Secukinumab in Moderate to Severe Hidradenitis Suppurativa: Primary Endpoint Analysis from the SUNSHINE and SUNRISE phase III Trials

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Poster N° 17

INTRODUCTION

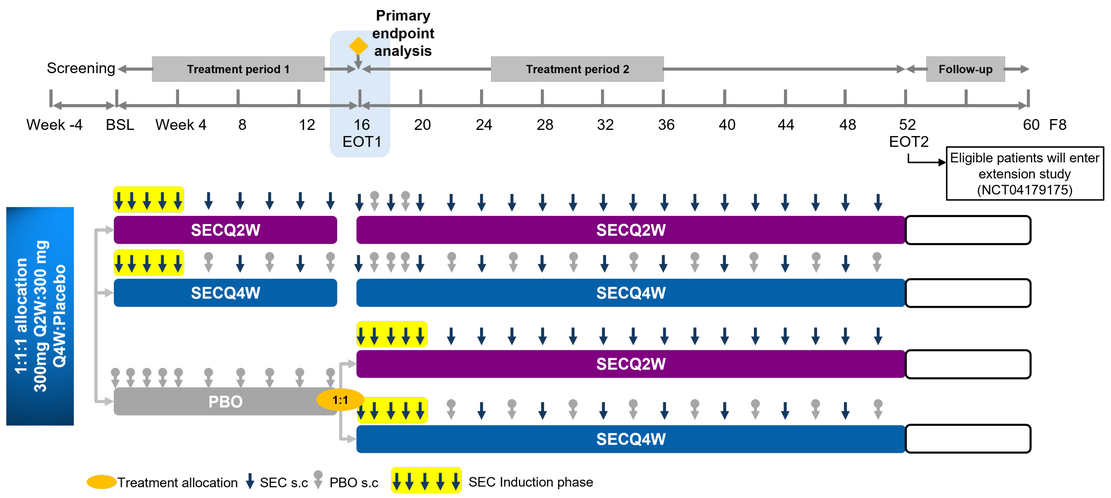
- Hidradenitis suppurativa (HS) is a difficult-to-manage, chronic, inflammatory skin disease, with limited effective treatment options available.
- Secukinumab (SEC), a fully human, monoclonal antibody which selectively neutralises interleukin 17A (IL-17A), was evaluated in patients with moderate to severe HS.
- Here, 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, are described.

METHODS

Study design

- Patients aged ≥18 years with moderate to severe HS were randomised to receive subcutaneous secukinumab 300 mg every two (SECQ2W) or four weeks (SECQ4W), or placebo. Figure 1 describes the SUNSHINE and SUNRISE study design.

Figure 1. SUNSHINE and SUNRISE study desgin



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

Study objectives

- The primary objective of both trials was to demonstrate the superiority of secukinumab over placebo with respect to the proportion of patients achieving a hidradenitis suppurativa clinical response (HiSCR) at Week 16 (HiSCR is defined as at least 50% decrease in abscess and inflammatory nodule count with no increase in the number of abscesses or in the number of draining fistulae relative to baseline).
- Key secondary endpoints included the percentage change from baseline in abscess and inflammatory nodule (AN) count at Week 16, the proportion of patients experiencing a flare over 16 weeks (flares are defined as at least a 25% increase in AN counts with a minimum increase of 2 AN relative to baseline), and the proportion of patients with NRS30 (skin pain) response (reported as pooled data from both trials) at Week 16. NRS30 is defined as at least a 30% reduction from baseline and at least a 2-unit reduction in patient's global assessment of skin pain at worst.

RESULTS

Study population

- 1,084 patients were randomised in SUNSHINE (n=541, SECQ2W [n=181]; SECQ4W [n=180]; placebo [n=180]) and SUNRISE (n=543, SECQ2W [n=180]; SECQ4W [n=180]; placebo [n=183]). Table 1 describes the baseline characteristics of the study populations.

Table 1. Baseline characteristics

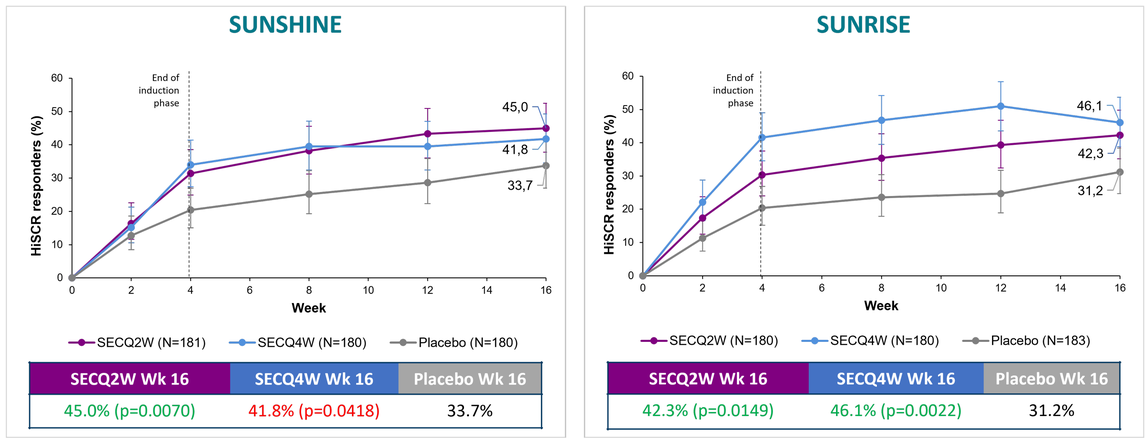
	SUNSHINE				SUNRISE			
Characteristic	SECQ2W N=181	SECQ4W N=180	Placebo N=180	Total N=541	SECQ2W N=180	SECQ4W N=180	Placebo N=183	Total N=543
Age group in years, n (%)								
<30	58 (32.0)	69 (38.3)	51 (28.3)	178 (32.9)	52 (28.9)	60 (33.3)	57 (31.1)	169 (31.1)
30–<40	56 (30.9)	45 (25.0)	70 (38.9)	171 (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.

Primary and key secondary endpoints

- The SECQ2W dose regimen met the primary endpoint (HiSCR at Week 16) in both studies (SUNSHINE: SECQ2W [45.0%] vs placebo [33.7%]; SUNRISE: SECQ2W [42.3%] vs placebo [31.2%]).
- SECQ2W met all of the secondary endpoints in both trials except for the proportion of patients experiencing a flare (met only in SUNSHINE); a significantly greater decrease in AN count (SUNSHINE: SECQ2W [-46.8%] vs placebo [-24.3%]; SUNRISE: SEC¬Q2W [-39.3%] vs placebo [-22.4%]) and significantly higher NRS30 response (pooled data: SECQ2W [38.9%] vs placebo [26.9%]) compared with placebo at Week 16.
- The SECQ4W dose regimen also demonstrated clinical efficacy, but primary and all secondary endpoints (excluding pain) were only met in SUNRISE; HiSCR (SECQ4W [46.1%] vs placebo [31.2%]), change in AN count (SECQ4W [-45.5%] vs placebo [-22.4%]) and proportion of patients experiencing flares (SECQ4W [15.6%] vs placebo [27.0%]).
- The primary endpoint is described in Figure 3.

Figure 3. Primary endpoint



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.

- Clinical response (HiSCR) to secukinumab is in line with sustained and continued improvement up to 52 weeks of treatment (long term data based on an interim analysis where 95% of patients completed or discontinued by week 52).

Safety

- Treatment with both dose regimens of secukinumab in both trials was well-tolerated with no new or unexpected safety signals compared to its well-established safety profile.
- Table 2 describes the safety profile of both SEC dosages in both trials.

Table 2. Safety profile

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 demonstrated sustained efficacy beyond the Week 16 primary efficacy analysis (long term data are based on an interim analysis where 95% of patients completed or discontinued by week 52).
- Secukinumab was well tolerated in patients with moderate to severe HS, consistent with the known favorable safety profile in other approved indications.
- Secukinumab is expected to be a new, safe, and effective biologic treatment option with a novel mode of action in moderate to severe HS.

DISCLOSURES

FB has received honoraria for consultance from AbbVie, Novartis and Leo Pharma. **ABK** is a consultant and investigator for Abbvie, Bristol Meyers Squibb, Janssen, Eli Lilly, Novartis, Pfizer, and UCB; investigator for Incyte and Anapyts Bio; consultant for Bayer, Boehringer Ingelheim, Ventyx, Moonlake, Lilly, Concert, EvoImmune, Sonoma Bio, Sanofi, receives fellowship funding from Janssen; and serves on the Board of Directors for Almirall. **AA** has received honoraria as a consultant or advisory board participant from AbbVie, Janssen, Novartis, Boehringer-Ingelheim, InflaRx, and UCB and is an investigator for Processa and Boehringer-Ingelheim. **GBEJ** has served as a consultant for AbbVie, Coloplast, Leo Pharma, Novartis, UCB, and InflaRX; as an investigator for AbbVie, Leo Pharma, Novartis, Regeneron, UCB, and InflaRX; has received unrestricted grants from AbbVie, Leo Pharma, and Novartis; has served on Adboards for AbbVie, Janssen-Pharma, MSD, and Novartis; and as a speaker for AbbVie, Coloplast, Leo Pharma, and Galderma. **AG** has received honoraria as an advisory board member, non-promotional speaker or consultant for: Amgen, AnaptsysBio, Avotres Therapeutics, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, Sun Pharmaceutical Industries, UCB, and Xbiotech (stock options for an RA project). **AG** has also received research/educational grants from: AnapytysBio, Janssen, Novartis, Ortho Dermatologics, Sun Pharmaceutical Industries, Bristol-Myers Squibb and UCB; all funds go to Icahn School of Medicine at Mount Sinai. **XW** is an employee at Novartis Pharma Shanghai, China. **MBW** is an employee and stockholder at Novartis Ireland Limited, Dublin. **LU,** and **ALM** are employees and stockholders at Novartis Pharma AG, Basel, Switzerland. **DK**, **RM**, **LC** and **EM** are employees and stockholders at Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA.

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