore of 0 or 1.

[e]Endoscopic remission (normalization) is defined as an endoscopy subscore of 0.

[f]HEMI is defined as achieving a combination of histologic and endoscopic improvement.

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- Within 1 hour of infusion, no AEs were considered serious or led to treatment discontinuation.[6]

**Treatment-emergent AEs through week 12[6]**

| | TREMFYA 200 mg IV (N=421) | Placebo IV (N=280) |
|---|---|---|
| Patients with ≥1 event, n (%) | | |
| AEs | 208 (49.4) | 138 (49.3) |
| SAEs | 12 (2.9) | 20 (7.1) |
| AEs leading to discontinuation of study agent | 7 (1.7) | 11 (3.9) |
| Infections[a] | 66 (15.7) | 43 (15.4) |
| Serious infections[a] | 3 (0.7) | 1 (0.4) |
| AEs within 1 hour of infusion | 6 (1.4) | 1 (0.4) |
| AEs leading to death | 1 (0.2) | 2 (0.7) |
| Most frequent AEs[b] | | |
| COVID-19 | 21 (5.0) | 12 (4.3) |
| Anemia | 21 (5.0) | 19 (6.8) |
| Worsening of UC | 10 (2.4) | 23 (8.2) |
| Headache | 13 (3.1) | 8 (2.9) |

[a]Infections were defined as any AE coded to the MedDRA system organ class "infections and infestations".
[b]Occurred in ≥3% of patients in any treatment group.

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- The percentage of patients with ≥1 AE was 70.0% in the TREMFYA 100 mg group, 64.5% in the TREMFYA 200 mg group, and 68.2% in the placebo group.[7]
- The most frequently reported AEs in the combined TREMFYA-treated group vs placebo group were COVID-19 (11.2% vs 14.1%), UC (11.2% vs 29.7%), and arthralgia (6.1% vs 6.8%).[7]
- In the combined TREMFYA-treated group, 2 cases of malignancy (clear cell renal carcinoma and rectal adenocarcinoma) and 1 case of a major cardiac AE (hemorrhagic stroke) were reported.[7]
- No cases of death, serious hepatic AEs, active tuberculosis, OIs, anaphylaxis, serum sickness, or Hy's law were reported in the primary safety population.[7]

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- There were no reports of death, active tuberculosis, OIs, anaphylaxis, serum sickness, or Hy's Law in patients treated with TREMFYA through week 92.[28]
- Detailed safety summary from week 44 through week 92 in all patients treated in the LTE is reported in the table below.[28]

**Safety summary from week 44 through week 92 (all patients treated in the LTE)[28]**

| | TREMFYA 100 mg SC Q8W | TREMFYA 200 mg SC Q4W | Placebo SC |
|---|---|---|---|
| All treated, N | 162 | 349 | 189 |
| Average duration of follow-up, weeks | 46.9 | 46.5 | 40.8 |
| Average exposure, weeks | 10.9 | 11.4 | 9.4 |
| Patients with event/100 patient-years of follow-up, n (95% CI) | | | |
| AE | 71.5 (58.4-86.6) | 75.9 (66.5-86.2) | 81.8 (67.9-97.8) |
| SAE | 2.8 (0.8-7.0) | 6.1 (3.7-9.5) | 10.8 (6.2-17.6) |
| AEs leading to discontinuation of study agent | 3.4 (1.1-8.0) | 4.8 (2.7-8.0) | 14.9 (9.3-22.5) |
| Infection[a] | 37.1 (27.9-48.4) | 40.5 (33.7-48.2) | 41.2 (31.6-53.0) |
| Serious infection[a] | 1.4 (0.2-5.0) | 1.0 (0.2-2.8) | 1.4 (0.2-4.9) |

Note: Includes all patients regardless of modified Mayo score at induction baseline who participated in the maintenance study and received treatment in the LTE. Data were summarized based on the study treatment patients were receiving upon entering the LTE.
[a]Infections were defined as any AE coded to the MedDRA system organ class "Infections and infestations".

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### Summary of safety results[1,2]

| Outcomes | Induction study | | Maintenance study | | |
|---|---|---|---|---|---|
| | TREMFYA 200 mg IV Q4W (N=421) | Placebo IV Q4W (N=280) | TREMFYA 100 mg Q8W SC (N=186) | TREMFYA 200 mg Q4W SC (N=190) | Placebo SC (N=192) |
| Mean duration of follow-up, weeks | 12.2 | 11.9 | 40.5 | 39.2 | 34.0 |
| Mean exposure (number of administrations) | 2.9 | 2.9 | 9.9 | 9.6 | 8.2 |
| AEs, n (%) | 208 (49) | 138 (49) | 120 (65) | 133 (70) | 131 (68) |
| SAEs, n (%) | 12 (3) | 20 (7) | 5 (3) | 12 (6) | 1 (1) |
| Deaths, n (%) | 1 (0.2)[a] | 2 (1)[b] | 0 | 0 | 0 |
| AEs leading to discontinuation of study agent, n (%) | 7 (2) | 11 (4) | 7 (4) | 5 (3) | 13 (7) |
| **Most frequent AEs (≥5% of patients in any treatment group), n (%)** | | | | | |
| UC | 10 (2) | 23 (8) | 17 (9) | 25 (13) | 57 (30) |
| Anemia | 21 (5) | 19 (7) | 4 (2) | 6 (3) | 5 (3) |
| COVID-19 | 21 (5) | 12 (4) | 24 (13) | 18 (9) | 27 (14) |
| Headache | 13 (3) | 8 (3) | 7 (4) | 8 (4) | 12 (6) |
| Arthralgia | 6 (1) | 6 (2) | 8 (4) | 15 (8) | 13 (7) |
| Upper RTI | 3 (1) | 1 (0.4) | 6 (3) | 13 (7) | 8 (4) |
| **Targeted AEs, n (%)** | | | | | |
| Serious infections[c] | 3 (1) | 1 (0.4) | 1 (1) | 2 (1) | 0 |
| OIs[c] | 0 | 1 (0.4)[d] | 0 | 0 | 0 |
| Active tuberculosis | 0 | 0 | 0 | 0 | 0 |
| MACE | 2 (0.5)[e] | 2 (1)[f] | 0 | 1 (1)[g] | 0 |
| Clinically important hepatic disorders[h] | 0 | 0 | 0 | 0 | 0 |
| Malignancies[i] | 0 | 0 | 0 | 1 (1)[j] | 2 (1)[k] |
| Nonmelanoma skin cancer | 2 (0.5) | 0 | 0 | 0 | 2 (1) |
| **Anaphylactic reactions, n (%)** | 0 | 0 | 0 | 0 | 0 |
| **Serum sickness reactions, n (%)** | 0 | 0 | 0 | 0 | 0 |

**Note:** For both studies, the primary safety populations included randomized, treated patients with a modified Mayo score from 4 to 9 at induction baseline. For the maintenance study, 2 patients who were randomly assigned to the TREMFYA 100 mg SC Q8W only received placebo at maintenance week 0 and discontinued the study intervention before their 1st scheduled TREMFYA dose at maintenance week 4; these patients were included in the placebo SC treatment group for safety analyses. For the maintenance study, data are from maintenance week 0 to maintenance week 44 or up to time of dose adjustment in patients who had a dose adjustment.

[a]Fatal acute MI in a patient with pre-existing cardiac risk factors. [b]Natural causes and cardiac arrest. [c]Infections were defined as any AE that was coded to MedDRA system organ class (version 26·0). [d]Cytomegalovirus colitis. [e]Nonfatal MI and fatal acute MI in patients with pre-existing cardiac risk factors. [f]Natural causes and cardiac arrest. [g]Hemorrhagic stroke. [h]Defined as hepatic AEs reported as SAEs or AEs leading to study drug discontinuation. [i]Excludes nonmelanoma skin cancer. [j]Rectal adenocarcinoma. [k]Breast cancer.

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This analysis evaluated the pharmacokinetics (PK) and exposure-response (E-R) for the efficacy and safety of TREMFYA IV and SC induction formulations (QUASAR and ASTRO studies).[30]

### Study design/methods

- The IV induction dosing regimen for phase 2b/3 QUASAR studies included 200 mg q4w x3 and SC induction for ASTRO study included 400 mg q4w x3.[30]
- Both QUASAR and ASTRO studies used the same SC maintenance dosing regimens (100 mg q8w or 200 mg q4w).[30]
- Individual post hoc PK parameter estimates were derived using the established QUASAR 2 compartment linear population PK (popPK) model with first-order absorption and elimination to compare TREMFYA PK exposure after IV and SC induction through week 12.[30]
- Patient dosing data from the QUASAR and ASTRO studies were used to simulate concentration-time profiles and calculate individual induction exposure metrics.[30]
- For key week 12 efficacy endpoints (clinical remission, clinical response, endoscopic improvement, and histologic-endoscopic mucosal improvement), comparative graphical E-R analysis (QUASAR vs ASRO) was conducted using overall exposure during induction ($C_{ave,\ week\ 0\text{-}12}$) and associated exposure quartiles from the combined study populations.[30]

### Results

- SC induction resulted in similar average serum concentrations and area under the concentration–time curve (AUC) from week 0 to week 12, lower peak concentrations at week 8, and higher trough levels at week 12 compared with IV induction. For details, see Table: **Comparison of model-predicted TREMFYA PK exposures at week 12 after induction regimens**.[30]

**Comparison of model-predicted TREMFYA PK exposures at week 12 after induction regimens[30]**

| | TREMFYA 200 mg IV q4w (n=644) | TREMFYA 400 mg SC q4w (n=331) |
|---|---|---|
| $C_{max,\ week\ 8}$ (µg/mL), mean (SD) | 68.9 (14.1) | 28.8 (8.81) |
| $C_{ave,\ week\ 0\text{-}12}$ (µg/mL), mean (SD) | 21.1 (5.80) | 19.0 (6.13) |
| $C_{trough,\ week\ 12}$ (µg/mL), mean (SD) | 9.91 (5.02) | 14.1 (6.27) |
| $AUC_{\ week\ 0\text{-}12}$ (day*µg/mL), mean (SD) | 1770 (487) | 1590 (515) |

- Steady-state serum concentration of TREMFYA was achieved by week 24.[30]
- Simulations based on the popPK model showed that serum TREMFYA levels were comparable by week 24 regardless of the induction route, when followed by the same maintenance regimen.[30]
- At week 12, efficacy outcomes were comparable across TREMFYA concentration quartiles for both IV and SC induction.[30]
- Similar positive E-R associations were observed following both IV and SC induction.[30]

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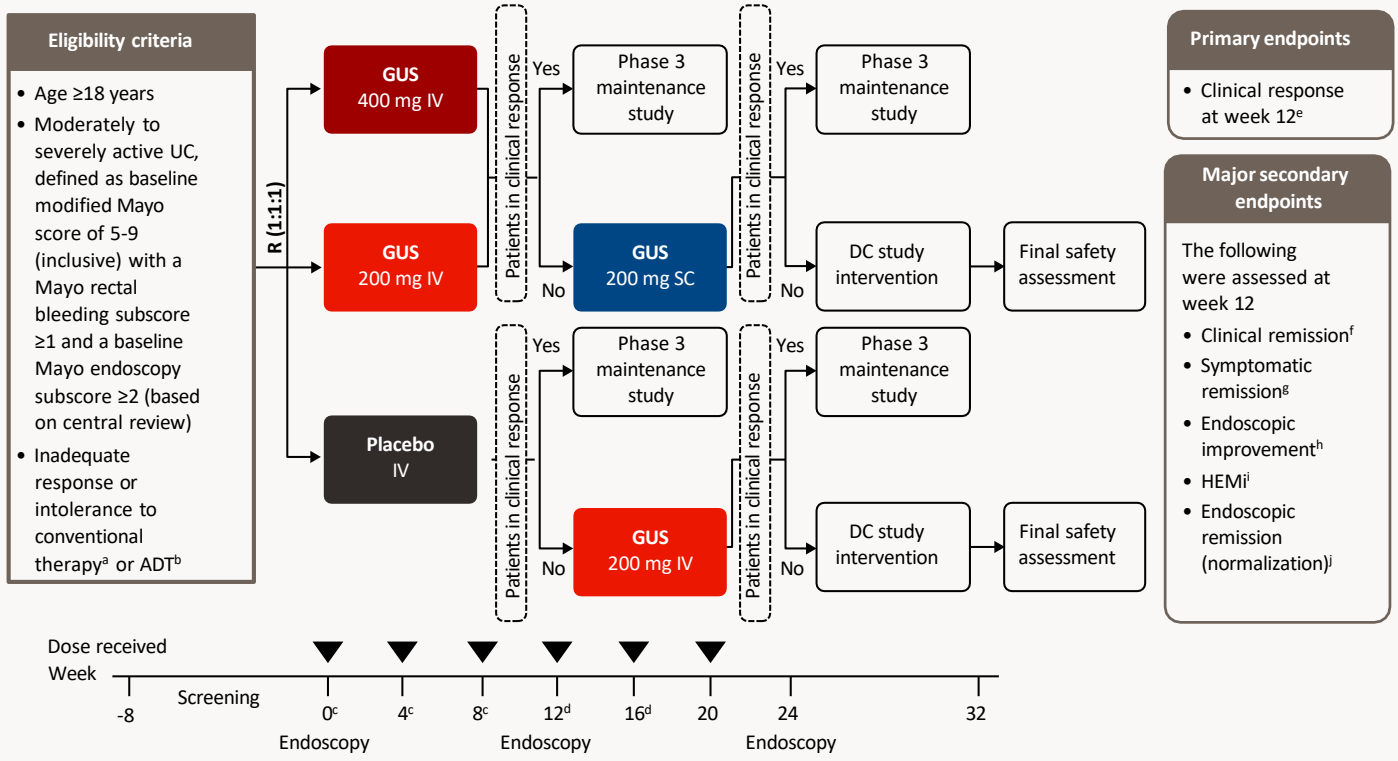
## Phase 2b study design[3,5]




[a]Corticosteroids or thiopurines.
[b]TNF alpha antagonists, vedolizumab, or tofacitinib.
[c]Study treatment administered.
[d]Study treatment administered to clinical nonresponders at week 12, with matching IV or SC placebo to maintain blinding.
[e]Clinical response was defined as a decrease from baseline in modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in rectal bleeding subscore or a rectal bleeding subscore of 0 or 1.
[f]Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 that had not increased from baseline; a rectal bleeding subscore of 0; and a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.
[g]Symptomatic remission was defined as a Mayo stool frequency subscore of 0 or 1 that had not increased from baseline and a Mayo rectal bleeding subscore of 0.
[h]Endoscopic improvement was defined as a Mayo endoscopy subscore of 0 or 1, with no friability observed on endoscopy.
[i]HEMI was defined as achievement of histologic (neutrophil infiltration in <5% of crypts; no crypt destruction; and no erosions, ulcerations, or granulation tissue based on the Geboes grading system [ie, Geboes score of ≤3.1]) and endoscopic improvement.
[j]Endoscopic remission (normalization) was defined as an endoscopy subscore of 0.

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### Patient characteristics at baseline

- There were 313 patients randomized in the primary analysis population. The mean age was 41.6 years, and the mean duration of UC was 7.55 years. The mean Mayo score was 9.2 and 70% of patients had endoscopy subscore of 3 (severe disease).[3]
- Of the 313 patients, 47.3% had a history of inadequate response or intolerance to ADT for UC.[3]
- At baseline, 90.4% of patients were receiving conventional therapy for UC including oral corticosteroids (39.6%), immunomodulatory therapy (21.7%), and oral aminosalicylates (77.3%).[3]

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- At week 12, a significantly greater proportion of patients in the TREMFYA 200 mg and 400 mg groups achieved clinical response compared with those in the placebo group (61.4% and 60.7% vs 27.6%, respectively; *P*<0.001 for both).[3]
- Major secondary efficacy outcomes are reported in the table below.[3]

**Major secondary efficacy endpoints at induction week 12[3,a]**

| **Proportion of patients, %** | **TREMFYA 200 mg IV (n=101)** | **TREMFYA 400 mg IV (n=107)** | **Placebo (n=105)** |
|---|---|---|---|
| Clinical remission | 25.7[b] | 25.2[b] | 9.5 |
| Symptomatic remission | 50.5[b] | 47.7[b] | 20.0 |
| Endoscopic improvement | 30.7[b] | 30.8[b] | 12.4 |
| HEMI | 19.8[b] | 27.1[b] | 8.6 |
| Endoscopic remission (normalization) | 17.8[b] | 14.0 | 6.7 |

[a]Patients who had a prohibited change in UC medication, an ostomy, or a colectomy or discontinued the study agent due to lack of efficacy or an AE of worsening of UC prior to the week 12 visit were considered not to have achieved these endpoints. Patients who were missing 1 or more components pertaining to a specified endpoint at week 12 were considered not to have achieved that endpoint.

[b]**Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established**

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### Efficacy results at week 12 by prior ADT status[31,a]

| Proportion of patients, % (95% CI) | TREMFYA 200 mg IV | TREMFYA 400 mg IV | TREMFYA combined | Placebo |
|---|---|---|---|---|
| Patients with a history of inadequate response/intolerance to ADT | | | | |
| n | 46 | 51 | 97 | 51 |
| Clinical response | 54.3[b] (39.0-69.1) | 47.1[b] (32.9-61.5) | 50.5[b] (40.2-60.8) | 25.5 (14.3-39.6) |
| Clinical remission | 17.4 (7.8-31.4) | 17.6 (8.4-30.9) | 17.5 (10.6-26.6) | 7.8 (2.2-18.9) |
| Symptomatic remission | 39.1[b] (25.1-54.6) | 37.3[b] (24.1-51.9) | 38.1[b] (28.5-48.6) | 17.6 (8.4-30.9) |
| Endoscopic improvement | 23.9 (12.6-38.8) | 21.6 (11.3-35.3) | 22.7 (14.8-32.3) | 9.8 (3.3-21.4) |
| Histo-endo mucosal improvement | 13.0 (4.9-26.3) | 19.6[b] (9.8-33.1) | 16.5 (9.7-25.4) | 5.9 (1.2-16.2) |
| Endoscopic remission (normalization) | 10.9 (3.6-23.6) | 5.9 (1.2-16.2) | 8.2 (3.6-15.6) | 5.9 (1.2-16.2) |
| Patients without a history of inadequate response/intolerance to ADT | | | | |
| N | 55 | 56 | 111 | 54 |
| Clinical response | 67.3[b] (53.3-79.3) | 73.2[b] (59.7-84.2) | 70.3[b] (60.9-78.6) | 29.6 (18.0-43.6) |
| Clinical remission | 32.7[b] (20.7-46.7) | 32.1[b] (20.3-46.0) | 32.4[b] (23.9-42.0) | 11.1 (4.2-22.6) |
| Symptomatic remission | 58.2[b] (44.1-71.3) | 57.1[b] (43.2-70.3) | 57.7[b] (47.9-67.0) | 22.2 (12.0-35.6) |
| Endoscopic improvement | 36.4[b] (23.8-50.4) | 39.3[b] (26.5-53.2) | 37.8[b] (28.8-47.5) | 14.8 (6.6-27.1) |
| Histo-endo mucosal improvement | 27.3[b] (16.1-41.0) | 33.9[b] (21.8-47.8) | 30.6[b] (22.2-40.1) | 11.1 (4.2-22.6) |
| Endoscopic remission (normalization) | 23.6[b] (13.2-37.0) | 21.4[b] (11.6-34.4) | 22.5[b] (15.1-31.4) | 7.4 (2.1-17.9) |

[a]Patients who had a prohibited change in UC medication, an ostomy, or a colectomy or discontinued the study agent due to lack of efficacy or an AE of worsening of UC prior to the week-12 visit were considered not to have achieved the endpoints. Data after discontinuation of the study agent due to COVID-19-related reasons (excluding COVID-19 infection) were considered missing. Patients who were missing 1 or more components pertaining to a specified endpoint at week 12 were considered not to have achieved that endpoint.

[b]**Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

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### Change in CRP concentrations from baseline through week 12[4,a]

| | TREMFYA 200 mg IV (n=101) | TREMFYA 400 mg IV (n=107) | TREMFYA combined (n=208) | Placebo (n=105) |
|---|---|---|---|---|
| Median baseline CRP (IQR), mg/L | n=99<br>4.31<br>(1.61 to 17.80) | n=104<br>4.38<br>(1.88 to 8.81) | n=203<br>4.37<br>(1.74 to 11.90) | n=105<br>4.89<br>(1.35 to 10.80) |
| Median change in CRP from baseline (IQR), mg/L | | | | |
| At week 4 | n=98<br>-2.18[b]<br>(-8.60 to -0.28) | n=101<br>-1.15[b]<br>(-5.45 to -0.06) | n=199<br>-1.45[b]<br>(-6.69 to -0.17) | n=104<br>0.00<br>(-1.32 to 1.37) |
| At week 8 | n=94<br>-2.60[b]<br>(-9.30 to -0.39) | n=102<br>-1.55[b]<br>(-4.80 to -0.18) | n=196<br>-2.10[b]<br>(-7.49 to -0.23) | n=103<br>0.00<br>(-2.49 to 1.74) |
| At week 12 | n=97<br>-2.31[b]<br>(-8.20 to -0.33) | n=100<br>-1.06[b]<br>(-4.76 to 0.07) | n=197<br>-1.86[b]<br>(-6.28 to -0.06) | n=102<br>0.06<br>(-2.23 to 2.94) |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC prior to the designated timepoint had their baseline value carried forward from the time of the event onward. Data after discontinuation of the study agent due to COVID-19-related reasons (excluding COVID-19 infection) were considered missing.
[b]**Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

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### Change in FCP concentrations from baseline through week 12[4,a]

| | TREMFYA 200 mg IV (n=101) | TREMFYA 400 mg IV (n=107) | TREMFYA combined (n=208) | Placebo (n=105) |
|---|---|---|---|---|
| Median baseline FCP (IQR), mg/kg | n=95<br>1667.00<br>(771.00 to 2859.00) | n=101<br>1578.00<br>(811.00 to 2859.50) | n=196<br>1619.50<br>(791.00 to 2859.50) | n=91<br>1457.00<br>(749.00 to 3054.00) |
| Median change in FCP from baseline (IQR), mg/kg | | | | |
| At week 4 | n=89<br>-358.00<br>(-1641.00 to 226.00) | n=95<br>-391.00[b]<br>(-1301.00 to 167.00) | n=184<br>-378.00[b]<br>(-1503.00 to 207.00) | n=89<br>-116.00<br>(-830.00 to 812.00) |
| At week 12 | n=82<br>-745.00[b]<br>(-1946.00 to 0.00) | n=88<br>-558.50[b]<br>(-1426.00 to -12.50) | n=170<br>-684.00[b]<br>(-1682.00 to -10.00) | n=77<br>0.00<br>(-855.00 to 1089.00) |

[a]Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an AE of worsening of UC prior to the designated timepoint had their baseline value carried forward from the time of the event onward. Data after discontinuation of the study agent due to COVID-19-related reasons (excluding COVID-19 infection) were considered missing.
**[b]Nominal *P*-value for TREMFYA vs placebo. The endpoint was not controlled for multiple comparisons. Therefore, the *P*-value is nominal, and statistical significance has not been established.**

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- Cumulative clinical response at week 12 or 24[5]:
  - In the TREMFYA 200 mg IV group and TREMFYA 200 mg IV→200 mg SC group (n=101), 80.2% of patients achieved cumulative clinical response at week 12 or 24.
  - In the TREMFYA 400 mg IV group and TREMFYA 400 mg IV→200 mg SC group (n=107), 78.5% of patients achieved cumulative clinical response at week 12 or 24.
- Among the week 12 clinical nonresponders who received additional TREMFYA treatment[5]:
  - In the TREMFYA 200 mg IV→200 mg SC group (n=35), 54.3% of patients achieved clinical response at week 24.
  - In the TREMFYA 400 mg IV→200 mg SC group (n=38), 50.0% of patients achieved clinical response at week 24
- Among randomized patients with a history of inadequate response or intolerance to advanced therapy[5]:
  - In the TREMFYA 200 mg IV group and TREMFYA 200 mg IV→200 mg SC group (n=46), 76.1% of patients achieved cumulative clinical response at week 12 or 24.
  - In the TREMFYA 400 mg IV group and TREMFYA 400 mg IV→200 mg SC group (n=51), 68.6% of patients achieved cumulative clinical response at week 12 or 24.
  - Among the week 12 clinical nonresponders who received additional TREMFYA treatment: 50.0% of patients in the TREMFYA 200 mg IV→200 mg SC group (n=20) and 44.0% of patients in the TREMFYA 400 mg IV→200 mg SC group (n=25) achieved clinical response at week 24.
- Among randomized patients without a history of inadequate response or intolerance to advanced therapy[5]:
  - In the TREMFYA 200 mg IV group and TREMFYA 200 mg IV→200 mg SC group (n=55), 83.6% of patients achieved cumulative clinical response at week 12 or 24.
  - In the TREMFYA 400 mg IV group and TREMFYA 400 mg IV→200 mg SC group (n=56), 87.5% of patients achieved cumulative clinical response at week 12 or 24.
  - Among the week 12 clinical nonresponders who received additional TREMFYA treatment: 60.0% of patients in the TREMFYA 200 mg IV→200 mg SC group (n=15) and 61.5% of patients in the TREMFYA 400 mg IV→200 mg SC group (n=13) achieved clinical response at week 24.
- Outcomes at week 24 among placebo nonresponders who crossed over to TREMFYA induction treatment (placebo IV→TREMFYA 200 mg IV; n=66)[5]:
  - Clinical response was achieved in 65.2%
  - Clinical remission was achieved in 22.7%
  - Symptomatic remission was achieved in 59.1%
  - Endoscopic improvement was achieved in 25.8%
  - HEMI was achieved in 18.2%
  - Endoscopic remission (normalization) was achieved in 16.7%

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- No AEs leading to death were reported throughout 32 weeks of treatment.[5]
- Among all the TREMFYA-treated patients (n=274), the most frequent AEs were anemia (7.7%), headache (5.1%), worsening UC (4.4%), COVID-19 (3.6%), arthralgia (2.9%), and abdominal pain (2.6%).[5]

**Safety events through final safety visit at week 32[5,a]**

| | PBO IV[b] | TREMFYA[b] 200 mg IV | TREMFYA[b] 400 mg IV | TREMFYA[b] Combination | Placebo IV → TREMFYA 200 mg IV[c] | TREMFYA IV → TREMFYA 200 mg SC[c] | Combination TREMFYA IV[d] | All TREMFYA[e] |
|---|---|---|---|---|---|---|---|---|
| Safety set, n | 105 | 101 | 107 | 208 | 66 | 78 | 274 | 274 |
| Average follow-up, weeks | 12.3 | 12.1 | 12.3 | 12.2 | 13.9 | 14.6 | 12.6 | 16.7 |
| Average exposure, no. of admins | 2.9 | 3.0 | 3.0 | 3.0 | 2.9 | 2.9 | 3.0 | 3.8 |
| Patients with ≥1 events, n (%) | | | | | | | | |
| AEs | 59 (56.2) | 45 (44.6) | 53 (49.5) | 98 (47.1) | 34 (51.5) | 33 (42.3) | 132 (48.2) | 143 (52.2) |
| SAEs | 7 (6.7) | 1 (1.0) | 3 (2.8) | 4 (1.9) | 2 (3.0) | 3 (3.8) | 6 (2.2) | 8 (2.9) |
| AEs leading to DC | 3 (2.9) | 1 (1.0) | 0 | 1 (0.5) | 2 (3.0) | 2 (2.6) | 3 (1.1) | 5 (1.8) |
| Reasonably related AEs[f] | 20 (19.0) | 13 (12.9) | 12 (11.2) | 25 (12.0) | 9 (13.6) | 11 (14.1) | 34 (12.4) | 43 (15.7) |
| Infections[g] | 13 (12.4) | 14 (13.9) | 10 (9.3) | 24 (11.5) | 10 (15.2) | 6 (7.7) | 34 (12.4) | 39 (14.2) |
| Serious infections | 2 (1.9) | 0 | 0 | 0 | 1 (1.5) | 0 | 1 (0.4) | 1 (0.4) |

[a]Includes only treated patients who had a modified Mayo score of 5-9 at induction baseline.
[b]Includes data up to week 12 for patients who received treatment at week 12. For patients who did not receive treatment at week 12, includes all data through the final safety visit.
[c]Includes data from week 12 onward.
[d]From the first TREMFYA IV dose onward. For patients who received TREMFYA 200 mg SC at week 12, includes data up to week 12.
[e]From the first TREMFYA dose onward.
[f]An AE that is categorized by the investigator as possibly, probably, or very likely related to the study agent or if the relationship to the study agent is missing.
[g]As assessed by the investigator.

# TREMFYA® (guselkumab)
# TREMFYA - Treatment of ulcerative colitis - QUASAR program

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| | | | |
|---|---|---|---|
| **ADAMDEC1** | ADAM-like decysin 1 | **ER** | Exposure response |
| **ADT** | Advanced therapy | **FC** | Fragment crystallizable |
| **ADT-IR** | Intolerance to advanced therapy | **FCP** | Fecal calprotectin |
| **AE** | Adverse event | **FDR** | False discovery rate |
| **ANCOVA** | Analysis of covariance | **GUS** | Guselkumab |
| **AUC** | Area under the curve | **HEMI** | Histo-endoscopic mucosal improvement |
| **BEST4** | Bestrophin 4 | **GUS** | Guselkumab |
| **BIO** | Biologic | **HEMI** | Histo-endoscopic mucosal improvement |
| **$C_{ave}$** | Average concentration | **HRQoL** | Health-related quality of life |
| **CCL11** | C-C motif chemokine ligand 11 | **IBDQ** | Inflammatory Bowel Disease Questionnaire |
| **CD** | Cluster of differentiation | **IFNγ** | Interferon gamma |
| **CI** | Confidence interval | **IL** | Interleukin |
| **$C_{max}$** | Maximum concentration | **IQR** | Interquartile range |
| **CMH** | Cochran-Mantel-Haenszel | **IV** | Intravenous |
| **COVID-19** | Coronavirus disease 2019 | **JAKi** | Janus kinase inhibitor |
| **CRP** | C-reactive protein | **LSM** | Least squares mean |
| **$C_{trough}$** | Trough concentration | **LTE** | Long-term extension |
| **CV** | Cardiovascular | **MACE** | Major adverse cardiovascular event |
| **DC** | Discontinued | **MCS** | Mental component summary |
| **ED** | Emergency department | **MedDRA** | Medical Dictionary for Regulatory Activities |
| **EpCam** | Epithelial cell adhesion molecule | **MI** | Myocardial infarction |

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| | | | |
|---|---|---|---|
| **NHI** | Nancy histological index | PK | Pharmacokinetics |
| **NRI** | Nonresponder imputation | **popPK** | Population PK |
| **NRS** | Numeric rating scale | **PRO** | Patient-reported outcomes |
| **OI** | Opportunistic infection | **PROMIS** | Patient-Reported Outcomes Measurement Information System |
| **OSM** | Oncostatin M | **Q4W** | Every 4 weeks |
| **PCS** | Physical component summary | | |

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A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) was conducted on 10 September 2025.

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# TREMFYA - Treatment of ulcerative colitis - QUASAR program

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1. Rubin DT, Allegretti JR, Panés J, et al. Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. *Lancet*. 2025;405(10472):33-49.
2. Rubin DT, Allegretti JR, Panés J, et al. Supplement to: Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. *Lancet*. 2025;405(10472):33-49.
3. Dignass A, Rubin D, Bressler B, et al. OP23 The efficacy and safety of guselkumab induction therapy in patients with moderately to severely active ulcerative colitis: phase 2b QUASAR study results through week 12. *J Crohns Colitis*. 2022;16(Suppl. 1):i025-i026.
4. Peyrin-Biroulet L, Dignass A, Sandborn W, et al. The effect of guselkumab induction therapy on inflammatory biomarkers in patients with moderately to severely active ulcerative colitis: QUASAR phase 2b induction results through week 12. Abstract presented at: 30th United European Gastroenterology (UEG) Week; October 8-11, 2022; Vienna, Austria, and Virtual.
5. Sands B, Rubin D, Lichtenstein G, et al. QUASAR induction study 1 cumulative response to guselkumab in patients with moderately to severely active ulcerative colitis. Poster presented at: American College of Gastroenterology (ACG) Meeting; October 21-26, 2022; Charlotte, NC, and Virtual.
6. Allegretti J, Peyrin-Biroulet L, Feagan B, et al. The efficacy and safety of guselkumab induction therapy in patients with moderately to severely active ulcerative colitis: results from the phase 3 QUASAR induction study. Abstract presented at: Digestive Disease Week (DDW); May 6-9, 2023; Chicago, IL, and Virtual.
7. Rubin DT, Allegretti JR, Panés J, et al. The efficacy and safety of guselkumab as maintenance therapy in patients with moderately to severely active ulcerative colitis: results from the phase 3 QUASAR maintenance study. Abstract presented at: Digestive Disease Week (DDW); May 18-21, 2024; Washington, DC, and Virtual.
8. Janssen Research & Development, LLC. A study of guselkumab in participants with moderately to severely active ulcerative colitis (QUASAR). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2025 August 19]. Available from: https://clinicaltrials.gov/ct2/show/NCT04033445 NLM Identifier: NCT04033445.
9. Lichtenstein GR, Dignass A, Rubin DT, et al. Early symptomatic improvement with guselkumab induction treatment in moderately to severely active ulcerative colitis: results from the phase 3 QUASAR induction study. Abstract presented at: 31st United European Gastroenterology (UEG) Week; October 14-15, 2023; Copenhagen, Denmark, and Virtual.
10. Panés J, Sands BE, Peyrin-Biroulet L, et al. Impact of guselkumab induction therapy on histologic and combined histologic and endoscopic outcomes in patients with moderately to severely active ulcerative colitis: week 12 results from the phase 3 QUASAR induction study. Abstract presented at: 31st United European Gastroenterology (UEG) Week; October 14-15, 2023; Copenhagen, Denmark, and Virtual.
11. Bressler B, Peyrin-Biroulet L, Allegretti JR, et al. The efficacy of induction treatment with guselkumab in patients with moderately to severely active ulcerative colitis: phase 3 QUASAR induction study results at week 12 by prior advanced therapy history. Abstract presented at: 31st United European Gastroenterology (UEG) Week; October 14-15, 2023; Copenhagen, Denmark, and Virtual.
12. Dimova M, Keng MJ, Naessens D, et al. Earlier use of guselkumab is projected to yield long-term sustained remission in patients with moderate-to-severe ulcerative colitis. Abstract presented at: 33rd United European Gastroenterology (UEG) Week; October 4-7, 2025; Berlin, Germany.
13. Hisamatsu T, Peyrin-Biroulet L, Dignass A, et al. Improvement in inflammatory biomarker levels through week 12 in moderately to severely active ulcerative colitis patients treated with guselkumab: results from the phase 3 QUASAR induction study. Abstract presented at: 31st United European Gastroenterology (UEG) Week; October 14-15, 2023; Copenhagen, Denmark, and Virtual.
14. Sridhar S, Hart A, Venkat S, et al. Guselkumab induction restores intestinal immune homeostasis and promotes epithelial repair in moderately to severely active ulcerative colitis [abstract]. *J Crohns Colitis*. 2024;18(Suppl. 1):i41. Abstract OP23.
15. Sridhar S, Hart A, Venkat S, et al. Guselkumab induction therapy results in molecular resolution of inflammation in moderately to severely active ulcerative colitis: results from the phase 3 QUASAR induction study. Abstract presented at: 20th European Crohn's and Colitis Organization (ECCO) Congress; February 19-22, 2025; Berlin, Germany.
16. Rubin DT, Sands BE, Lichtenstein GR, et al. Cumulative response to guselkumab through week 24 of induction in patients with moderately to severely active ulcerative colitis: results from the phase 3 QUASAR induction study. Poster presented at: American College of Gastroenterology (ACG) Annual Meeting; October 20-25, 2023; Vancouver, Canada.

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17. Bressler B, Feagan BG, Panés J, et al. Guselkumab improves health-related quality of life in patients with moderately to severely active ulcerative colitis: results from the QUASAR phase 3 induction study. Poster presented at: American College of Gastroenterology (ACG) Annual Meeting; October 20-25, 2023; Vancouver, Canada.

18. Panes J, Dignass A, Lichtenstein G, et al. Guselkumab improves health-related quality of life as measured by PROMIS-29 in patients with moderately to severely active ulcerative colitis: phase 3 QUASAR induction study [abstract]. *J Crohns Colitis*. 2024;18(Suppl. 1):i61-i62. Abstract DOP49.

19. Rubin DT, Panes J, Feagan BG, et al. Guselkumab improves abdominal pain and bowel urgency symptoms in patients with moderately to severely active ulcerative colitis: results from the phase 3 QUASAR induction study. Poster presented at: American College of Gastroenterology (ACG) Annual Meeting; October 20-25, 2023; Vancouver, Canada.

20. Dignass A, Panes J, Rubin DT, et al. Guselkumab improves symptoms of fatigue in patients with moderately to severely active ulcerative colitis: phase 3 QUASAR induction study results at week 12 [abstract]. *J Crohns Colitis*. 2024;18(Suppl. 1):i65-i66. Abstract DOP52l.

21. Wu E, Kachroo S, Miao Y, et al. Ulcerative colitis-related medical encounters in patients treated with guselkumab: an analysis of the QUASAR phase 3 induction study. Abstract presented at: Digestive Disease Week (DDW) Congress; May 3-6, 2025; San Diego, CA.

22. Allegretti JR, Hisamatsu T, Bressler B, et al. Efficacy of guselkumab in moderately to severely active ulcerative colitis by extent of disease and inflammatory burden: subgroup analysis of the phase 3 QUASAR maintenance study. Abstract presented at: 33rd United European Gastroenterology (UEG) Week; October 4-7, 2025; Berlin, Germany.

23. Bressler B, Allegretti J, Rubin DT, et al. Corticosteroid sparing effects of treatment with guselkumab in patients with moderate to severely active ulcerative colitis: phase 3 QUASAR maintenance study results through week 44. Abstract presented at: 32nd United European Gastroenterology (UEG) Week; October 12-15, 2024; Vienna, Austria, and Virtual.

24. Panes J, Dignass A, Hisamatsu T, et al. Impact of guselkumab maintenance therapy on histologic and combined endoscopic outcomes in patients with moderately to severely active ulcerative colitis: week 44 results from the phase 3 QUASAR maintenance study. Abstract presented at: 32nd United European Gastroenterology (UEG) Week; October 12-15, 2024; Vienna, Austria, and Virtual.

25. Rubin DT, Dignass A, Allegretti J, et al. Efficacy and safety of guselkumab maintenance therapy among guselkumab induction week 24 clinical responders: results from phase 3 QUASAR maintenance study. Abstract presented at: 32nd United European Gastroenterology (UEG) Week; October 12-15, 2024; Vienna, Austria, and Virtual.

26. Allegretti J, Panes J, Peyrin-Biroulet L, et al. The efficacy of maintenance treatment with guselkumab in patients with moderately to severely active ulcerative colitis: phase 3 QUASAR maintenance study results at week 44 by biologic/Janus kinase inhibitor history. Abstract presented at: 32nd United European Gastroenterology (UEG) Week; October 12-15, 2024; Vienna, Austria, and Virtual.

27. Bressler B, Peyrin-Biroulet L, Afif W, et al. Guselkumab maintenance treatment improves health-related quality of life in patients with moderately to severely active ulcerative colitis: phase 3 QUASAR maintenance study. Abstract presented at: 20th European Crohn's and Colitis Organization (ECCO) Congress; February 19-22, 2025; Berlin, Germany.

28. Hart A, Sridhar S, Venkat S, et al. Guselkumab maintenance therapy mediates further improvements in intestinal immune homeostasis and mucosal healing in patients with ulcerative colitis. Abstract presented at: 20th European Crohn's and Colitis Organization (ECCO) Congress; February 19-22, 2025; Berlin, Germany.

29. Lichtenstein GR, Allegretti JR, Rubin DT, et al. Efficacy and safety of guselkumab for ulcerative colitis through week 92 of the QUASAR LTE study. Abstract presented at: Digestive Disease Week (DDW) Congress; May 3-6, 2025; San Diego, CA.

30. Peyrin-Biroulet L, Xu Z, Shao J, et al. Pharmacokinetics and exposure-response relationships of guselkumab intravenous or subcutaneous induction in participants with ulcerative colitis. Abstract presented at: American College of Gastroenterology (ACG); October 24-29, 2025; Phoenix, Arizona.

31. Panes J, Allegretti J, Sands B, et al. The effect of guselkumab induction therapy in patients with moderately to severely active ulcerative colitis: QUASAR phase 2b induction results at week 12 by prior inadequate response or intolerance to advanced therapy. Abstract presented at: 30th United European Gastroenterology (UEG) Week; October 8-11, 2022; Vienna, Austria, and Virtual.

32. Hisamatsu T, Panés J, Magro F, et al. Maintenance of endoscopic and histologic efficacy with guselkumab for ulcerative colitis at week 92 of the QUASAR long-term extension study. Abstract presented at: 33rd United European Gastroenterology (UEG) Week; October 4-7, 2025; Berlin, Germany.


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