# SIMPONI® (subcutaneous golimumab)
# Treatment of Ulcerative Colitis with SIMPONI: Dose Increase Above 100 mg Every 4 Weeks or Dosing Interval Reduction

## SUMMARY


- The company cannot recommend any practices, procedures, or usage that deviate from the approved labeling.
- Please refer to the local labeling for relevant information on dosage and administration for SIMPONI.
- GOLILOR was an open-label, phase 4, prospective, multicentric study that evaluated the effectiveness and safety of SIMPONI dose escalation in adult patients with active ulcerative colitis (UC) who had loss of response to SIMPONI maintenance therapy. Among 47 patients with loss of response after a median of 20.4 months of maintenance, 50 dose escalations were done: 25 patients underwent escalation from 50 mg to 100 mg every 4 weeks (q4w); and 25 patients had the dose escalated from 100 mg q4w to 100 mg every 2 weeks (q2w).[1]
- Results from a multicenter, open-label, retrospective, cohort study of adult patients with moderate-to-severe UC demonstrated that among the 13 secondary nonresponders receiving a SIMPONI maintenance dose of 100 mg q4w, the dose was escalated from 100 mg to 200 mg q4w in 1 patient and to 100 mg q2w in 2 patients.[2]


## CLINICAL DATA

### Prospective Cohort Study

**Fumery et al (2023)**[1] evaluated the effectiveness and safety of SIMPONI dose escalation in GOLILOR (NCT03182166), an open-label, phase 4, prospective, multicentric study that included adult patients with active UC who had loss of response to SIMPONI maintenance therapy.

#### *Study Design/Methods*

- All consecutive patients with active UC who had loss of response to SIMPONI were included in the study. Loss of response was defined as a Mayo score between 5 and 12 and an endoscopic Mayo subscore >1.
- Patients received an induction dose of 200 mg at week 0, 100 mg at week 2, followed by 50 mg or 100 mg q4w for patients weighing <80 kg or ≥80 kg, respectively, from week 6 onwards.
- Patients with loss of response at 50 mg or 100 mg q4w underwent dose intensification to 100 mg q4w or 100 mg q2w, respectively. Two consecutive intensifications were permitted.
- The primary endpoint was clinical response (≥3-point decrease in the partial Mayo score) approximately 4-8 weeks after drug intensification.
- The secondary endpoints were clinical remission (partial Mayo score ≤1) and endoscopic remission (endoscopic Mayo score ≤1).

#### *Results*

- A total of 47 patients (50 mg q4w, 53% [n=25]; 100 mg q4w, 47% [n=22]) who had loss of response after a median of 20.4 months of maintenance treatment were included in the study. The median baseline partial and endoscopic Mayo scores for these patients were 6 (interquartile range [IQR], 5-7) and 3 (IQR, 2-3), respectively.
- Overall, 50 dose escalations (100 mg q4w, n=25; 100 mg q2w, n=25) were performed.
- At weeks 2-4, clinical response was achieved in 40% (16/40) of patients; clinical remission, in 10% (4/40); endoscopic response, in 33% (10/30); and endoscopic remission, in 23% (7/30).

- At weeks 4-8, clinical response was achieved in 44% (16/36) of patients; clinical remission, in 22% (8/36); endoscopic response, in 45% (17/37); and endoscopic remission, in 41% (15/37).
- Serum golimumab levels post dose escalation (weeks 2-4 and weeks 4-8) were not significantly different between patients who achieved clinical or endoscopic response/remission.
- SIMPONI dose escalation to 100 mg q4w vs 100 mg q2w was significantly associated with clinical remission at weeks 4-8 (odds ratio, 1.98; 95% confidence interval [CI], 1.06-3.70; *P*=0.032).
- Golimumab levels at baseline or the presence of anti-drug antibodies were not associated with the effectiveness of dose escalation.
- Among the 29 patients with data at week 26, 12 were still treated with SIMPONI and 6 patients were in clinical remission.
- A total of 35 AEs were observed among the 47 patients who received ≥1 escalated dose of SIMPONI. Serious AEs were reported in 4.2% (n=2) of patients (UC exacerbation, n=1; infection, n=1). No death, cancer, or severe infection were observed.

**Retrospective Cohort Study**

**Taxonera et al (2017)**[2] conducted a multicenter, open-label, uncontrolled, retrospective cohort study of adult patients with moderate-to-severe UC assessing the short-term and long-term efficacy and safety of SIMPONI used as the first, second, or third anti-TNF agent. As a secondary objective, SIMPONI dose escalation efficacy and safety was also evaluated after a secondary loss of response.

***Study Design/Methods***

- Patients received an induction dose of 200 mg at week 0, 100 mg at week 2, and thereafter maintenance (50 or 100 mg q4w for patients weighing <80 kg or ≥80 kg, respectively) doses of SIMPONI.
- Patients were evaluated for short-term (clinical response and clinical remission at week 8) and long-term (cumulative chance of SIMPONI failure-free survival and colectomy free survival during follow-up) efficacy.
- Clinical response was defined as a 3-point or ≥50% decrease from baseline in the partial Mayo score and a final partial Mayo score of ≤2. Clinical remission was defined as a partial Mayo score of 0 or 1.
- SIMPONI failure was defined as discontinuation of SIMPONI therapy due to drug intolerance or absence or loss of response (primary nonresponse or secondary loss of response or tertiary loss of response despite SIMPONI dose escalation). Patients who experienced a secondary loss of response on SIMPONI but were dose escalated and regained response were not considered failures.
- During follow-up, the proportion of patients who experienced secondary loss of response and the amount who were dose escalated were evaluated.
- A safety analysis of SIMPONI was also conducted.

***Results***

- A total of 142 patients were included in the study. One-hundred patients were initiated on the 50 mg maintenance dose and 40 patients on the 100 mg maintenance dose. Two patients were withdrawn by week 6.
- At week 8, clinical response was achieved in 64.8% (92/142; 95% CI, 56.6-73) of patients and clinical remission in 31.7% (45/142; 95% CI, 23.7-39.7) of patients.
- After a median 12-month follow-up, 42.2% (60/142; 95% CI, 33.8-50.7) of patients experienced SIMPONI failure due to primary nonresponse (28/142), secondary loss of response (19/142), tertiary loss of response after SIMPONI dose escalation (9/142) and AEs (4/142).

- A total of 50 out of 114 patients who were on maintenance therapy had a secondary loss of response and of these patients, 19 discontinued SIMPONI.
- SIMPONI dose escalation was required in 62% (31/50) of patients to overcome secondary loss of response. SIMPONI dose was escalated from 50 to 100 mg every 4 weeks in 28 patients, 100 to 200 mg q4w in one patient, and to 100 mg q2w in two patients.
- Seventy-one percent (22/31) of the patients requiring SIMPONI dose escalation regained clinical response and avoided SIMPONI failure at the last follow-up. A total of 9 patients had SIMPONI failure due to tertiary loss of response. Additionally, one patient required colectomy after dose escalation.
- The safety analysis of the 142 patients in the study represented SIMPONI exposure for a total of 1824 months (217 months with escalated doses). A total of 2.8% (n=4) of patients experienced AEs (paresthesia, cutaneous infection, pneumonitis and recurrence of cervical neoplasia; all n=1) leading to SIMPONI discontinuation. Of note, rates of AEs leading to discontinuation were found to be similar for patients receiving standard or escalated doses.

## LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) was conducted on 09 November 2023.

## REFERENCES

1. Fumery M, Nancey S, Filippi J, et al. Effectiveness of golimumab intensification in ulcerative colitis: a multicentric prospective study. *Aliment Pharmacol Ther*. 2023;57(11):1290-1298.

2. Taxonera C, Rodriguez C, Bertoletti F, et al. Clinical outcomes of golimumab as first, second or third anti-TNF agent in patients with moderate-to-severe ulcerative colitis. *Inflamm Bowel Dis*. 2017;23(8):1394-1402.