

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

This late-breaking oral presentation took place on 10<sup>th</sup> September 2022 as part of the 31<sup>st</sup> European Academy of Dermatology and Venereology (EADV) Congress, held in Milan, Italy, 7<sup>th</sup>–10<sup>th</sup> September 2022

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**Disclosure:**

Kimball is a consultant and investigator for Abbvie, Bristol Myers Squibb, Janssen, Eli Lilly, Novartis, Pfizer, and UCB; an investigator for Incyte and AnaptysBio; a consultant for Bayer, Boehringer Ingelheim, Ventyx, Moonlake, Eli Lilly, Concert, Evolmmune, Sonoma Bio, and Sanofi; receives fellowship funding from Janssen; and serves on the Board of Directors for Almirall. Alavi 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. Jemec 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, LeoPharma, and Novartis; has served on advisory boards for AbbVie, Janssen Pharmaceuticals, MSD, and Novartis; and as a speaker for AbbVie, Coloplast, Leo Pharma, and Galderma. Gottlieb has received honoraria as an advisory board member, non-promotional speaker, or consultant for Amgen, Anaptys Bio, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, Sun Pharmaceutical Industries, UCB, and Xbiotech;

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### Meeting Summary

The primary endpoint analyses from the SUNSHINE and SUNRISE Phase III trials of secukinumab in moderate-to-severe hidradenitis suppurativa (HS) were featured in an oral presentation as part of the late-breaking news session at the 31<sup>st</sup> annual European Academy of Dermatology and Venereology (EADV) congress. Known collectively as the SUNNY trials, the SUNSHINE and SUNRISE studies represent the largest Phase III trials conducted in HS to date. The primary endpoint was met in both studies for the every 2 weeks (Q2W) regimen, and in one for the every 4 weeks (Q4W) regimen, demonstrating the superiority of secukinumab over placebo in patients with moderate-to-severe HS. Secukinumab delivered rapid symptom relief and showed a favourable safety profile consistent with its use in other indications. Available data on file from the Week 52 database lock support the sustained efficacy beyond Week 16 with no new safety findings. Based on the positive outcomes of these milestone clinical trials, secukinumab is expected to be a new, safe, and effective biologic treatment option with a novel mode of action, targeting IL-17A, for moderate-to-severe HS.

### Primary Endpoint Analysis from the SUNSHINE and SUNRISE Phase III Trials

Alexa Kimball, Harvard Medical School and Clinical Laboratory for Epidemiology and Applied Research in Skin (CLEARS), Department of Dermatology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA, presented the Week 16 results from the two identical Phase III SUNSHINE and SUNRISE trials.<sup>1</sup> Both studies were randomised, double-blind, multicentre clinical trials that assessed the short- (16 weeks) and long-term (up to 1 year) efficacy, safety, and tolerability of secukinumab, a monoclonal antibody selectively neutralising IL-17A in adult patients with moderate-to-severe HS.

Patients were randomised 1:1:1 to one of two subcutaneous secukinumab dosing regimens: 300 mg Q2W or 300 mg Q4W, or placebo. Key inclusion criteria included  $\geq 5$  inflammatory lesions affecting at least two distinct anatomical areas at baseline, and diagnosis of HS  $\geq 1$  year prior to enrolment. Patients in the antibiotic stratum were permitted to enter the study on stable treatment with selected antibiotics (i.e., doxycycline, minocycline, and tetracycline, representing only 10–14% of patients). Patients with HS with a total fistulae count  $\geq 20$  at baseline, active inflammatory disease, or previous exposure to secukinumab or other IL-17(A)-biologics were excluded. Together, the SUNSHINE and SUNRISE trials randomised a

total of 1,084 patients with HS across 219 sites worldwide between January 2019 and July 2022. Retention was very high, with a completion rate of approximately 94% across the two studies. Overall, patients were well-balanced between treatment arms, although Kimball highlighted the higher proportion of Hurley Stage III patients in the SUNRISE trial, particularly in the secukinumab Q2W arm (45.6%), indicating a more severe patient population.

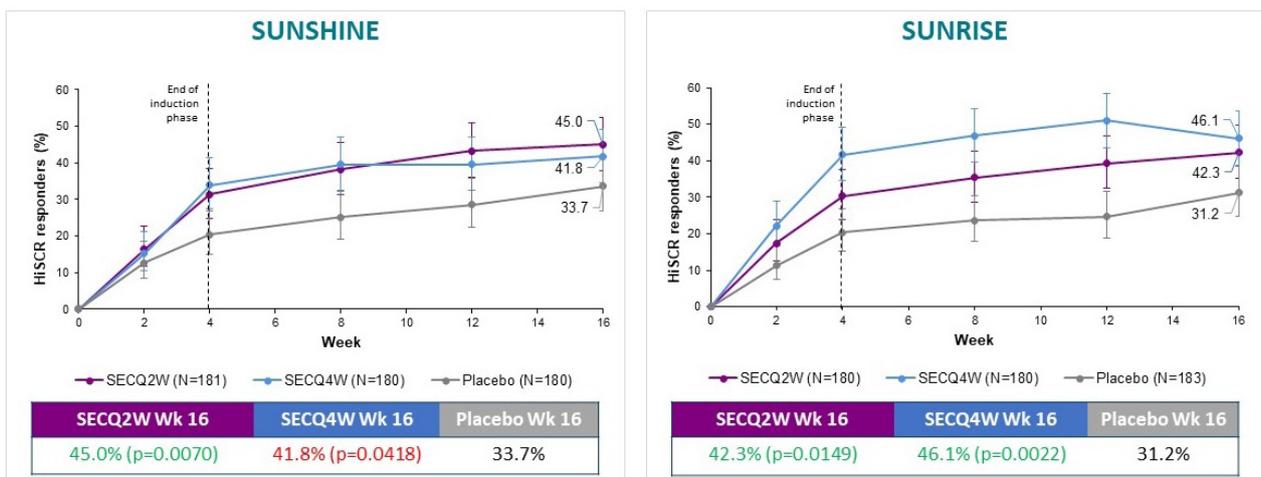
Both the SUNSHINE and SUNRISE studies met their primary endpoint based on HS clinical response (HiSCR), defined as at least a 50% decrease in abscess and inflammatory nodule (AN) count with no increase in the number of abscesses, or in the number of draining fistulae relative to baseline (Figure 1). Across both studies, numerically greater HiSCR response rates for secukinumab compared to placebo were seen at all time points from Week 2 to Week 16, with secukinumab demonstrating a rapid onset of action by Week 2. In the SUNSHINE and SUNRISE trials, treatment with secukinumab 300 mg Q2W demonstrated superiority compared to placebo in regard to the proportion of HiSCR responders (primary endpoint) in patients with moderate-to-severe HS at Week 16. In the SUNRISE trial only, secukinumab 300 mg Q4W was superior versus

placebo at Week 16 for HiSCR. Despite not achieving superiority, numerical differences at Week 16 were also observed in the SUNSHINE trial following the Q4W dosing regimen. The clinical response (HiSCR) to secukinumab at Week 16 is in line with the sustained and continued improvement that was seen up to 52 weeks of treatment, based on available data on file from the Week 52 database lock.

Secukinumab also achieved statistical significance and clinical improvements in key secondary endpoints evaluated in the SUNSHINE and SUNRISE trials. In both studies, secukinumab significantly reduced the AN count in patients with moderate-to-severe HS. The decrease in AN count with secukinumab appeared as early as Week 2 of treatment, and further improved up to Week 16. Overall, patients in the secukinumab treatment groups attained reductions from baseline of 39–47% in their AN count by Week 16, compared to decreases of approximately 23% with placebo.

Secukinumab was also shown to reduce the number of flares experienced by patients with moderate-to-severe HS, an outcome that Kimball described as an important “mirror” of efficacy. Across both studies, the proportion of patients experiencing flares was lower with secukinumab

Figure 1: SUNSHINE and SUNRISE both met their primary endpoints.



HiSCR: hidradenitis suppurativa clinical response; Q2W: every 2 weeks; Q4W: every 4 weeks; SEC: secukinumab; Wk: Week.

versus placebo at all time points from Week 2 to Week 16. Again, secukinumab demonstrated a rapid onset of action, with improvement seen as early as Week 2.

Finally, secukinumab reduced pain in patients with moderate-to-severe HS, which Kimball highlighted as an important and debilitating feature of this disease. A significantly higher proportion of patients with HS achieved a skin pain response (using the high hurdle of the numeric rating scale [NRS30] score), analysed based on pooled data from SUNSHINE and SUNRISE, compared with placebo at Week 16 following secukinumab 300 mg Q2W treatment. Despite not achieving statistical significance, numerical superiority at Week 16 was also observed with the Q4W dosing regimen. Only patients with a baseline NRS  $\geq 3$  were included in this analysis of skin pain.

Alongside its clinical efficacy, secukinumab also demonstrated substantial improvements in the quality of life of patients with moderate-to-severe HS in exploratory analyses from the SUNSHINE and SUNRISE trials. In both studies, Dermatology Life Quality Index (DLQI) response, defined as a >5 point reduction, was evident as early as Week 2. The proportion of patients achieving DLQI response was greater in both secukinumab regimens at Week 16 compared to placebo.

Safety data from the SUNSHINE and SUNRISE trials showed secukinumab to be well tolerated, consistent with its established safety profile in other disease states. Rates of adverse events

(AE) and all non-fatal serious AEs were very similar in both secukinumab arms compared to placebo. Rates of infections, including Candida infections, were low and not substantially different to placebo. The number of patients discontinuing study treatment due to AEs was also low across the secukinumab treatment groups in both trials. Discontinuations due to AEs in the secukinumab Q2W and Q4W arms were 2.8% and 0.6%, respectively, in the SUNSHINE trial and 0.6% and 2.2%, respectively, in the SUNRISE trial, compared to discontinuation rates of 0.6% and 2.2%, respectively, for placebo. Kimball described these safety data as “reassuring”, with secukinumab demonstrating “a very clean profile overall.”

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## Conclusion

Both the SUNSHINE and SUNRISE Phase III trials successfully met the primary endpoint, demonstrating superiority of secukinumab over placebo in HiSCR, with rapid symptom relief in patients with moderate-to-severe HS. Secukinumab reportedly also demonstrated sustained efficacy beyond the Week 16 primary efficacy analysis. Overall, secukinumab was well tolerated in patients with moderate-to-severe HS, consistent with its known safety profile. Collectively, these results highlight that secukinumab is expected to be a new, safe, and effective addition to the treatment armamentarium for moderate-to-severe HS, Kimball concluded.

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# Dermatoscopic Rainbow Pattern in Extragenital Lichen Sclerosus et Atrophicus

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## BACKGROUND

Lichen sclerosus et atrophicus (LSEA) is an inflammatory skin disease that most frequently affects pre-pubertal and post-menopausal females. It commonly affects anogenital skin; however, extragenital lesions are not uncommon and occur in isolation or concomitantly with genital lesions. Autoimmunity, genetic factors, and hormonal influences are the main factors suspected in aetiology; however, the exact cause remains unknown. Histopathologic and dermatoscopic features of LSEA have been included in several studies; however, the dermatoscopic rainbow pattern has been rarely reported. Herein, the authors discuss a case of extragenital LSEA with a prominent rainbow pattern under polarised dermatoscopy.

## CASE STUDY

A female in their 50s presented with a 2-year history of multiple itchy lesions on the right inner thigh. Physical examination revealed porcelain white crinkled violaceous patches extending from the right inner thigh to the inguinal fold.

Dermatoscopic examination showed brown follicular plugs, white lines, and a rainbow pattern arranged over white polygonal clods on polarised mode (Dermlite DL4; DermLite, San Juan Capistrano, California, USA [Figure 1]). A punch biopsy of the lesion was performed, and histopathology was consistent with LSEA. In light of clinical symptoms as well as histopathologic and dermatoscopic findings, the patient was diagnosed with extragenital LSEA and started on topical steroid therapy. The lesions resolved completely and no relapse was noted in the following 2 years.

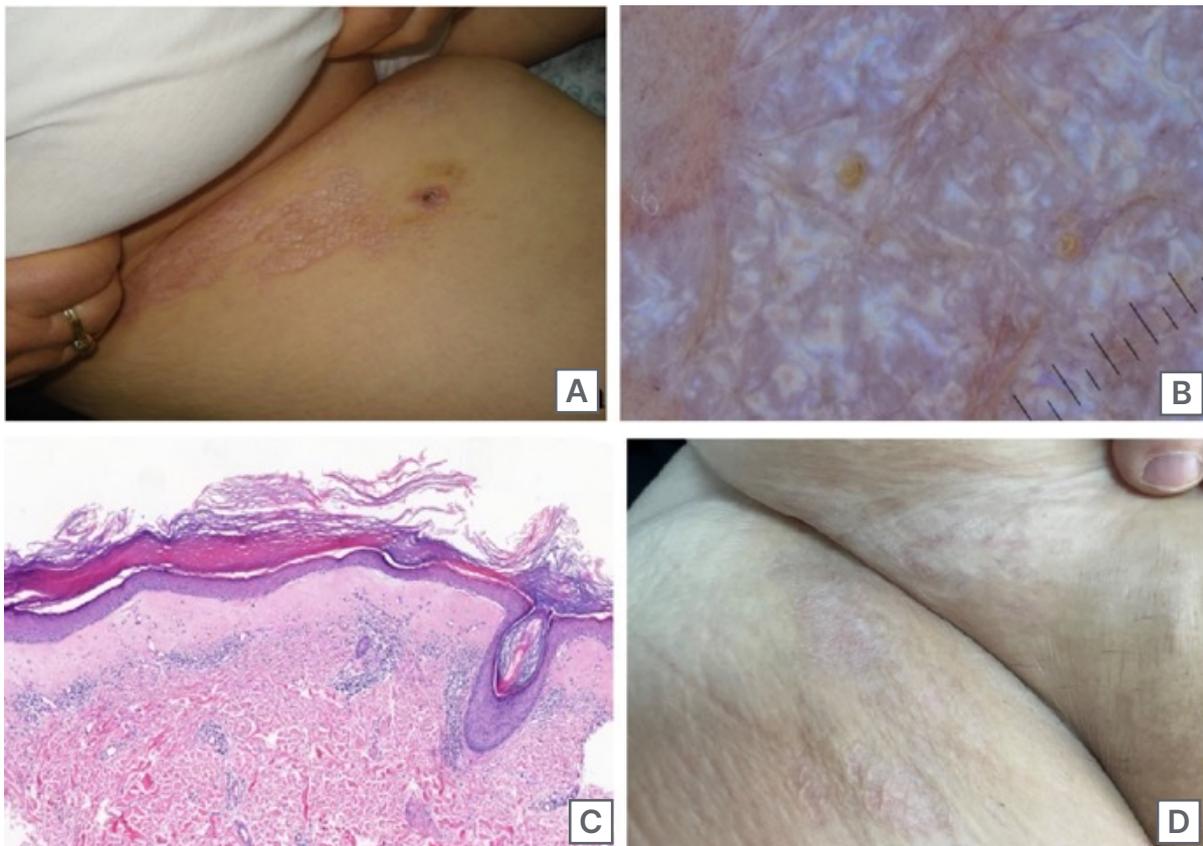
## DISCUSSION

Extragenital LSEA mostly occurs as multiple, oval, bluish-whitish macules or papules located on the neck, shoulders, and upper trunk. Lesions are predominantly asymptomatic. Itching is the most common complaint in symptomatic cases and leads to increased frequency of scratching followed by scarring. Diagnosis is mostly clinical; however, in ambiguous cases, dermatoscopy and histopathology lead to diagnosis. Dermatoscopic features of LSEA are characterised by white structureless areas, follicular plugs, purple dots, shiny white streaks, and peppering.<sup>1</sup> In the authors' patient, a prominent rainbow pattern arranged over white polygonal clods on polarised dermatoscopy was observed. The rainbow pattern has been reported in a few LSEA cases in the literature.<sup>2</sup> In previous studies, this pattern has been associated with a rich vascular network; however, the authors' histological examination did not reveal a vascular-rich pattern. The authors observed epidermal hyperkeratosis, atrophy, and homogeneous dense fibrosis in the papillary dermis and dense lymphocytic infiltrate below the fibrosis. Although the mechanism behind this appearance is not clear, it can be secondary to diffuse and dense homogenous fibrosis in the superficial dermis, giving a sharp and brighter appearance along with increased dermal capillaries and inflammatory cell infiltration.

## CONCLUSION

Extragenital LSEA should be considered in the differential diagnosis in the presence of

Figure 1: Dermatoscopic examination of the patient.



A) Clinical image of lichen sclerosus et atrophicus extending from the left inner thigh to the inguinal fold showing porcelain white crinkled violaceous patches. B) Dermatoscopic findings revealing brown follicular plugs, white lines, and a prominent rainbow pattern arranged over white polygonal cods on polarised mode (Dermlite DL4; DermLite, San Juan Capistrano, California, USA). C) Histologic findings revealing epidermal hyperkeratosis, atrophy, follicular plugs with basal vacuolar degeneration, and homogenous dense fibrosis in the papillary dermis with dense lymphocytic infiltrate beneath the fibrosis (haematoxylin and eosin stain, 7.3x magnification). D) Clinical image of lichen sclerosus et atrophicus showing regression of the lesions except mild atrophy and depigmentation after 2 years of topical steroid use.

dermatoscopic rainbow pattern, shiny white lines, and follicular plaques along with clinical features. ●

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