SUPPORTING INFORMATION

Supplement to: Agreement between local and central reading of endoscopic disease activity in ulcerative colitis: results from the tofacitinib OCTAVE trials

This appendix has been provided by the authors to give readers additional information about their work.

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1. Permitted concomitant and prohibited concomitant medications in the OCTAVE clinical programme

Patients were permitted concomitant treatment with oral 5-aminosalicylates (5-ASA) or sulfasalazine (providing the dose was not changed), and oral corticosteroids (up to 25 mg/day prednisone or equivalent; stable dose for ≥2 weeks prior to baseline of OCTAVE Induction 1 or 2); corticosteroid tapering was mandatory from baseline of OCTAVE Sustain.

1.1. Concomitant medications

OCTAVE Induction 1 and 2

The following treatments for ulcerative colitis (UC) were allowed providing they were stable for the specified period of time prior to the first dose of study medication and were not permitted to change (dose reduction or increase) during the study treatment period:

- Oral 5-ASA or sulfasalazine were allowed providing the dose was stable for at least 4 weeks prior to baseline
- Chronic treatment for UC with antibiotics (e.g. metronidazole, rifaximin) was allowed, providing that the dose was stable for at least 2 weeks prior to baseline
- Oral corticosteroids were allowed during the study up to 25 mg/day oral prednisone or equivalent, and up to 9 mg/day budesonide, providing that the dose was stable within 2 weeks of baseline. Note: for subjects that were taking >20 mg/day oral corticosteroids, the dose could have been decreased down to 20 mg/day at the investigator’s discretion starting at Week 4/visit 4 and stayed at this reduced dose thereafter for the remainder of the induction study, provided their partial Mayo score
was ≤2, with no individual subscore >1 and they had a rectal bleeding subscore of 0 at Week 4. If the subject subsequently experienced signs or symptoms of worsening of UC, in the opinion of the investigator, due to the reduction in corticosteroid daily dose, the daily corticosteroid dosage for the subject could have been reverted to the preceding daily dosage instructed by the investigator; however, in those cases, no further dose decrease was allowed for the remainder of the induction study.

**OCTAVE Sustain**

The following treatments for UC were allowed providing their doses were not changed (dose reduction or increase), with the exception of oral corticosteroids (see below) during the study treatment period:

- Oral 5-ASA or sulfasalazine
- Chronic treatment for UC with antibiotics (e.g. metronidazole, rifaximin)
- Oral corticosteroids were allowed during the study. Since the subjects were transferred from OCTAVE Induction 1 and 2, the maximum corticosteroid dose was 25 mg/day oral prednisone or equivalent, and 9 mg/day budesonide. Tapering corticosteroids was mandatory starting the first week of the study.

**OCTAVE Open**

The following treatments for UC were allowed providing their doses were not changed (reduced or increased), with the exception of oral 5-ASA or sulfasalazine and oral corticosteroids (see below) during the study treatment period:

- Oral 5-ASA or sulfasalazine dose modifications during the study were permitted
• Chronic treatment for UC with antibiotics (e.g. metronidazole, rifaximin) if continued from the preceding study

• Oral corticosteroids were allowed for subjects entering OCTAVE Open on oral corticosteroids (maximum dose of 25 mg/day oral prednisone or equivalent), and tapering was required to commence starting the first week of the study

• The daily dose of oral prednisone or equivalent was decreased at a rate of 5 mg/week until the dose reached 20 mg/day, then reduced by 2.5 mg to 5.0 mg weekly until the dose reached 0 mg.

1.2. Prohibited concomitant medications

OCTAVE Induction 1 and 2, OCTAVE Sustain and OCTAVE Open

The following medications were prohibited:

• Azathioprine, 6-mercaptopurine, and methotrexate

• Cyclosporine, mycophenolate mofetil/mycophenolic acid, and tacrolimus

• Interferon

• Tumour necrosis factor (TNF) antagonists (e.g. infliximab, adalimumab, or certolizumab)

• Intravenous corticosteroids

• Rectally administered formulation of corticosteroids or 5-ASA

• Natalizumab, vedolizumab (specified in the OCTAVE Open protocol), or other anti-adhesion molecule therapy (including investigational agents)

• Other investigational or marketed immunosuppressants or biologics with immunomodulatory properties
• Leukocyte apheresis, including selective lymphocyte, monocyte, or granulocyte apheresis (e.g. Cellsorba®) or plasma exchange
• Moderate to potent CYP3A inducers or inhibitors due to potential for drug interactions or confounding of data interpretation
• Antimotility agents for control of diarrhoea (i.e. diphenoxylate hydrochloride with atropine sulphate or loperamide) (not prohibited in OCTAVE Open).

2. Summary of study design

Patients in OCTAVE Induction 1 and 2 received tofacitinib 10 mg twice daily (b.d.) or placebo, with final efficacy assessment at Week 8 (Figure 1). Patients who achieved clinical response (a decrease from induction study baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1; centrally read) in OCTAVE Induction 1 and 2 were eligible to enter OCTAVE Sustain. In OCTAVE Sustain, patients received placebo, tofacitinib 5 mg b.d., or tofacitinib 10 mg b.d., with final efficacy assessment at Week 52 (Figure 1).

OCTAVE Open included induction non-responders from OCTAVE Induction 1 and 2 and completers or treatment failures from OCTAVE Sustain (Figure 1); patients in remission at Week 52 of OCTAVE Sustain (centrally read) received tofacitinib 5 mg b.d.; all others received tofacitinib 10 mg b.d. All patients underwent endoscopy at Month 2 of OCTAVE Open; induction non-responders without clinical response at Month 2 (centrally read) were withdrawn.

3. Assessment of Mayo endoscopic subscore (MES)

For central reading, a single read was performed by a reader who was unaware of treatment assignment, study, visit and the patient’s clinical status. For local reading, sites were trained.
on the scoring of the MES, and methods for optimising the quality of the video recordings. Per protocol, MES was scored as: normal or inactive disease = 0; mild disease (erythema, decreased vascular pattern) = 1; moderate disease (marked erythema, absent vascular pattern, any friability, erosions) = 2; or severe disease (spontaneous bleeding, ulceration) = 3. Of note, the inclusion of any friability in the criteria for a score of 2 was a modification to the original MES (which formally assigned ‘mild friability’ as a score of 1),\(^1\) to align with current US Food and Drug Administration guidance.\(^2\)

4. Treatment failure definition

Treatment failure was defined as an increase from OCTAVE Sustain study baseline total Mayo score of $\geq 3$ points, with an increase in rectal bleeding subscore of $\geq 1$ point and an increase in MES of $\geq 1$ point yielding a MES of $\geq 2$, after a minimum of 8 weeks of tofacitinib treatment in OCTAVE Sustain.

5. Evaluation of agreement and disagreement between the local and central endoscopy scoring methods

Agreement between central and local reads was first displayed graphically in a four-by-four table based upon the four categories of the MES. The variability amongst the 16 cells was initially evaluated by inspecting the distribution of agreement around the theoretical line of complete agreement specified by a diagonal line (e.g. a central read of 0 and local read of 0; a central read of 1 and local read of 1 etc.). In these tables, random variation in scoring should generate a distribution in the differences scattered equally on either side of the line of complete agreement, whilst a systematic variation, consistent with bias, would show a distribution skewed to one side of the line or the other.
6. Cochran-Mantel-Haenszel (CMH) chi-squared test to compare the proportion of patients in clinical remission and endoscopic response

Non-responder imputation was used for missing data, meaning that patients were treated as non-responders after the time of discontinuation up to the visit they would have reached if they had stayed in the study. No imputation for missing data was applied for patients who continued participation. The CMH chi-squared test was used to compare the proportion of patients in clinical remission and endoscopic response in the tofacitinib and placebo groups. For OCTAVE Induction 1 and 2, the CMH chi-squared test was stratified by treatment group, prior TNF antagonist treatment, corticosteroid use at induction study baseline and geographic region. For OCTAVE Sustain, the CMH chi-squared test was stratified by treatment assignment in the induction study and remission status at OCTAVE Sustain baseline.

7. References

1. Vuitton L, Peyrin-Biroulet L, Colombel JF, et al. Defining endoscopic response and remission in ulcerative colitis clinical trials: an international consensus. *Aliment Pharmacol Ther* 2017;45:801–813.

2. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Ulcerative colitis: clinical trial endpoints. Guidance for industry. 2016. [http://www.fda.gov/downloads/Drugs/Guidances/UCM515143.pdf](http://www.fda.gov/downloads/Drugs/Guidances/UCM515143.pdf). Accessed July 8, 2021.
Table S1. Proportion of patients with a difference between centrally and locally read MES (two-level response) at Week 8 in OCTAVE Induction 1 and 2, Week 52 in OCTAVE Sustain and in induction non-responders at Month 2 of OCTAVE Open

| Age at baseline | Week 8 in OCTAVE Induction 1 and 2 | Week 52 in OCTAVE Sustain | Month 2 in OCTAVE Open |
|----------------|-----------------------------------|---------------------------|------------------------|
|                | (N = 1061)                         | (N = 333)                 | (induction non-responders) |
|                | N1 CR ≥1 point higher or lower than LR n (%) | No difference between CR and LR n (%) | N1 CR ≥1 point higher or lower than LR n (%) | No difference between CR and LR n (%) | N1 CR ≥1 point higher or lower than LR n (%) | No difference between CR and LR n (%) |
| <30 years      | 245 84 (34.3) 161 (65.7) 59 23 (39.0) 36 (61.0) 95 36 (37.9) 59 (62.1) | 30 to <40 years | 284 96 (33.8) 188 (66.2) 78 40 (51.3) 38 (48.7) 115 44 (38.3) 71 (61.7) | 40 to <50 years | 232 82 (35.3) 150 (64.7) 73 27 (37.0) 46 (63.0) 78 35 (44.9) 43 (55.1) | ≥50 years | 300 122 (40.7) 178 (59.3) 123 58 (47.2) 65 (52.8) 94 38 (40.4) 56 (59.6) |
| Sex            | Male 619 226 (36.5) 393 (63.5) 191 85 (44.5) 106 (55.5) 237 85 (35.9) 152 (64.1) | Female 442 158 (35.7) 284 (64.3) 142 63 (44.4) 79 (55.6) 145 68 (46.9) 77 (53.1) |  |  |  |  |
| Body mass index | <25 kg/m² 618 216 (35.0) 402 (65.0) 177 82 (46.3) 95 (53.7) 224 87 (38.8) 137 (61.2) | 25 to <30 kg/m² 300 123 (41.0) 177 (59.0) 107 48 (44.9) 59 (55.1) 101 38 (37.6) 63 (62.4) |  |  |  |  |
|                | ≥30 kg/m² 142 45 (31.7) 97 (68.3) 49 18 (36.7) 31 (63.3) 55 27 (49.1) 28 (50.9) |  |  |  |  |  |  |
## Race

|       | 847 | 286 (33.8) | 561 (66.2) | 256 | 109 (42.6) | 147 (57.4) | 300 | 112 (37.3) | 188 (62.7) |
|-------|-----|------------|------------|-----|------------|------------|-----|------------|------------|
| White |     |            |            |     |            |            |     |            |            |
| Black | 8   | 5 (62.5)   | 3 (37.5)   | 2   | 0 (0.0)    | 2 (100.0)  | 4   | 1 (25.0)   | 3 (75.0)   |
| Asian | 134 | 61 (45.5)  | 73 (54.5)  | 50  | 26 (52.0)  | 24 (48.0)  | 53  | 30 (56.6)  | 23 (43.4)  |
| Other | 38  | 18 (47.4)  | 20 (52.6)  | 14  | 8 (57.1)   | 6 (42.9)   | 12  | 4 (33.3)   | 8 (66.7)   |

## Geographic region

| Geographical region | 222 | 89 (40.1) | 133 (59.9) | 62  | 27 (43.5) | 35 (56.5) | 82  | 35 (42.7) | 47 (57.3) |
|---------------------|-----|----------|------------|-----|----------|----------|-----|----------|----------|
| North America††     |     |          |            |     |          |          |     |          |          |
| Asia‡‡               | 115 | 55 (47.8)| 60 (52.2)  | 43  | 24 (55.8)| 19 (44.2)| 46  | 28 (60.9)| 18 (39.1)|
| Australia and New Zealand | 64 | 27 (42.2)| 37 (57.8)  | 14  | 7 (50.0) | 7 (50.0) | 25  | 13 (52.0)| 12 (48.0)|
| Eastern Europe§§     | 307 | 95 (30.9)| 212 (69.1)| 124 | 46 (37.1)| 78 (62.9)| 92  | 36 (39.1)| 56 (60.9)|
| Western Europe¶¶     | 317 | 102 (32.2)| 215 (67.8)| 77  | 39 (50.6)| 38 (49.4)| 128 | 38 (29.7)| 90 (70.3)|
| Other                | 36  | 16 (44.4)| 20 (55.6)  | 13  | 5 (38.5) | 8 (61.5) | 9   | 3 (33.3) | 6 (66.7) |
### Oral corticosteroid use at baseline

|        | Yes  | No   |
|--------|------|------|
|        | 491  | 570  |
| Yes    | 187 (38.1) | 197 (34.6) |
| No     | 304 (61.9)  | 373 (65.4)  |
|        | 131  | 202  |
| Yes    | 55 (42.0)  | 93 (46.0)   |
| No     | 76 (58.0)  | 109 (54.0)  |
|        | 154  | 228  |
| Yes    | 52 (33.8)  | 101 (44.3)  |
| No     | 102 (66.2) | 127 (55.7)  |

### Oral corticosteroid dose at induction study baseline

|        | <15 mg/day | ≥15 mg/day | Other | None |
|--------|------------|------------|-------|------|
|        | 145        | 303        | 43    | 570  |
| Yes    | 53 (36.6)  | 122 (40.3) | 12 (27.9) | 197 (34.6) |
| No     | 92 (63.4)  | 181 (59.7) | 31 (72.1) | 373 (65.4) |
|        | 49         | 75         | 12     | 202  |
| Yes    | 19 (38.8)  | 32 (42.7)  | 6 (50.0)  | 93 (46.0)  |
| No     | 30 (61.2)  | 43 (57.3)  | 6 (50.0)  | 109 (54.0) |
|        | 43         | 95         | 17     | 228  |
| Yes    | 16 (37.2)  | 32 (33.7)  | 5 (29.4)  | 101 (44.3) |
| No     | 27 (62.8)  | 63 (66.3)  | 12 (70.6) | 127 (55.9) |

### Prior TNF antagonist failure at induction study baseline

|        | Yes  | No   |
|--------|------|------|
|        | 549  | 512  |
| Yes    | 176 (32.1) | 208 (40.6) |
| No     | 373 (67.9)  | 304 (59.4)  |
|        | 140  | 193  |
| Yes    | 62 (44.3)  | 86 (44.6)   |
| No     | 78 (55.7)  | 107 (55.4)  |
|        | 228  | 154  |
| Yes    | 75 (32.9)  | 78 (50.6)   |
| No     | 153 (67.1) | 76 (49.4)   |

### Prior immunosuppressant failure at induction study baseline

|        | Yes  | No   |
|--------|------|------|
|        | 770  | 291  |
| Yes    | 272 (35.3) | 112 (38.5) |
| No     | 498 (64.7)  | 179 (61.5)  |
|        | 229  | 104  |
| Yes    | 99 (43.2)  | 49 (47.1)   |
| No     | 130 (56.8) | 55 (52.9)   |
|        | 293  | 89   |
| Yes    | 114 (38.9) | 39 (43.8)   |
| No     | 179 (61.1) | 50 (56.2)   |

### Baseline total Mayo score

|        | <9   | ≥9   | <3   | ≥3   |
|--------|------|------|------|------|
|        | 381  | 677  | -    | -    |
| Yes    | 158 (41.5) | 225 (33.2) | -    | -    |
| No     | 223 (58.5)  | 452 (66.8)  | -    | -    |
|        | -    | -    | 128  | -    |
| Yes    | -    | -    | 55 (43.0) | -    |
| No     | -    | -    | 73 (57.0) | -    |
|        | -    | -    | 205  | -    |
| Yes    | -    | -    | 93 (45.4) | -    |
| No     | -    | -    | 112 (54.6) | -    |

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| Baseline partial Mayo score\(^5\) | <6 | ≥6 | <2 | ≥2 |
|---|---|---|---|---|
|  | 255 | 109 (42.7) | 146 (57.3) | - |
| <6 | 803 | 274 (34.1) | 529 (65.9) | - |
| ≥6 | - | - | - | - |
| <2 | - | - | 166 | 74 (44.6) |
| ≥2 | - | - | 167 | 74 (44.3) |
| Partial Mayo score at assessment\(\ddagger\ddagger\ddagger\) | <6 | ≥6 |
|  | 774 | 316 (40.8) | 458 (59.2) | 283 |
| <6 | 286 | 68 (23.8) | 218 (76.2) | 7 |
| ≥6 | - | - | - | - |
| CRP concentration at baseline\(^6\) | <3 mg/L | ≥3 mg/L |
|  | 381 | 162 (42.5) | 219 (57.5) | 260 |
| <3 mg/L | 666 | 219 (32.9) | 447 (67.1) | 73 |
| ≥3 mg/L | - | - | - | - |
| CRP concentration at assessment\(\ddagger\ddagger\ddagger\) | <3 mg/L | ≥3 mg/L |
|  | 633 | 270 (42.7) | 363 (57.3) | 225 |
| <3 mg/L | 424 | 114 (26.9) | 310 (73.1) | 74 |
| ≥3 mg/L | - | - | - | - |
| Number of patients randomised at site based on induction data | <5 | ≥5 | <10 | ≥10 |
|  | 300 | 111 (37.0) | 189 (63.0) | 168 |
| <5 | 761 | 273 (35.9) | 488 (64.1) | 165 |
| ≥5 | 688 | 254 (36.9) | 434 (63.1) | 242 |
| <10 | 373 | 130 (34.9) | 243 (65.1) | 91 |
| ≥10 | - | - | - | - |
Abbreviations: b.d., twice daily; CR, central read; CRP, C-reactive protein; LR, local read; MES, Mayo endoscopic subscore; N, number of patients in each treatment group with non-missing local and central read data; n, number of patients in each subgroup with the specified level of difference; N1, number of patients in each subgroup; TNF, tumour necrosis factor.

Proportions were based on a two-level response: no difference between central and local read; central read ≥1 point higher or lower than local read.

†Includes patients receiving placebo (n = 216) or tofacitinib 10 mg b.d. (n = 845).
‡Includes patients receiving placebo (n = 68) or tofacitinib 10 mg b.d. (n = 265).
§Includes patients who were non-responders after receiving tofacitinib 10 mg b.d. (n = 261) or placebo (n = 121) in OCTAVE Induction 1 or 2, all of whom received tofacitinib 10 mg b.d. in OCTAVE Open.
¶Baseline of OCTAVE Induction 1 or 2, OCTAVE Sustain or OCTAVE Open.
††Canada and the USA.
‡‡Japan, Korea and Taiwan.
§§Croatia, Czechia, Estonia, Hungary, Latvia, Poland, Romania, Russia, Serbia, Slovakia and Ukraine.
¶¶Austria, Belgium, Denmark, France, Germany, Israel, Italy, Netherlands, Spain and the UK.
†††One patient with proctitis was enrolled into OCTAVE Induction 2 as a protocol deviation and assigned to receive tofacitinib 10 mg b.d.
‡‡‡Week 8 for OCTAVE Induction 1 and 2, Week 52 for OCTAVE Sustain and Month 2 for OCTAVE Open Induction non-responders.
§§§Week 8 for OCTAVE Induction 1 and 2 and Week 52 for OCTAVE Sustain.
Table S2. Proportion of patients with a difference between centrally and locally read MES (three-level response) at Week 8 in OCTAVE Induction 1 and 2, Week 52 in OCTAVE Sustain and in induction non-responders at Month 2 of OCTAVE Open

|                      | Week 8 in OCTAVE Induction 1 and 2<sup>†</sup> (N = 1061) | Week 52 in OCTAVE Sustain<sup>‡</sup> (N = 333) | Month 2 in OCTAVE Open (induction non-responders)<sup>§</sup> (N = 382) |
|----------------------|----------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------|
|                      | N1            | CR ≥1 point lower than LR n (%) | No difference between CR and LR n (%) | CR ≥1 point higher than LR n (%) | N1            | CR ≥1 point lower than LR n (%) | No difference between CR and LR n (%) | CR ≥1 point higher than LR n (%) | N1            | CR ≥1 point lower than LR n (%) | No difference between CR and LR n (%) | CR ≥1 point higher than LR n (%) |
| Age at baseline<sup>¶</sup> |               |                                |                                |                                |               |                                |                                |                                |               |                                |                                |                                |
| <30 years            | 245           | 29 (11.8)                      | 161 (65.7)                      | 55 (22.4)                      | 59            | 8 (13.6)                       | 36 (61.0)                      | 15 (25.4)                      | 95            | 11 (11.6)                      | 59 (62.1)                      | 25 (26.3)                      |
| 30 to <40 years      | 284           | 28 (9.9)                       | 188 (66.2)                      | 68 (23.9)                      | 78            | 9 (11.5)                       | 38 (48.7)                      | 31 (39.7)                      | 115           | 7 (6.1)                        | 71 (61.7)                      | 37 (32.2)                      |
| 40 to <50 years      | 232           | 14 (6.0)                       | 150 (64.7)                      | 68 (29.3)                      | 73            | 5 (6.8)                        | 46 (63.0)                      | 22 (30.1)                      | 78            | 3 (3.8)                        | 43 (55.1)                      | 32 (41.0)                      |
| ≥50 years            | 300           | 26 (8.7)                       | 178 (59.3)                      | 96 (32.0)                      | 123           | 13 (10.6)                      | 65 (52.8)                      | 45 (36.6)                      | 94            | 6 (6.4)                        | 56 (59.6)                      | 32 (34.0)                      |
| Sex                  |               |                                |                                |                                |               |                                |                                |                                |               |                                |                                |                                |
| Male                 | 619           | 58 (9.4)                       | 393 (63.5)                      | 168 (27.1)                     | 191           | 26 (13.6)                      | 106 (55.5)                     | 59 (30.9)                      | 237           | 16 (6.8)                       | 152 (64.1)                     | 69 (29.1)                      |
| Female               | 442           | 39 (8.8)                       | 284 (64.3)                      | 119 (26.9)                     | 142           | 9 (6.3)                        | 79 (55.6)                      | 54 (38.0)                      | 145           | 11 (7.6)                       | 77 (53.1)                      | 57 (39.3)                      |
| Body mass index<sup>¶</sup> |               |                                |                                |                                |               |                                |                                |                                |               |                                |                                |                                |
| <25 kg/m²            | 618           | 57 (9.2)                       | 402 (65.0)                      | 159 (25.7)                     | 177           | 17 (9.6)                       | 95 (53.7)                      | 65 (36.7)                      | 224           | 16 (7.1)                       | 137 (61.2)                     | 71 (31.7)                      |
| 25 to <30 kg/m²      | 300           | 30 (10.0)                      | 177 (59.0)                      | 93 (31.0)                      | 107           | 14 (13.1)                      | 59 (55.1)                      | 34 (31.8)                      | 101           | 9 (8.9)                        | 63 (62.4)                      | 29 (28.7)                      |
| ≥30 kg/m²            | 142           | 10 (7.0)                       | 97 (68.3)                       | 35 (24.6)                      | 49            | 4 (8.2)                        | 31 (63.3)                      | 14 (28.6)                      | 55            | 2 (3.6)                        | 28 (50.9)                      | 25 (45.5)                      |
| Race        | Total | <6 years | ≥6 years | Extent of disease | Total | <6 years | ≥6 years |
|-------------|-------|----------|----------|------------------|-------|----------|----------|
| White       | 847   | 22%      | 78%      | 153              | 153   | 10%      | 90%      |
| Black       | 8     | 14%      | 86%      | 548              | 548   | 14%      | 86%      |
| Asian       | 134   | 7%       | 93%      | 354              | 354   | 7%       | 93%      |
| Other       | 38    | 5%       | 95%      | 354              | 354   | 5%       | 95%      |

**Geographic region**

| Region        | Total | <6 years | ≥6 years | Extent of disease | Total | <6 years | ≥6 years |
|---------------|-------|----------|----------|------------------|-------|----------|----------|
| North America | 222   | 15%      | 85%      | 513              | 513   | 15%      | 85%      |
| Asia          | 115   | 14%      | 86%      | 548              | 548   | 14%      | 86%      |
| Australia     | 64    | 7%       | 93%      | 354              | 354   | 7%       | 93%      |
| Other         | 36    | 5%       | 95%      | 354              | 354   | 5%       | 95%      |

**Disease duration**

| Duration | Total | <6 years | ≥6 years | Extent of disease | Total | <6 years | ≥6 years |
|----------|-------|----------|----------|------------------|-------|----------|----------|
| <6 years | 513   | 15%      | 85%      | 153              | 153   | 10%      | 90%      |
| ≥6 years | 548   | 14%      | 86%      | 548              | 548   | 14%      | 86%      |

**Extent of disease**

| Extent | Total | <6 years | ≥6 years | Extent of disease | Total | <6 years | ≥6 years |
|--------|-------|----------|----------|------------------|-------|----------|----------|
| Prolonged sigmoiditis or proctitis | 153   | 16%      | 84%      | 153              | 153   | 10%      | 90%      |
| Left-sided colitis | 354   | 42%      | 58%      | 354              | 354   | 13%      | 87%      |

**Notes:**

††† Proctosigmoiditis and proctitis are considered together in the Extent of disease section.
| Extensive colitis or pancolitis | 551 | 39 (7.1) | 365 (66.2) | 147 (26.7) | 171 | 16 (9.4) | 93 (54.4) | 62 (36.3) | 196 | 14 (7.1) | 116 (59.2) | 66 (33.7) |
|--------------------------------|-----|----------|------------|------------|-----|--------|----------|----------|-----|-------|----------|---------|

**Oral corticosteroid use at baseline**

| Yes | 491 | 52 (10.6) | 304 (61.9) | 135 (27.5) | 131 | 15 (11.5) | 76 (58.0) | 40 (30.5) | 154 | 8 (5.2) | 102 (66.2) | 44 (28.6) |
|-----|-----|-----------|------------|------------|-----|--------|----------|----------|-----|-------|----------|---------|
| No  | 570 | 45 (7.9)  | 373 (65.4) | 152 (26.7) | 202 | 20 (9.9) | 109 (54.0) | 73 (36.1) | 228 | 19 (8.3) | 127 (55.7) | 82 (36.0) |

**Oral corticosteroid dose at induction study baseline**

| <15 mg/day | 145 | 12 (8.3) | 92 (63.4) | 41 (28.3) | 49 | 6 (12.2) | 30 (61.2) | 13 (26.5) | 43 | 3 (7.0) | 27 (62.8) | 13 (30.2) |
|------------|-----|----------|------------|-----------|----|--------|----------|----------|----|-------|----------|---------|
| ≥15 mg/day | 303 | 35 (11.6) | 181 (59.7) | 87 (28.7) | 75 | 10 (13.3) | 43 (57.3) | 22 (29.3) | 95 | 4 (4.2) | 63 (66.3) | 28 (29.5) |
| Other      | 43  | 5 (11.6)  | 31 (72.1)  | 7 (16.3)  | 12 | 0 (0.0)  | 6 (50.0)  | 6 (50.0)  | 17 | 1 (5.9) | 12 (70.6) | 4 (23.5) |
| None       | 570 | 45 (7.9)  | 373 (65.4) | 152 (26.7) | 197 | 19 (9.6) | 106 (53.8) | 72 (36.5) | 227 | 19 (8.4) | 127 (55.9) | 81 (35.7) |

**Prior TNF antagonist failure at induction study baseline**

| Yes | 549 | 39 (7.1) | 373 (67.9) | 137 (25.0) | 140 | 11 (7.9) | 78 (55.7) | 51 (36.4) | 228 | 13 (5.7) | 153 (67.1) | 62 (27.2) |
|-----|-----|----------|------------|------------|-----|--------|----------|----------|-----|-------|----------|---------|
| No  | 512 | 58 (11.3) | 304 (59.4) | 150 (29.3) | 193 | 24 (12.4) | 107 (55.4) | 62 (32.1) | 154 | 14 (9.1) | 76 (49.4) | 64 (41.6) |

**Prior immunosuppressant failure at induction study baseline**

| Yes | 770 | 69 (9.0) | 498 (64.7) | 203 (26.4) | 229 | 11 (5.9) | 130 (56.8) | 75 (32.8) | 293 | 24 (8.2) | 179 (61.1) | 90 (30.7) |
|-----|-----|----------|------------|------------|-----|--------|----------|----------|-----|-------|----------|---------|
| No  | 291 | 28 (9.6) | 179 (61.5) | 84 (28.9)  | 104 | 11 (10.6) | 55 (52.9) | 38 (36.5) | 89  | 3 (3.4) | 50 (56.2) | 36 (40.4) |

**Baseline total Mayo score**

| <9      | 381 | 45 (11.8) | 223 (58.5) | 113 (29.7) | -   | -      | -        | -        | 178 | 19 (10.7) | 99 (55.6) | 60 (33.7) |
|---------|-----|-----------|------------|------------|-----|--------|----------|----------|-----|-------|----------|---------|
| ≥9      | 677 | 52 (7.7)  | 452 (66.8) | 173 (25.6) | -   | -      | -        | -        | 204 | 8 (3.9)  | 130 (63.7) | 66 (32.4) |
| <3      | -   | -         | -          | -          | 128 | 15 (11.7) | 73 (57.0) | 40 (31.3) | -   | -      | -        | -        |
| Baseline partial Mayo score | <6 | ≥6 | <2 | ≥2 | <6 | ≥6 | <2 | ≥2 | <6 | ≥6 | <2 | ≥2 |
|-----------------------------|----|----|----|----|----|----|----|----|----|----|----|----|
| <6                          | 255| 803| -  | -  | 31 (12.2)| 66 (8.2)| -  | -  | 166| 167| -  | -  |
| ≥6                          | 146| 529| 259| 167| 146 (57.3)| 529 (65.9)| 259| 167| 19 (11.4)| 16 (9.6)| 19 (11.4)| 16 (9.6)| 232| 232| 11 (4.7)| 11 (4.7)| 144 (62.1)| 144 (62.1)| 77 (33.2)| 77 (33.2)| 205| 205| 20 (9.8)| 20 (9.8)| 73 (35.6)| 73 (35.6)| 112 (54.6)| 112 (54.6)| 85 (56.7)| 85 (56.7)| 49 (32.7)| 49 (32.7) |
| <2                          | -  | -  | -  | -  | 166| 167| -  | -  | 166| 167| -  | -  |
| ≥2                          | -  | -  | -  | -  | 166| 167| -  | -  | 166| 167| -  | -  |

Partial Mayo score at assessment

| CRP concentration at baseline |
|-------------------------------|
| <3 mg/L                       | 381| 666| -  | -  | 51 (13.4)| 46 (6.9)| -  | -  | 219 (57.5)| 447 (67.1)| -  | -  |
| ≥3 mg/L                       | 219| 447| -  | -  | 111 (29.1)| 173 (26.0)| -  | -  | 242 (31.3)| 218 (76.2)| -  | -  |

CRP concentration at assessment

| Number of patients randomised at site based on induction data |
|--------------------------------------------------------------|
| <5               | 300| 761| 688|<5 | 63 (9.2)| 434 (63.1)| 191 (27.8)| 242| 23 (9.5)| 140 (57.9)| 79 (32.6)| 275| 17 (6.2)| 160 (58.2)| 98 (35.6) |
| ≥5               | 20 (6.7)| 189 (63.0)| 91 (30.3)| 168| 12 (7.1)| 97 (57.7)| 59 (35.1)| 130| 13 (10.0)| 69 (53.1)| 48 (36.9) |
| <10              | 77 (10.1)| 488 (64.1)| 196 (25.8)| 165| 23 (13.9)| 88 (53.3)| 54 (32.7)| 252| 14 (5.6)| 160 (63.5)| 78 (31.0) |
| $\geq 10$ | 373 | 34 (9.1) | 243 (65.1) | 96 (25.7) | 91 | 12 (13.2) | 45 (49.5) | 34 (37.4) | 107 | 10 (9.3) | 69 (64.5) | 28 (26.2) |

Abbreviations: b.d., twice daily; CR, central read; CRP, C-reactive protein; LR, local read; N, number of patients in each treatment group with non-missing local and central read data; n, number of patients in each subgroup with the specified level of difference; N1, number of patients in each subgroup; TNF, tumour necrosis factor.

Proportions were based on a three-level response: central read $\geq 1$ point lower than local read; no difference between central and local read; central read $\geq 1$ point higher than local read.

†Includes patients receiving placebo ($n = 216$) or tofacitinib 10 mg b.d. ($n = 845$).
‡Includes patients receiving placebo ($n = 68$) or tofacitinib 10 mg b.d. ($n = 265$).
§Includes patients who were non-responders after receiving tofacitinib 10 mg b.d. ($n = 261$) or placebo ($n = 121$) in OCTAVE Induction 1 or 2, all of whom received tofacitinib 10 mg b.d. in OCTAVE Open.
¶Baseline of OCTAVE Induction 1 or 2, OCTAVE Sustain, or OCTAVE Open.
††Canada and the USA.
‡‡Japan, Korea and Taiwan.
§§Croatia, Czechia, Estonia, Hungary, Latvia, Poland, Romania, Russia, Serbia, Slovakia and Ukraine.
¶¶Austria, Belgium, Denmark, France, Germany, Israel, Italy, Netherlands, Spain and the UK.
†††One patient with proctitis was enrolled into OCTAVE Induction 2 as a protocol deviation and assigned to receive tofacitinib 10 mg b.d.
‡‡‡Week 8 for OCTAVE Induction 1 and 2, Week 52 for OCTAVE Sustain and Month 2 for OCTAVE Open Induction non-responders.
§§§Week 8 for OCTAVE Induction 1 and 2 and Week 52 for OCTAVE Sustain.