SIMPONI® (subcutaneous golimumab)
SIMPONI - Treatment of Ankylosing Spondylitis

SUMMARY

- The safety and efficacy of SIMPONI for the treatment of patients with active ankylosing spondylitis (AS) was evaluated in the phase 3 GO-RAISE trial.[1]
- At week 14, treatment with SIMPONI 50 mg (59.4%) resulted in a significantly greater proportion of patients who achieved ≥20% improvement in the ASsessment in AS International Working Group criteria (ASAS 20) compared to placebo (21.8%; *P*<0.001).[1]
- Through week 24, ≥1 adverse event (AE) was reported in 79.9% of all SIMPONI-treated patients and 76.6% of placebo-treated patients, and 4.7% and 6.5% of patients, respectively, had ≥1 serious adverse event (SAE).[1]

CLINICAL DATA

Phase III - GO-RAISE

The efficacy and safety of SIMPONI for the treatment of patients with active AS was evaluated in a randomized, double-blind, placebo-controlled, phase 3 study (GO-RAISE).[1]

Study Design/Methods

The design and methods of the GO-RAISE study are described below.[1-3]

- A total of 356 patients were randomly assigned to receive injections of SIMPONI 50 mg, SIMPONI 100 mg, or placebo at baseline and every 4 weeks thereafter.
- Patients were eligible for inclusion in the study if they had AS according to the modified New York Criteria for ≥3 months, a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; 0-10) score of ≥4, a spinal back pain score of ≥4 using a visual analog scale (VAS; 0-10) scoring system, and an inadequate response to current or previous nonsteroidal antiinflammatory drugs (NSAIDs) or disease-modifying antirheumatic drugs (DMARDs).
- Patients were permitted to continue concomitant methotrexate, sulfasalazine, hydroxychloroquine, corticosteroids, and NSAIDs at stable doses through week 24. After week 24, adjustment of select concomitant medications was permitted.
- Patients receiving placebo or SIMPONI 50 mg who had <20% improvement from baseline in both total back pain and morning stiffness measures entered early escape in a double-blind fashion at week 16 (patients in the placebo group received SIMPONI 50 mg and patients in the SIMPONI 50 mg group received SIMPONI 100 mg).
- All other patients remained on their previous medication until week 24.
- Beginning at week 24, patients who were still receiving placebo crossed over to receive subcutaneous (SC) injections of SIMPONI 50 mg every 4 weeks in a blinded manner. All other assigned treatments, including from randomization or early escape, were continued.
- The study was blinded through week 104 (to placebo or SIMPONI during the placebo-controlled phase and to the SIMPONI dose through week 104) and patients were followed for up to 5 years (final SIMPONI injection at week 252).
- SIMPONI dosage modifications or concomitant DMARD, corticosteroid, and NSAID therapy adjustments were permitted at the investigator's discretion after unblinding at week 104. Patients receiving SIMPONI 50 mg could have their dose increased to 100 mg and patients receiving SIMPONI 100 mg could have their dose decreased to 50 mg.
- The primary efficacy endpoint was the proportion of patients with an ASAS 20 response at week 14.
- Secondary endpoints included ≥40% improvement in the ASessment in AS International Working Group criteria (ASAS 40), ASsessment in AS (ASAS) partial remission (value <2 in each of the 4 ASAS domains), and 20% improvement in 5 of 6 ASAS domains (ASAS 5/6).

- Other endpoints included assessments of disease activity according to the BASDAI, back pain VAS, night pain VAS, patient's global assessment and C-reactive protein (CRP) level, an assessment of physical function according to the Bath AS Functional Index (BASFI), assessments of range of motion according to the Bath AS Metrology Index (BASMI) and chest expansion, and assessment of health-related quality of life (HR-QoL) according to Short Form 36 (SF-36).
- A post-hoc analysis included an evaluation of inactive and moderate disease activity according to the AS Disease Activity Score (ASDAS) <1.1 and <2.1, respectively.

Results

The results of the GO-RAISE study are described below.[1,3]

Patient Characteristics

- Baseline demographics and disease characteristics were similar among the 3 treatment groups.
- Patients had active disease with moderately high levels of pain and inflammation as evidenced by baseline disease activity values.
- Across treatment groups, concomitant DMARDs were received by 29%-36% of patients at baseline.
- A total of 66 patients entered early escape at week 16 (41 patients, placebo/SIMPONI 50 mg; 25 patients, SIMPONI 50 mg/SIMPONI 100 mg).

Efficacy

- As noted in Table: Proportion of Patients Achieving Clinical Response to SIMPONI Therapy at Weeks 14 and 24, both SIMPONI regimens resulted in statistically significant improvement in the signs and symptoms of AS, as measured by ASAS responses, compared to placebo.
- However, no clear difference in efficacy was evident between the 50 mg and 100 mg dose groups through week 24.
- ASAS 20 responses were achieved by greater proportions of patients in the SIMPONI groups at the first assessment, 4 weeks after the first SC injection.

Proportion of Patients Achieving Clinical Response to SIMPONI Therapy at Weeks 14 and 24[1,4]

Assessment	Placebo (n=78)	SIMPONI 50 mg (n=138)	SIMPONI 100 mg (n=140)	SIMPONI Combined (n=278)
Week 14				
ASAS 20	21.8%	59.4%[a]	60% (84)[a]	59.7% (166)[a]
ASAS 40	15.4%	44.9%[a]	49.3% (69)[a]	47.1% (131)[a]
ASAS 5/6	7.7%	50.0%[a]	48.6% (68)[a]	49.3% (137)[a]
ASAS partial remission	5.1%	23.2%[a]	20.7% (29)[b]	21.9% (61)[a]
BASDAI 50	15.4%	45.9%[a]	40.9%[a]	43.3%[a]
BASFI (0-10 scale)	0.1 (-1.1, 1.1)	-1.4 (-3.1, -0.1)[a]	-1.5 (-3.0, -0.1)[a]	-1.4 (-3.1, -0.1)[a]
BASMI (0-10 scale)	0 (-1.0, 0.0)	0 (-1.0, 0.0)	0 (-1.0, 0.0)	0 (-1.0, 0.0)
SF-36 PCS score (0-50 scale)	2.4 (-1.4, 7.8)	7.3 (1.5, 15.3)[a]	8.4 (2.3, 14.1)[a]	7.8 (1.9, 14.5)[a]
SF-36 MCS score (0-50 scale)	0.1 (-4.3, 5.3)	1.5 (-2.2, 7.8)[c]	3.7 (-3.2, 12.1)[d]	2.5 (-2.6, 9.4)[d]
Week 24				
ASAS 20	23.1%	55.8%[a]	65.7%[a]	60.8%[a]
ASAS 40	15.4%	43.5%[a]	54.3%[a]	48.9%[a]
ASAS 5/6	12.8%	49.3%[a]	50.7%[a]	50.0%[a]
BASDAI 50	14.7%	50.8%[a]	47.8%[a]	49.3%[a]

BASFI (0-10 scale)	0.4 (-1.1, 1.3)	-1.6 (-3.4, 0.0)[a]	-1.6 (-3.5, -0.3)[a]	-1.6 (-3.5, -0.2)[a]
BASMI (0-10 scale)	0.0 (-1.0, 0.0)	0.0 (-1.0, 0.0)	-0.2 (-1.0, 0.0)	0.0 (-1.0, 0.0)
SF-36 PCS score (0-50 scale)	2.0 (-2.4, 7.7)	7.9 (1.1, 17.6)[a]	8.1 (2.1, 15.0)[a]	8.1 (2.0, 16.6)[a]
SF-36 MCS score (0-50 scale)	-0.3 (-3.2, 6.3)	1.4 (-3.3, 6.6)	5.2 (-2.3, 12.8)[d]	2.9 (-2.8, 9.7)[c]

Except where indicated otherwise, values are the median (interquartile range).
Abbreviations: ASAS, ASsessment in Ankylosing Spondylitis International Working Group criteria; ASAS 20, ≥20% improvement in the ASAS; ASAS 40, ≥40% improvement in the ASAS; ASAS 5/6, 20% improvement in 5 of 6 ASAS domains; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASDAI 50, ≥50% improvement from baseline in the baseline BASDAI score; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; MCS score, mental component summary score; PCS score, physical component summary score; SC, subcutaneous; SF-36, Short Form 36; VAS, visual analog scale.
[a]*P*<0.001.
[b]*P*=0.002.
[c]*P*<0.05.
[d]*P*<0.01.

- Of the 355 treated patients, 101 patients discontinued study agent through week 252 due to AEs (n=33), unsatisfactory therapeutic effects (n=35), lost to follow-up (n=11), or other reasons (n=22).
- Through week 256, the overall intent-to-treat (ITT) ASAS 20 and ASAS 40 response rates were 66.0% (235/356) and 57.0% (203/356), respectively, as compared with 61.8% (220/356) and 44.6% (166/356) rates, respectively, at week 24.
- At week 256, ASAS partial remission based on an ITT analysis was reported in 121/356 patients (34.0%) treated with SIMPONI compared with 82/356 patients (23.0%) at week 24.
- Response rates using observed data for the 255 patients (72%) who continued SIMPONI through week 252 were consistent.
- Of the patients who received an increased dose of SIMPONI from 50 mg to 100 mg, 60.6% (20/33) and 44.7% (17/38) achieved ASAS 20 and ASAS 40 responses, respectively, following ≥2 doses of SIMPONI 100 mg. None of the 33 (ASAS 20) or 38 patients (ASAS 40) in this analysis had achieved these respective responses before dose escalation.

Safety

Through Week 24

- Through week 24, ≥1 AE was reported in 79.9% of all SIMPONI-treated patients and 76.6% of placebo-treated patients, and 4.7% and 6.5% of patients, respectively, had ≥1 SAE.
- There was an increased incidence of infections in patients treated with SIMPONI 50 mg (46.4%) and SIMPONI 100 mg (48.6%) compared with patients receiving placebo (36.4%).
- Serious infections were reported in 3 patients: 1 placebo-treated patient (gastrointestinal inflammation) and 2 SIMPONI 100 mg-treated patients (mononucleosis and chronic otitis media).
- Injection site reactions were reported in 8.7%, 6.4%, and 2.6% of patients, respectively. None of these were considered to be serious.
- Antibodies to SC golimumab were detected in 4.1% of patients through week 24.
- Two patients, 1 in the placebo group and 1 in the SIMPONI 100 mg group, developed a malignancy; both had basal cell carcinoma.
- There were no deaths, opportunistic infections, or cases of tuberculosis (TB) reported.

Through Week 268

- Through week 268, the safety of SIMPONI was similar to the safety reported through week 24 (regardless of dose).

- Overall, 97.5% (344/353) of all patients treated with SIMPONI developed at least 1 AE with 9.1% (32/353) of patients discontinuing study agent due to AEs.
- The incidence of SAEs was 20.4% (72/353 SIMPONI-treated patients) and included osteoarthritis requiring hospitalization (2.0%), pneumonia (1.1%), worsening of AS (1.1%), and depression (1.1%).
    - There was no increase in SAEs in successive years of SIMPONI treatment.
    - A total of 5.9% (21/353) of SIMPONI-treated patients developed a serious infection and there was no increase in serious infections observed in successive years of SIMPONI treatment.
- One death was reported during the study in a patient who was randomized to receive SIMPONI 50 mg. After 3 years in the study, the patient developed lymphoma and subsequently died from pancreatic cancer.
    - For SIMPONI-treated patients, the overall incidence of death was 0.07/100 patient-years (95% confidence interval [CI] 0.00-0.38) with no difference seen between doses.
- Two other malignancies were reported which were 2 SIMPONI-treated patients both with nonmelanoma skin cancer (NMSC). No increase in the incidence of malignancies was observed in successive years of SIMPONI treatment.
- It didn't appear that the incidences (per 100 patient-years) for lymphoma, NMSC, other malignancies and all malignancies were dose-related. Also, these incidences were not higher relative to those expected in the United States of America population according to the Surveillance, Epidemiology and End Results (SEER) database (excluding NMSC, which is excluded from the SEER database).
- The incidence of injection site reaction(s) was 12.2% (43/353 SIMPONI-treated patients).

LITERATURE SEARCH

A literature search of Ovid MEDLINE®, Embase®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 03 January 2024.

REFERENCES

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