# Secukinumab in Moderate to Severe Hidradenitis Suppurativa: Primary Endpoint Analysis From the SUNSHINE and SUNRISE Phase 3 Trials

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## SYNOPSIS


- Hidradenitis suppurativa (HS) is a chronic autoinflammatory keratinization disease of the skin involving the hair follicle characterized by nodules, abscesses and draining tunnels[1]
- HS is characterized by high patient burden and a recognized need for novel therapeutic options[2]
- The IL-17 pathway has been implicated as a key orchestrator of inflammation in HS[3]
- The SUNSHINE and SUNRISE studies investigated the efficacy and safety of secukinumab, an anti-IL-17A agent, in the treatment of moderate to severe HS


## OBJECTIVE

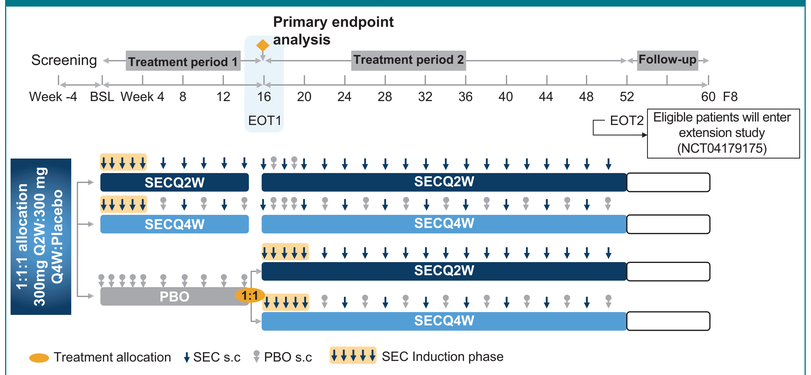

- To describe the primary endpoint analysis (Week 16) results from SUNSHINE (NCT03713619) and SUNRISE (NCT03713632), two double-blind, identical, Phase 3 randomised controlled trials of secukinumab in patients with moderate to severe HS


## METHODS

### Study Design

- SUNSHINE and SUNRISE were two randomised, double-blind, multicentre studies assessing short (16 weeks) and long-term (up to 1 year) efficacy, safety, and tolerability of two subcutaneous (s.c.) SEC dose regimens in adult patients with moderate to severe HS
- A total of 1084 patients (mean age 36.2, 56.3% female) across 219 sites worldwide were randomized in SUNSHINE (n=541) and SUNRISE (n=543)
- In each study, adult patients with moderate to severe HS were randomly assigned in a 1:1:1 fashion to receive s.c. secukinumab 300 mg every 2 (SECQ2W) or 4 weeks (SECQ4W), or placebo (**Figure 1**)

**Figure 1. Sunshine and Sunrise Study Design**




BSL, baseline; EOT1/EOT2: end of treatment period 1/2; F8, end of 8-week follow-up period; PBO, placebo; PRO, patient-reported outcome; Q2W, every two weeks; Q4W, every four weeks; s.c., subcutaneous; SEC, secukinumab 300 mg.

### Endpoints/assessments

- **Primary endpoint (week 16):** To demonstrate superiority of secukinumab versus placebo based on HiSCR (defined as at least a 50% decrease in AN count with no increase in the number of abscesses and/or in the number of draining fistulae relative to baseline).
- **Secondary endpoints (Week 16):** Percentage change in AN count from baseline, flares, and achievement of NRS30 among patients with a baseline skin pain NRS ≥3 (defined as at least a 30% reduction and at least a 2-unit reduction in baseline patient's global assessment of skin pain at worst)
- **Exploratory objectives:** To evaluate long-term safety, efficacy, and tolerability of secukinumab and its effect on patient reported outcomes (PROs) and biomarkers

## RESULTS

### Patient demographics and baseline characteristics

- N=541 (SUNSHINE) and N=543 (SUNRISE) randomized; 509 (94.1%) and 506 (93.2%) patients completed Treatment Period 1 (Week 16), respectively
- Discontinuation rate of treatment up to Week 16 was very low and balanced despite COVID-19 pandemic (**Table 1**)

**Table 1. SUNSHINE and SUNRISE: Patient Disposition**

| Disposition/ reason, n (%) | SUNSHINE | | | | SUNRISE | | | |
|---|---|---|---|---|---|---|---|---|
| | SECQ2W N=181 | SECQ4W N=180 | Placebo N=180 | Total N=541 | SECQ2W N=180 | SECQ4W N=180 | Placebo N=183 | Total N=543 |
| Completed Week 16 | 168 (**92.8**) | 169 (**93.9**) | 172 (**95.6**) | 509 (**94.1**) | 170 (**94.4**) | 169 (**93.9**) | 167 (**91.3**) | 506 (**93.2**) |
| Discontinued treatment | 13 (**7.2**) | 11 (**6.1**) | 8 (**4.4**) | 32 (**5.9**) | 10 (**5.6**) | 11 (**6.1**) | 16 (**8.7**) | 37 (**6.8**) |
| **Primary reason for discontinuing treatment up to Week 16** | | | | | | | | |
| Patient decision | 4 (2.2) | 9 (5.0) | 5 (2.8) | 18 (3.3) | 6 (3.3) | 6 (3.3) | 8 (4.4) | 20 (3.7) |
| Adverse event | 4 (2.2) | 0 (0.0) | 1 (0.6) | 5 (0.9) | 1 (0.6) | 4 (2.2) | 4 (2.2) | 9 (1.7) |
| Other* | 5 (2.8) | 2 (1.2) | 2 (1.2) | 9 (1.7) | 3 (1.7) | 1 (0.6) | 4 (2.2) | 8 (1.5) |

*Other includes the following reasons: lost to follow-up, physician decision, technical problems, lack of efficacy and pregnancy.
COVID-19, coronavirus disease 2019; N, number of patients in group; n, number of patients with characteristic; Q2W, every two weeks; Q4W, every four weeks; SEC, secukinumab 300 mg.

- 59% of participants were categorized as Hurley stage II and 37% as Hurley stage III (**Table 2**)
- About one quarter of participants had received previous systemic biologic therapy (mostly anti-TNFs)

### Efficacy: Primary endpoints

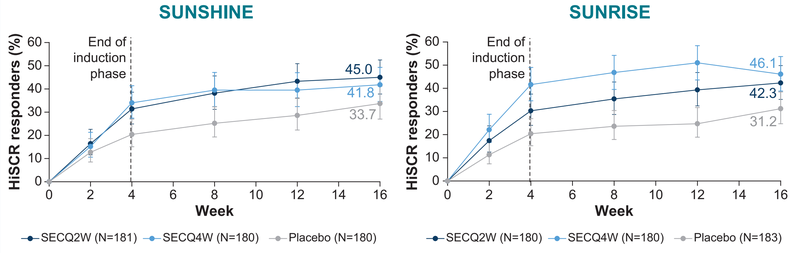
- The primary endpoint was met in both the SUNSHINE and SUNRISE studies
- Greater response rates for secukinumab compared to placebo were seen at all time-points from Week 2 to Week 16, with a rapid onset of action by Week 2 (**Figure 2**)

**Table 2. SUNSHINE and SUNRISE Results: Baseline Characteristics**

| Characteristic | SUNSHINE | | | | SUNRISE | | | |
|---|---|---|---|---|---|---|---|---|
| | SECQ2W N=181 | SECQ4W N=180 | Placebo N=180 | Total N=541 | SECQ2W N=180 | SECQ4W N=180 | Placebo N=183 | Total N=543 |
| **Age group in years, n (%)** | | | | | | | | |
| <30 | 58 (32.0) | 69 (38.3) | 51 (28.3) | 178 (32.9) | 52 (28.9) | 60 (33.3) | 57 (31.1) | 169 (31.1) |
| 30–<40 | 56 (30.9) | 45 (25.0) | 70 (38.9) | 171 (31.6) | 48 (26.7) | 61 (33.9) | 65 (35.5) | 174 (32.0) |
| 40–<65 | 64 (35.4) | 63 (35.0) | 58 (32.2) | 185 (34.2) | 77 (42.8) | 57 (31.7) | 59 (32.2) | 193 (35.5) |
| ≥65 | 3 (1.7) | 3 (1.7) | 1 (0.6) | 7 (1.3) | 3 (1.7) | 2 (1.1) | 2 (1.1) | 7 (1.3) |
| **Sex, n (%)** | | | | | | | | |
| Female | 102 (56.4) | 100 (55.6) | 102 (56.7) | 304 (56.2) | 98 (54.4) | 103 (57.2) | 105 (57.4) | 306 (56.4) |
| **Weight groups (kg), n (%)** | | | | | | | | |
| ≥90 | 99 (54.7) | 100 (55.6) | 97 (53.9) | 296 (54.7) | 94 (52.2) | 91 (50.6) | 91 (49.7) | 276 (50.8) |
| **Time since diagnosis of HS, mean±SD** | | | | | | | | |
| Years | 7.4±7.98 | 6.6±6.73 | 7.5±7.00 | 7.1±7.25 | 7.1±7.04 | 8.2±8.42 | 7.0±6.65 | 7.4±7.41 |
| **Baseline Hurley stage, n (%)** | | | | | | | | |
| II | 104 (57.5) | 107 (59.4) | 121 (67.2) | 332 (61.4) | 92 (51.1) | 106 (58.9) | 110 (60.1) | 308 (56.7) |
| III | 70 (38.7) | 63 (35.0) | 51 (28.3) | 184 (34.0) | 82 (45.6) | 68 (37.8) | 70 (38.3) | 220 (40.5) |
| **Previous exposure to systemic biologic therapy, n (%)** | | | | | | | | |
| Yes | 44 (24.3) | 39 (21.7) | 46 (25.6) | 129 (23.8) | 36 (20.0) | 42 (23.3) | 48 (26.2) | 126 (23.2) |
| **Current systemic antibiotic use (i.e., *antibiotic strata*), n (%)** | | | | | | | | |
| Yes | 26 (14.4) | 25 (13.9) | 18 (10.0) | 69 (12.8) | 18 (10.0) | 21 (11.7) | 19 (10.4) | 58 (10.7) |

HS, hidradenitis suppurativa; N, number of patients in group; n, number of patients with characteristic; Q2W, every two weeks; Q4W, every four weeks; SD, standard deviation; SEC, secukinumab 300 mg.

**Figure 2. Primary Efficacy Endpoint: HiSCR up to Week 16**




| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| 45.0% (p=0.0070) | 41.8% (p=0.0418) | 33.7% |

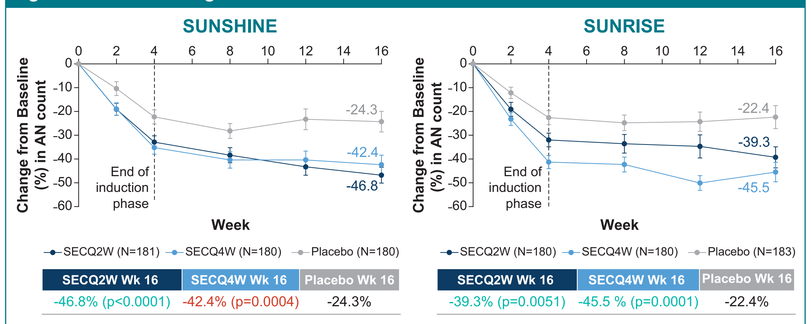
| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| 42.3% (p=0.0149) | 46.1% (p=0.0022) | 31.2% |

One-sided nominal p-values are based on a logistic regression model, the primary estimand, and multiple imputation. Error bars represent 95% CI.
Green represents statistical significance and red represents non-significance compared with placebo.
CI, confidence intervals; HiSCR, hidradenitis suppurativa clinical response; N, number of patients in group; Q2W, every two weeks; Q4W, every four weeks; SEC, secukinumab 300 mg; Wk, week.

### Efficacy: Secondary endpoints

- In both studies, secukinumab reduced the abscess and inflammatory nodule count in patients with moderate to severe HS (**Figure 3**)
  - A decrease in AN count with secukinumab appeared as early as Week 2, and further improved up to Week 16 in both studies

**Figure 3. Percent change From Baseline in AN Count**



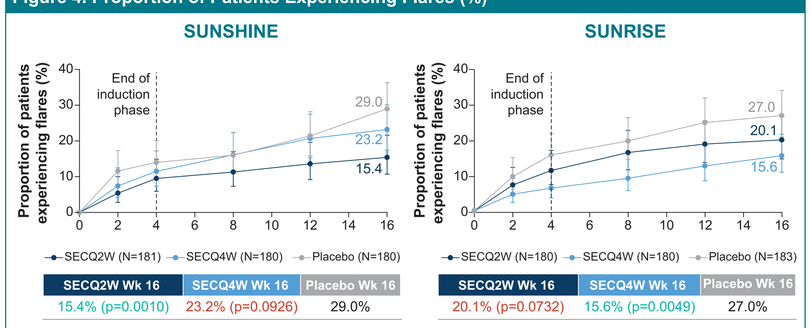

| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| -46.8% (p<0.0001) | -42.4% (p=0.0004) | -24.3% |

| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| -39.3% (p=0.0051) | -45.5 % (p=0.0001) | -22.4% |

One-sided nominal p-values are based on an ANCOVA, the secondary estimand, and multiple imputation. Error bars represent SE. Green represents statistical significance and red represents non-significance compared with placebo.
AN, abscess and inflammatory nodule; ANCOVA, analysis of covariance; HS, hidradenitis suppurativa; N, number of patients in group; Q2W, every two weeks; Q4W, every four weeks; SE, standard error; SEC, secukinumab 300 mg; Wk, week.

- The proportion of patients experiencing flares was lower with secukinumab compared to placebo at all timepoints from Week 2 to Week 16, with a rapid onset of action starting at Week 2 in both studies (**Figure 4**)

**Figure 4. Proportion of Patients Experiencing Flares (%)***



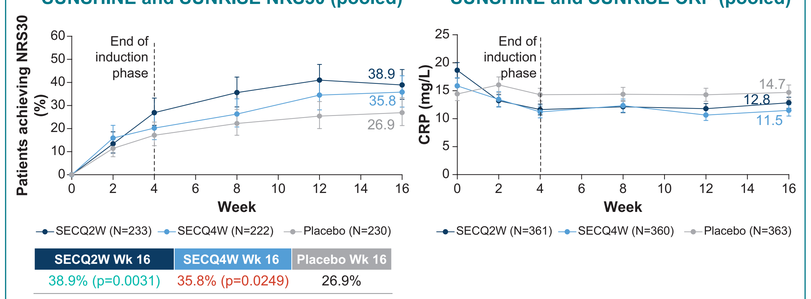

| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| 15.4% (p=0.0010) | 23.2% (p=0.0926) | 29.0% |

| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| 20.1% (p=0.0732) | 15.6% (p=0.0049) | 27.0% |

*Flares are defined as as at least a 25% increase in AN count with a minimum increase of 2 AN relative to baseline.
One-sided nominal p-values are based on a logistic regression model, the secondary estimand, and multiple imputation. Error bars represent 95% CI.
Green represents statistical significance and red represents non-significance compared with placebo. AN, abscess and inflammatory nodule;
CI, confidence intervals; HS, hidradenitis suppurativa; N, number of patients in group; Q2W, every two weeks; Q4W, every four weeks;
SEC, secukinumab 300 mg; Wk, week.

- Secukinumab reduced skin pain in patients with moderate to severe HS (**Figure 5**)
  - NRS30 was defined as ≥30% reduction and a ≥2-unit reduction from baseline in Patient's Global Assessment of Skin Pain. Only patients with a baseline NRS≥3 were included in the analysis of skin pain
  - Pooled CRP levels demonstrate numerical reductions from placebo group
- A larger treatment effect was achieved with secukinumab compared with the placebo regimen as early as Week 4 and sustained up to Week 16

**Figure 5. Patients' Reduction in Pain**




| SECQ2W Wk 16 | SECQ4W Wk 16 | Placebo Wk 16 |
|---|---|---|
| 38.9% (p=0.0031) | 35.8% (p=0.0249) | 26.9% |

One-sided nominal p-values are based on a logistic regression model, the secondary estimand, and multiple imputation. Error bars represent 95% CI (NRS30) or SE (CRP). Green represents statistical significance and red represents non-significance compared with placebo.
CI, confidence intervals; CRP, C-reactive protein; HS, hidradenitis suppurativa; N, number of patients in group; NRS, numerical rating score; Q2W, every two weeks; Q4W, every four weeks; SE, standard error; SEC, secukinumab 300 mg; Wk, week.

### Safety

- Secukinumab was well tolerated, consistent with the known safety profile in other approved indications (**Table 3**)

**Table 3. Summary of Secukinumab Safety Through Week 16**

| Outcome, n (%) | SUNSHINE | | | SUNRISE | | |
|---|---|---|---|---|---|---|
| | SECQ2W N=181 | SECQ4W N=180 | Placebo N=180 | SECQ2W N=180 | SECQ4W N=180 | Placebo N=183 |
| **Safety overview** | | | | | | |
| Any AEs | 122 (67.4) | 118 (65.6) | 120 (66.7) | 113 (62.8) | 114 (63.3) | 116 (63.4) |
| All non-fatal SAEs | 3 (1.7) | 3 (1.7) | 6 (3.3) | 6 (3.3) | 6 (3.3) | 5 (2.7) |
| Deaths | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Discontinued study treatment due to AEs | 5 (2.8) | 1 (0.6) | 1 (0.6) | 1 (0.6) | 4 (2.2) | 4 (2.2) |
| **AEs of special interest** | | | | | | |
| Infections and infestations (SOC) | 59 (32.6) | 51 (28.3) | 53 (29.4) | 52 (28.9) | 59 (32.8) | 62 (33.9) |
| *URTI (HLT)* | 33 (18.2) | 26 (14.4) | 22 (12.2) | 27 (15.0) | 21 (11.7) | 29 (15.8) |
| Fungal infectious disorders (HLGT) | 12 (6.6) | 1 (0.6) | 7 (3.9) | 7 (3.9) | 13 (7.2) | 3 (1.6) |
| *Candida infections (HLT)* | 2 (1.1) | 1 (0.6) | 4 (2.2) | 5 (2.8) | 5 (2.8) | 2 (1.1) |
| Hypersensitivity (SMQ, narrow) | 12 (6.6) | 9 (5.0) | 9 (5.0) | 7 (3.9) | 5 (2.8) | 7 (3.8) |
| Malignant or unspecified tumours* (SMQ) | 0 (0.0) | 0 (0.0) | 1 (0.6) | 0 (0.0) | 1 (0.6) | 1 (0.5) |
| MACE | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| IBD† | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.6) | 1 (0.6) | 0 (0.0) |

*Excludes non-melanoma skin cancers; †one case of IBD and one case of ulcerative colitis was reported.
AE, adverse event; AESI, adverse event of special interest; HLGT, high-level group terms; HLT, high-level term; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular events; MedDRA, medical dictionary for regulatory activities; n, number of patients with outcome; N, number of patients in group; Q2W, every two weeks; Q4W, every four weeks; SAE, serious adverse event; SEC, secukinumab; SMQ, standardised MedDRA queries; SOC, system organ class; URTI, upper respiratory tract infection.

## CONCLUSIONS

- The SUNSHINE and SUNRISE Phase 3 trials both met their primary endpoint (HiSCR) demonstrating superiority of secukinumab over placebo with rapid symptom relief in patients with moderate to severe HS
- Secukinumab achieved the majority of its secondary endpoints of AN count, flares and pain while demonstrating positive numeric trends in safety and efficacy in DLQI and CRP
- Secukinumab was well tolerated in patients with moderate to severe HS, consistent with the known favorable safety profile in other approved indications

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