SUNSHINE and SUNRISE Extension Trial: Week 104 Results

MLR ID: 442373-1
November 2024

NOVARTIS | Reimagining Medicine

Disclaimers

- This material may be used for external presentation **in response to an unsolicited request** for medical information subject to local approval. It should not be left behind
- **For proactive use,** CPO medical and CPO legal approval is required following thorough review and consideration of the content
- This material may include data/information on investigational uses of compounds/drugs that have not yet been approved by regulatory authorities
- Before local implementation, CPOs must ensure compliance with all applicable laws and regulations, local industry codes and local Novartis companies' policies

Hidradenitis suppurativa (HS) Is a chronic, recurrent, inflammatory skin disease[1–3]

HS is characterized by recurrent inflammatory lesions in the apocrine gland-bearing skin of the axillary, inguinal and anogenital regions[2,4]

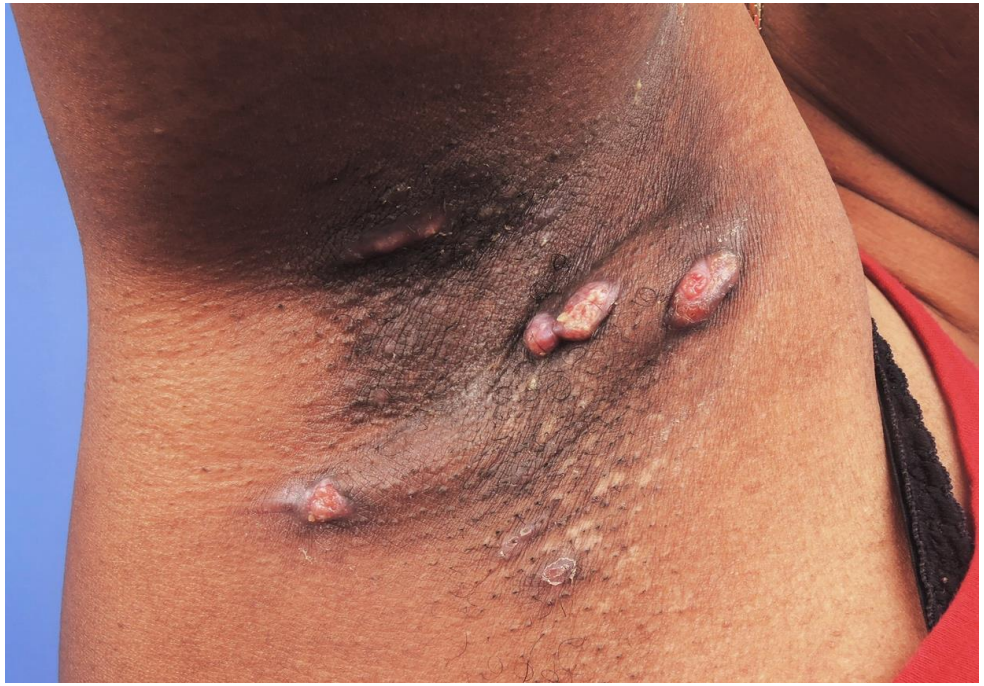


Image provided by Science Source.

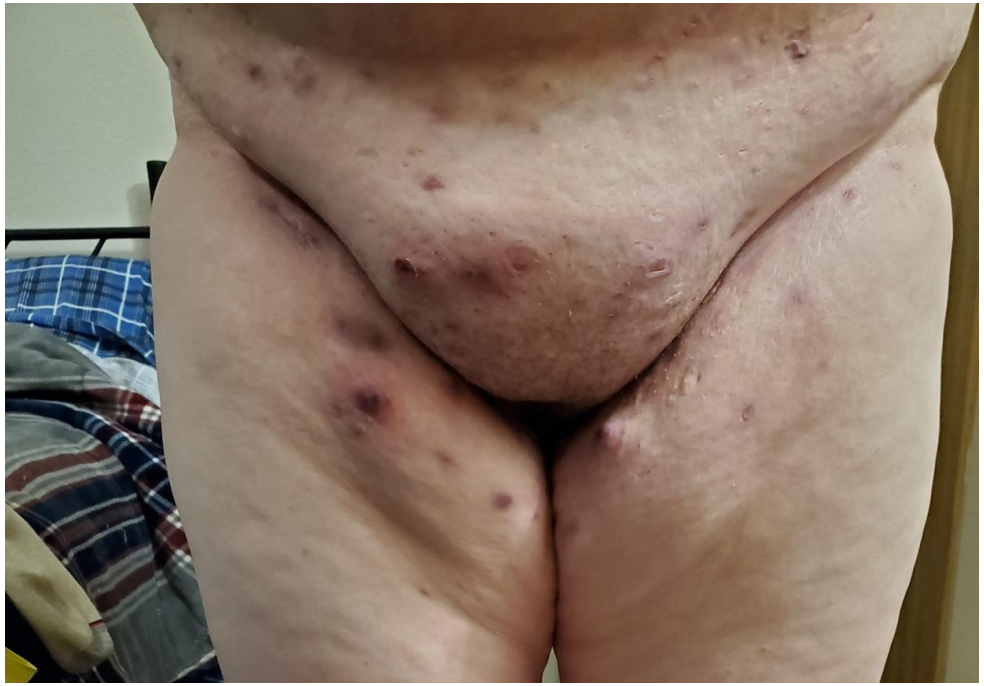


Image provided by Dr Collin Blattner.

1. Jansen I, et al. *J Eur Acad Dermatol Venereol*. 2001;15:532–540; 2. Sabat R, et al. *Nat Rev Dis Primers*. 2020;6(1):18;3. 3. Goldburg SR, et al. *J Am Acad Dermatol*. 2020;82:1045–1058; 4. Zouboulis CC, et al. *J Eur Acad Dermatol Venereol*. 2015;29(4):619–644.
HS, hidradenitis suppurativa.

HS is a heterogenous condition characterized by temporary disease exacerbations[1]

- The natural course of disease in HS is not well defined, although it is understood to include fluctuations in disease severity and temporary disease exacerbations[1,2]
- There are few robust and validated objective clinical outcome measures to assess changes in HS disease severity[3–6]
- Given the natural disease fluctuations in HS,[1–2] and lack of appropriate clinical outcome measures,[3–6] assessing long-term disease activity and maintenance of response to therapies is complex

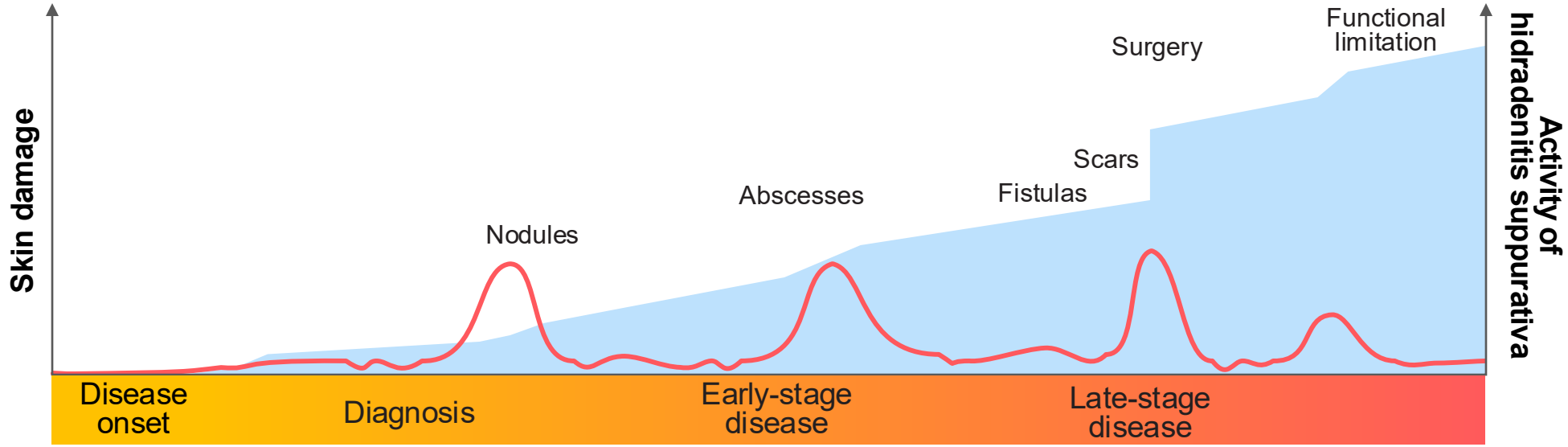


Figure adapted from Martorell A, et al. *Actas Dermosifiliogr*. 2016;107(Suppl 2):32–42.

1. Frew JW, et al. *JAAD Int*. 2020;1(2):208–221. 2. Martorell A, et al. *Actas Dermosifiliogr*. 2016;107 (Suppl 2):32–42.
3. Maghfour J, et al. *JMIR Dermatol*. 2021;4(2):e27869. 4. Mastacouris N, et al. *JAMA Dermatol*. 2023;159(11):1258–1266.
5. Koerts NDK, et al. *Clin Dermatol*. 2023;41(5):601–610. 6. Frew JW, et al. *J Am Acad Dermatol*. 2020;82(5):1150–1157.
HS, hidradenitis suppurativa.

Long-term extension trials of biologics in HS

Strengths of the SUNSHINE and SUNRISE extension trial

- The SUNSHINE and SUNRISE clinical development program represents the largest development plan ever completed to date (2024) in HS, following patients for up to five years[1–6]
- The SUNSHINE and SUNRISE extension trial included the longest RWP of the current long-term extension trials of biologics in HS[2–6]

	Secukinumab[1–4]	Adalimumab[5,6]	Bimekizumab[7]
Study design	RWP (Week 104) and OL	RWP (Week 36) and OL	OL
Primary outcome	Time to LOR through Week 104 in HiSCR-R from core trial	HiSCR* over time up to Week 168	TEAE up to Week 196
Enrolment	700 patients[2]	508 patients	658 patients
Duration	260 weeks	216 weeks	196 weeks

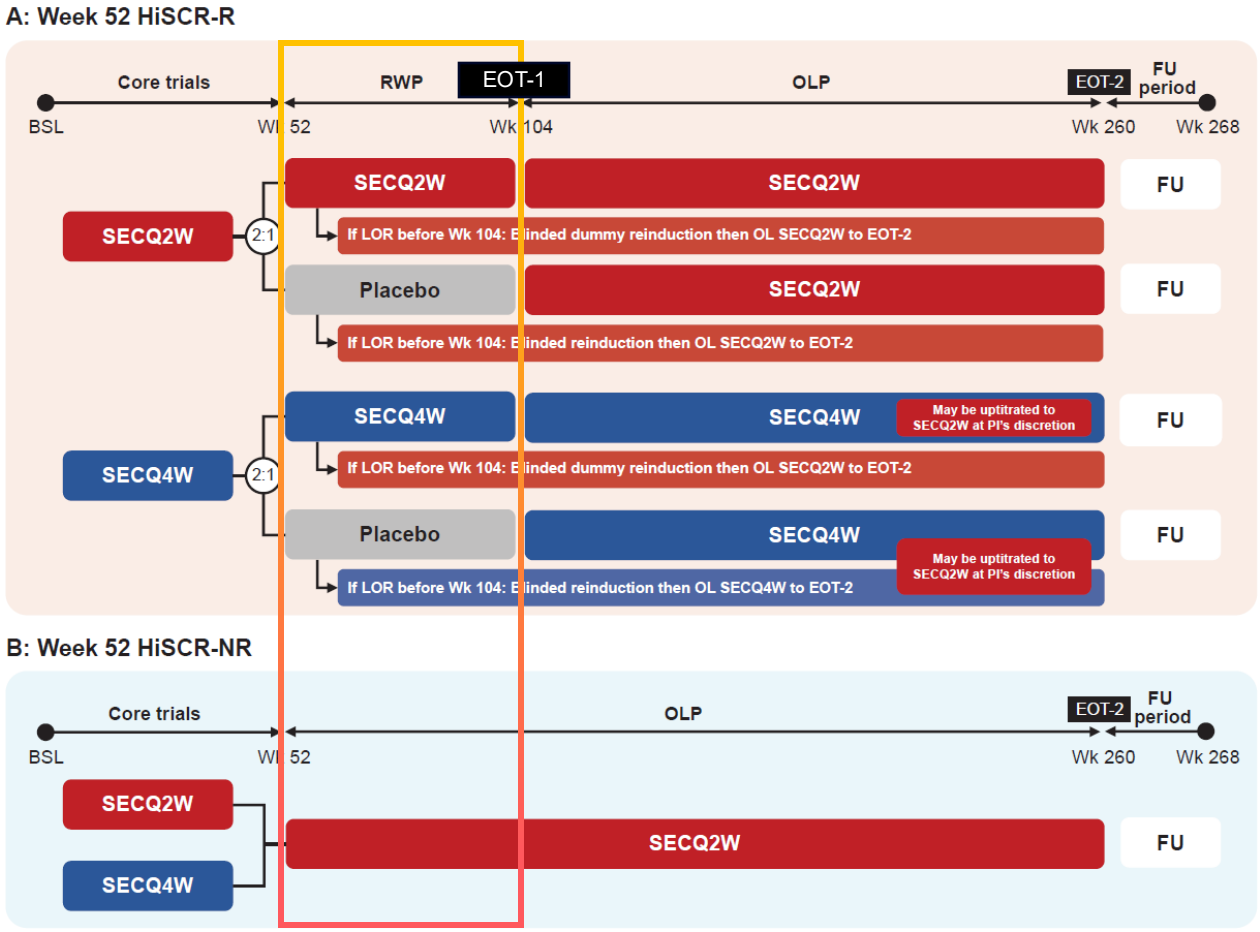
*HiSCR responders and partial responders

1. Kimball AB, et al. *Lancet*. 2023;401(10378):747–761. 2. Data on File.
3. NCT04179175. https://clinicaltrials.gov/study/NCT04179175. Accessed: 03 December 2024.
4. Kimball AB, et al. *Br J Dermatol*. 2024;ljae469. 5. Zouboulis CC, et al. *J Am Acad Dermatol*. 2019;80(1):60–69.e2.
6. NCT01635764. https://clinicaltrials.gov/study/NCT01635764. Accessed: 03 December 2024.
7. NCT04901195. https://clinicaltrials.gov/study/NCT04901195. Accessed: 03 December 2024.

HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; OL, open-label; R, Week 52 HiSCR responders; RWP, randomized withdrawal period; TEAE, treatment-emergent adverse event.

The SUNSHINE and SUNRISE extension trial was a four-year multicenter, double-blind, randomized withdrawal trial

- **The design of the extension trial differs based on the clinical outcome of patients at Week 52 of the core trials**
- HiSCR responders **(A):**
  - RWP from Week 52 (baseline of extension trial) up to EOT-1 (defined as either LOR or Week 104)
  - OLP from EOT-1 to EOT-2 (Week 260)
- HiSCR non-responders **(B):**
  - OLP from Week 52 to EOT-2



Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AN, abscess and inflammatory nodule; BSL, baseline; EOT-1/2, end of treatment period 1/2; FU, follow-up; HiSCR, Hidradenitis Suppurativa Clinical Response; LOR, loss of response; NR, Week 52 HiSCR non-responder; OL, open-label; OLP, open-label period; PI, principal investigator; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; RWP, randomized withdrawal period; SEC, secukinumab 300 mg; Wk, week.

The primary endpoint of the extension trial was time to loss of response

LOR definition

The **definition of LOR** used in this study was **newly defined and non-validated**

LOR was newly defined for this trial and occurred if the following criteria were met:

- A ≥50% increase in AN count at any visit
- An increase of ≥3 in the absolute AN count when compared with the average of the previous 3 visits or the Week 52 visit (whichever was lower)
- If a patient experienced a ≥30% increase in AN count and an increase of ≥2 in the absolute AN count, they were reassessed within 2–4 weeks
    - A further increase of ≥2 in AN count at the reassessment visit was also considered LOR

Primary objective

To demonstrate the efficacy of secukinumab 300 mg in patients with moderate to severe HS who were Week 52 HiSCR responders, with respect to time to LOR through Week 104, versus placebo

- **SECQ2W-R-Q2W** versus **SECQ2W-R-PBO** and **SECQ4W-R-Q4W** versus **SECQ4W-R-PBO**

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AN, abscess and inflammatory nodule; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

Additional endpoints reported in the SUNNY extension trial

Secondary endpoints[1,2]

- **Number of patients with TEAE**

Exploratory endpoints[2]

- **HiSCR over time versus baseline of the core trials**
- **Skin pain response/NRS30 versus baseline of the core trials**
  - Defined as a ≥30% reduction and ≥2-point reduction in skin pain from baseline in the Patient's Global Assessment of Skin Pain–at worst on a continuous NRS
  - Only assessed in patients with a core baseline NRS ≥3
- **DLQI response versus baseline of the core trials**
  - Defined as a ≥5-point decrease in total DLQI score

Supportive post hoc analyses[2]

- **HiSCR**
- **Skin pain response/NRS30**
- **DLQI response**

→ **Analysis of patients on continuous secukinumab from Week 52 to Week 104**
- Included all patients on active treatment, including those in the RWP who met LOR criteria and continued in the trial on OL treatment

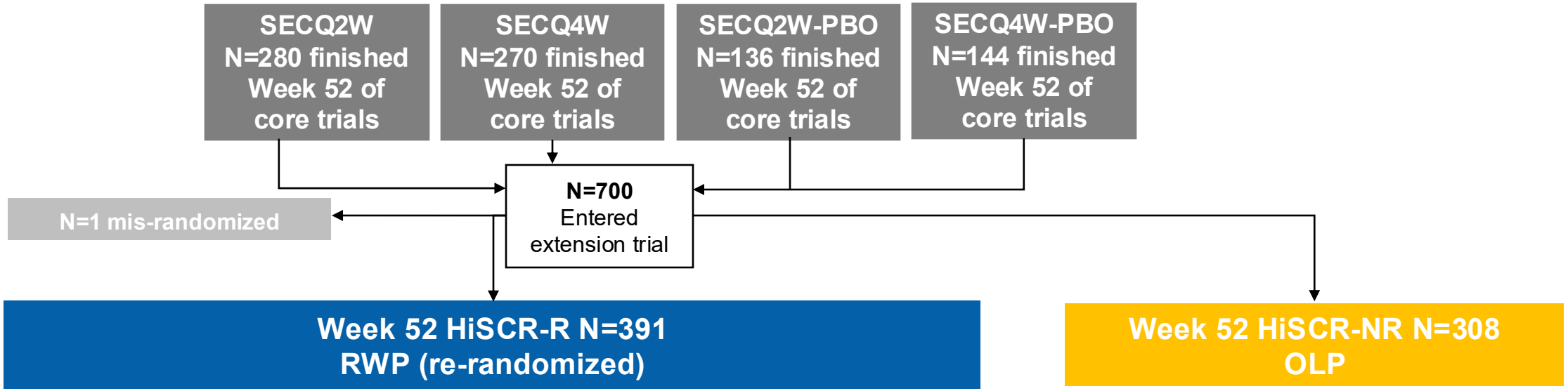
- **Change in AN count and time to regain AN count status after meeting LOR**
  - Assessment of the absolute change in AN count from baseline of core trials to Week 52, time of LOR or Week 104
  - The time to regain AN count status was the time difference between the date of regaining AN count status and the start date (LOR declaration)

1. NCT04179175. https://clinicaltrials.gov/study/NCT04179175. Accessed: 03 December 2024.
2. Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AN, abscess and inflammatory nodule; DLQI, Dermatology Life Quality Index; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; NRS, numerical rating scale; OL, open-label; RWP, randomized withdrawal period; TEAE, treatment-emergent adverse events.

Patient rollover to extension trial from core trials

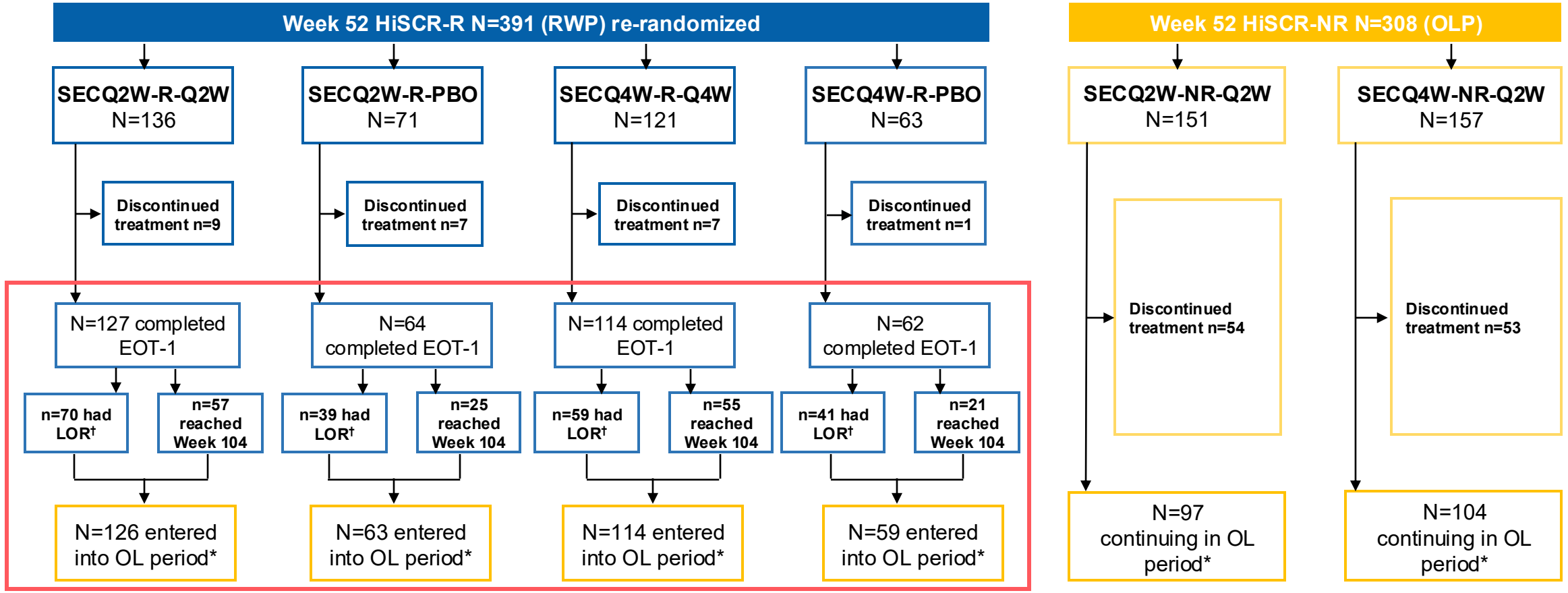
- Of all patients completing Week 52 of the core trials, 84.3% entered the extension trial
  - **55.9%** were **Week 52 HiSCR responders** and entered the RWP
  - **44.0%** were **Week 52 HiSCR non-responders** and directly entered the OLP



Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.
HiSCR, Hidradenitis Suppurativa Clinical Response; N, number of patients evaluated; NR, Week 52 HiSCR non-responder; OLP, open-label period; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; RWP, randomized withdrawal phase; SEC, secukinumab 300 mg.

The majority of patients are still ongoing in the extension trial*

- In the RWP, 94% of patients completed EOT-1, 93% entered into OL treatment and the majority are still ongoing in the trial



*At the time of data cut-off (26-May-2023). †Patients meeting the LOR criteria before Week 104 could enter directly into OL treatment. EOT-1 was applied for HiSCR-R only and was defined as Week 104 or the time at LOR declaration, if before.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AE, adverse event; EOT, end of treatment period 1; FU, follow-up; HiSCR, Hidradenitis Suppurativa Clinical Response; LOR, loss of response; N, number of patients evaluated; n, number of patients with outcome; NR, Week 52 HiSCR non-responder; OL, open-label; OLP, open-label period; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responder; RWP, randomized withdrawal period; SEC, secukinumab 300 mg.

Baseline demographics and disease characteristics

	RWP: Week 52 HiSCR-R				OLP: Week 52 HiSCR-NR	
Characteristic[a]	SECQ2W-R-Q2W (N=136)	SECQ2W-R-PBO (N=71)	SECQ4W-R-Q4W (N=121)	SECQ4W-R-PBO (N=63)	SECQ2W-NR-Q2W (N=151)	SECQ4W-NR-Q2W (N=157)
Age, years, mean ± SD	35.7 ± 11.3	34.8 ± 10.6	35.4 ± 12.6	36.0 ± 11.3	37.3 ± 11.0	37.1 ± 11.1
Sex, Female, n (%)	73 (53.7)	38 (53.5)	64 (52.9)	28 (44.4)	91 (60.3)	38 (49.7)
BMI, kg/m^2, mean ± SD	32.0 ± 7.8	31.6 ± 7.5	31.8 ± 7.7	31.7 ± 7.5	32.0 ± 7.5	32.7 ± 7.3
Smoking status, n (%)						
Current	79 (58.1)	35 (49.3)	52 (43.0)	39 (61.9)	86 (57.0)	88 (56.1)
Former	15 (11.0)	12 (16.9)	20 (16.5)	6 (9.5)	24 (15.9)	29 (18.5)
Hurley stage, n (%)						
II	78 (57.4)	41 (57.7)	78 (64.5)	37 (58.7)	80 (53.0)	86 (54.8)
III	51 (37.5)	29 (40.8)	35 (28.9)	23 (36.5)	65 (43.0)	66 (42.0)
Time since HS diagnosis,[b] years, mean ± SD	8.7 ± 7.2	7.2±5.5	8.0 ± 7.4	7.2 ± 6.4	7.6 ± 6.1	7.6 ± 6.8
Draining tunnel count, mean ± SD	2.4 ± 3.1	2.8 ± 3.6	2.0 ± 2.8	3.1 ± 3.9	3.0 ± 3.8	3.0 ± 3.2
NRS/skin pain, mean ± SD	5.0 ± 2.2 (N=127)	5.6 ± 2.6 (N=65)	5.0 ± 2.6 (N=109)	4.8 ± 2.6 (N=58)	5.6 ± 2.5 (N=141)	5.2 ± 2.5 (N=145)
Previous exposure to systemic biologics, n (%)	33 (24.3)	13 (18.3)	25 (20.7)	14 (22.2)	30 (19.9)	37 (23.6)

[a]All baseline demographics and disease characteristics are from baseline of the core trials. [b]The date of first diagnosis collected in the core trials is evaluated with respect to the extension trial informed consent signature.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

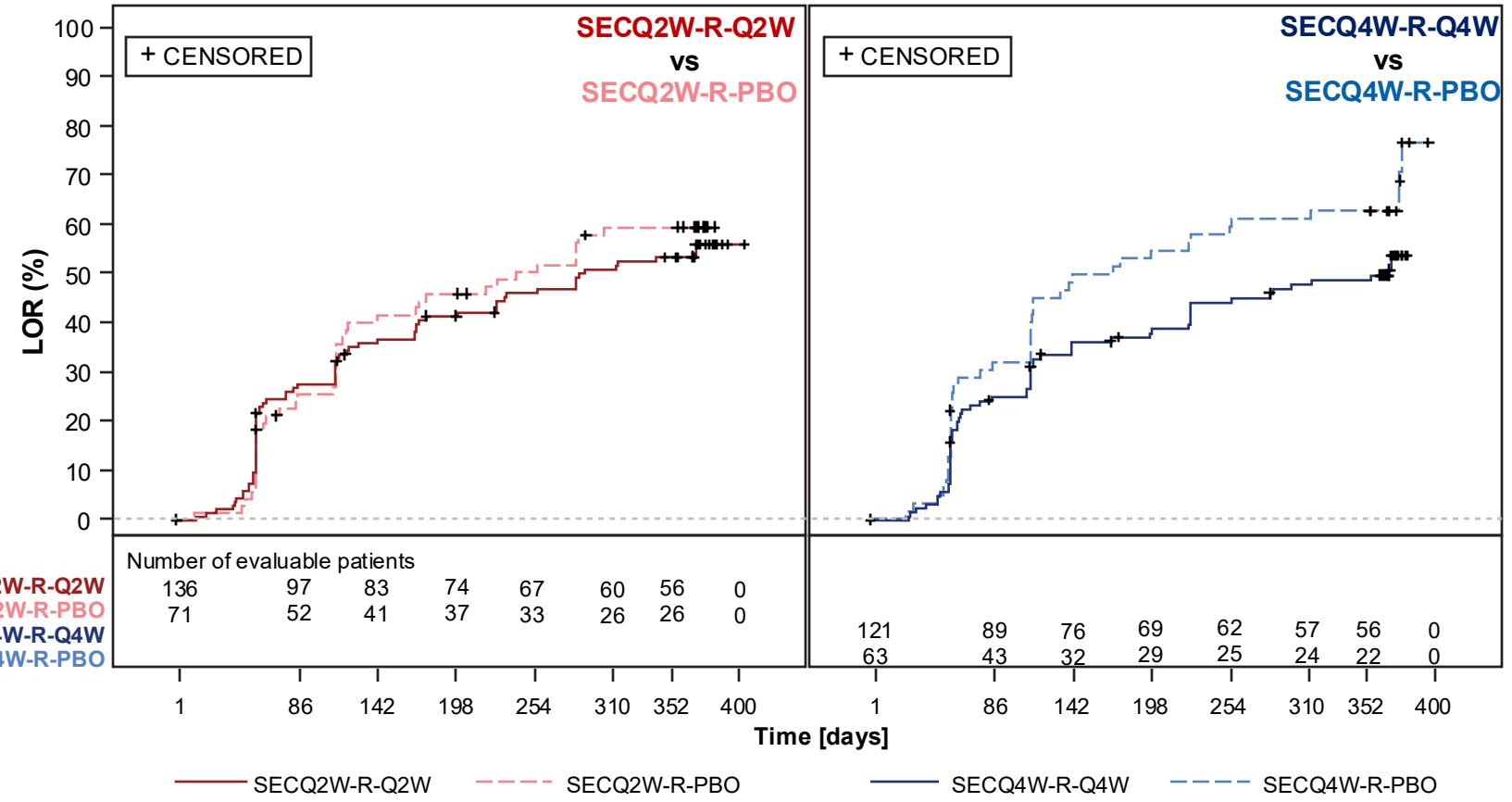
BMI, body mass index; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; n, number of patients with event; N, number of patients evaluated; NR, Week 52 HiSCR non-responder; NRS, numerical rating scale; OLP, open-label period; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; RWP, randomized withdrawal period; SD, standard deviation; SEC, secukinumab 300 mg.

The primary endpoint of the extension trial, time to LOR in the randomized withdrawal phase, was not met for either of the secukinumab dosing regimens

Primary endpoint missed

- The estimated risk reduction in LOR for **SECQ2W-R-Q2W** versus **SECQ2W-R-PBO** was **13%*** (one-sided *p*=0.250)
- The estimated risk reduction in LOR for **SECQ4W-R-Q4W** versus **SECQ4W-R-PBO** was **30%†** (one-sided *p*=0.044)

Cumulative incidence rate of LOR in Week 52 HiSCR-R



*HR: 0.87, 95% CI: 0.59–1.29. †HR: 0.70, 95% CI: 0.47–1.05. Figures show 1 minus the Kaplan-Meier estimates. Patients who did not experience LOR through Week 104, those with ≥2 consecutive assessments missing, and those who permanently discontinued the trial (except for discontinuation due to lack of efficacy or AE) were censored at the last recorded visit.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AE, adverse event; CI, confidence interval; HR, hazard ratio; HS, hidradenitis suppurativa; HiSCR, Hidradenitis Suppurativa Clinical Response; LOR, loss of response; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

The median time to LOR was numerically longer for patients on continuous secukinumab (both dosing regimens) versus placebo

The difference in the median time to LOR was:

- **44 days** later for **SECQ2W-R-Q2W**, versus SECQ2W-R-PBO
- **194 days** later for **SECQ4W-R-Q4W**, versus **SECQ4W-R-PBO**

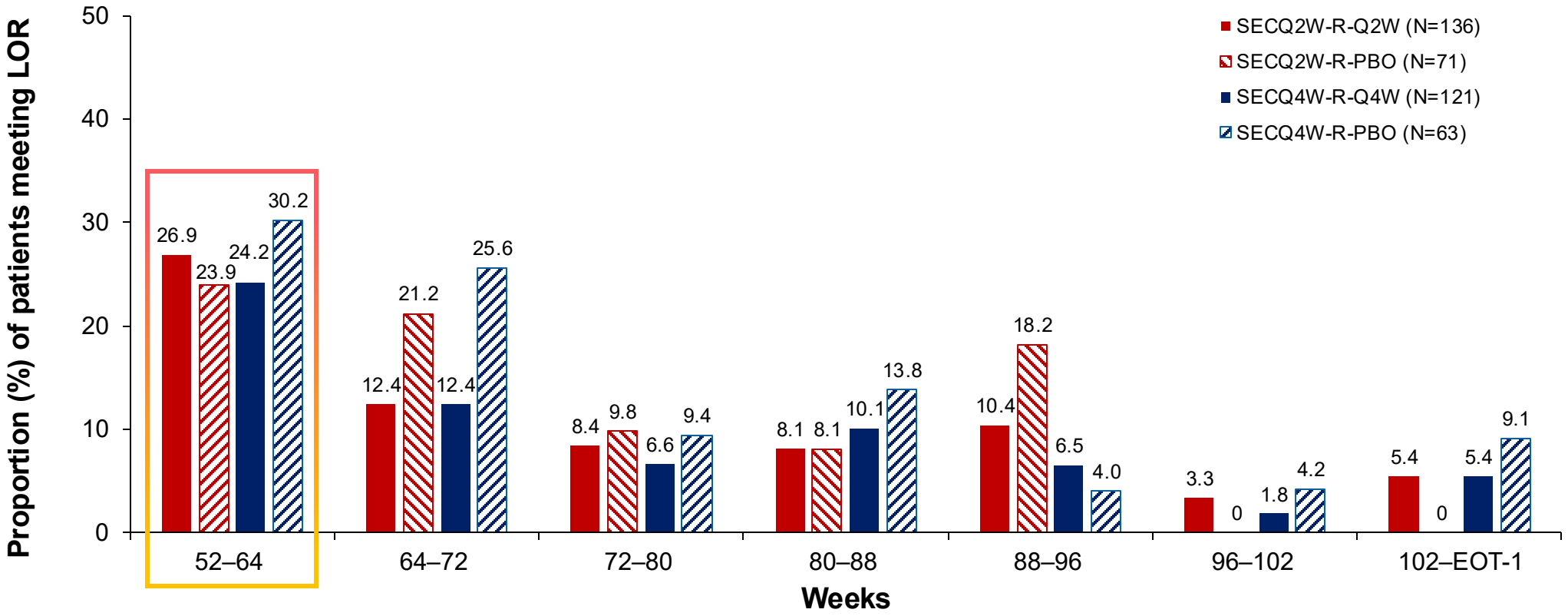
				KM estimates		HR estimates		
	N	n	n/N (%)	Median (days)	95% CI	Estimate	95% CI	p value
SECQ2W-R-Q2W	136	73	73/136 (53.7)	**283**	**(176, -)**	0.87	(0.59, 1.29)	0.250
SECQ2W-R-PBO	71	41	41/71 (57.7)	**239**	**(120, -)**			
SECQ4W-R-Q4W	121	60	60/121 (49.6)	**365**	**(225, -)**	0.70	(0.47, 1.05)	0.044
SECQ4W-R-PBO	63	41	41/63 (65.1)	**171**	**(113, 337)**			

Stratified Cox proportional hazards regression models, with treatment arm as an explanatory variable and stratified by regionand body weight category (<90 kg, ≥90 kg), were used to estimate treatment effects (in terms of HR and the associated 95% CIs). A onesided alpha of 0.0125 was used for statistical testing for each comparison of SEC with the corresponding PBO.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

CI, confidence interval; HiSCR, Hidradenitis Suppurativa Clinical Response; HR, hazard ratio;HS, hidradenitis suppurativa; KM, Kaplan-Meier; LOR, loss of response; n, number of patients with event; N, number of patients evaluated; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

Exploratory analysis observed that ~25% of patients who met the LOR criteria did so within the first 12 weeks, indicating the high sensitivity of the LOR criteria



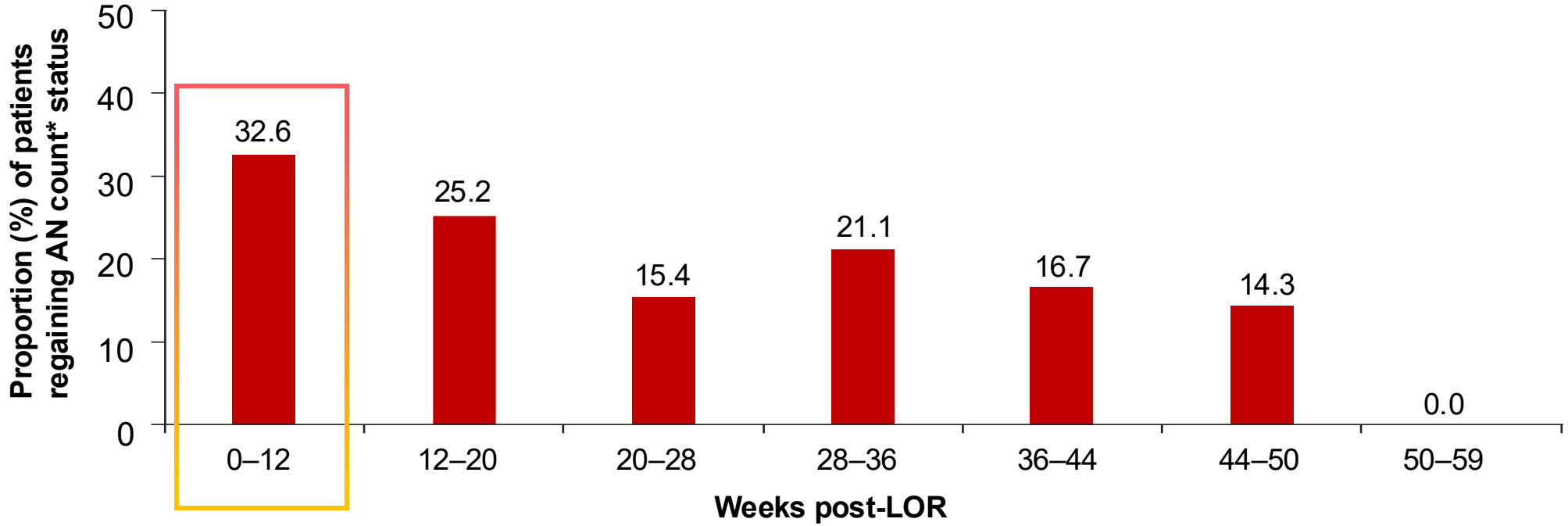
The proportions are computed by dividing the number of LOR events recorded within the specific time frame by the number of patients at risk at the beginning of the specific time frame. The assessment is based on the primaryestimand. Weeks 102–EOT-1 refer to events (LOR) occurring within Days 352–399 of extension (data exists beyond Week 104 due to late EOT-1 visit).

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

LOR, loss of response; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

Post hoc analysis observed that 33% of patients across all treatment arms who met LOR criteria had regained their AN count status within 12 weeks, reflecting the natural disease fluctuations in HS

- Among all patients meeting LOR (N=215), 187 were eligible for post hoc evaluation of time to regain AN count status
  - **64.7%** regained AN count status* by Week 104, relative to the reference used to declare LOR (i.e. Week 52 or average of the previous three visits, whichever was lower)

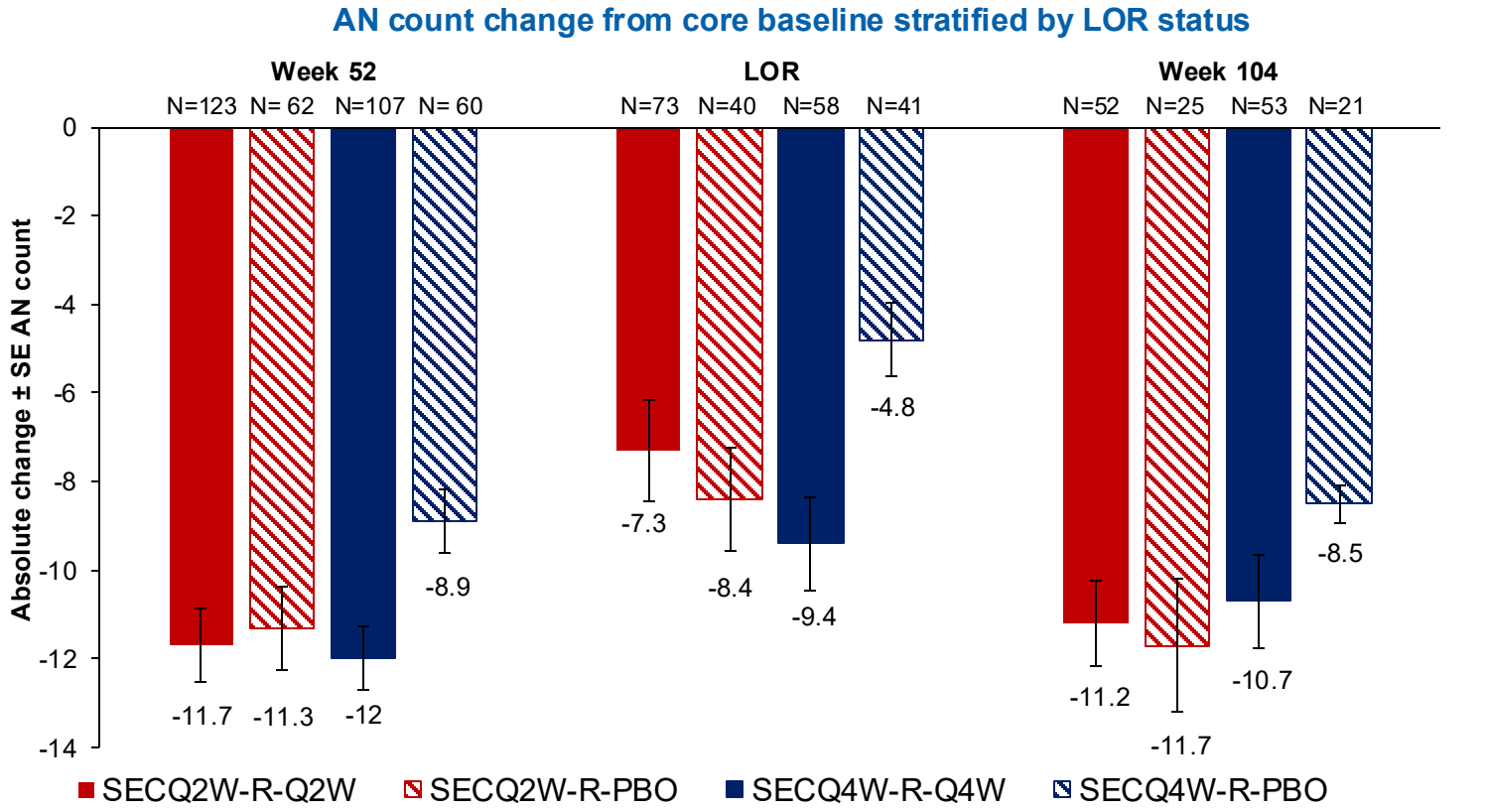


*Timepoint where AN count was less than or equal to the reference AN count used for LOR declaration.
The proportions are computed by dividing the number of regain events recorded within the specific time frame by the number of patients at risk at the beginning of the specific time frame. Weeks 50–EOT-1 refer to events (AN count regain) occurring within Days 352–399 of extension after LOR declaration (data exists beyond Week 104 due to late EOT-1 visit).
Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.
AN, abscess and inflammatory nodule; EOT-1, end of treatment period 1; N, number of patients with available data at each timepoint; LOR, loss of response.

Post hoc analysis showed that patients meeting LOR still reported meaningful reductions in absolute AN count versus baseline of the core trials, indicating that patients did not revert to baseline disease severity levels

Change in absolute AN count from baseline of core trials to time of LOR in Week 52 HiSCR responders:

- **SECQ2W-R-Q2W, –7.3 ± 1.14**
- **SECQ2W-R-PBO, –8.4 ± 1.15**
- **SECQ4W-R-Q4W, –9.4 ± 1.06**
- **SECQ4W-R-PBO, –4.8 ± 0.84**



NOVARTIS | Reimagining Medicine

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.
AN, abscess and inflammatory nodule; HiSCR, Hidradenitis Suppurativa Clinical Response; LOR, loss of response; N, number of patients with available data at each timepoint; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SE, standard error; SEC, secukinumab 300 mg.

Limitations of the LOR criteria

The SUNNY extension trial presents the first time this newly defined and non-validated LOR criteria were used; results suggest the criteria were too sensitive in the context of the natural disease fluctuations in HS

Regression to the mean phenomenon

- The reference visit for detecting LOR was patient-specific and not fixed in time
- It was at a timepoint where patients were managing symptoms well, with a low AN count versus their core trial baseline values, making it easy to trigger the LOR criteria even with a small AN count increase

Time-to-event endpoint unsuitable in HS

- Time-to-event analysis may not be clinically meaningful for a chronic disease with an inherent waxing and waning clinical course
- HS disease activity naturally fluctuates,[1] making the patient-specific nature of the LOR definition prone to detecting transient increases in disease activity

High placebo effect in HS

- Extension trial placebo arms did not represent a true placebo group*
- Fluctuations in HS disease activity contributes to the higher placebo response rates observed across clinical trials in patients with HS[1–3]
- LOR analyses are particularly susceptible to interference from higher placebo response rates, inherent to HS[2,3]

*Patients originally assigned to placebo at baseline of the extension trial had received secukinumab between Weeks 16 and 52 of the core trials and entered the extension trial without any washout or treatment free period. Thus, there may have been some residual effects of secukinumab in these treatment arms at the beginning of the randomized withdrawal period.

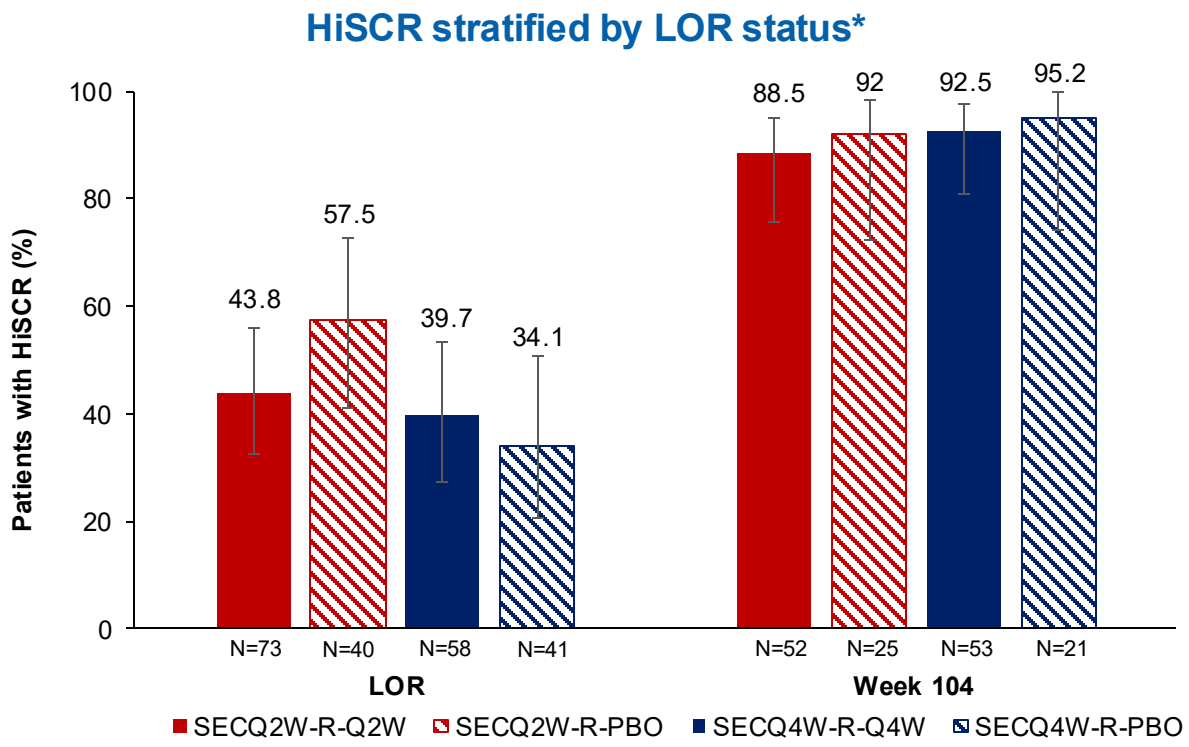
Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.
1. Frew JW, et al. *JAAD Int.* 2020;1(2):208–221. 2. Kimball AB et al. *J Am Acad Dermatol.* 2020; 83: e431. 3. Amir Ali A, et al. *J Am Acad Dermatol.* 2020;82:45–53.

AN, abscess and inflammatory nodule; HS, hidradenitis suppurativa; LOR, loss of response.

The definition of LOR is not the same as the definition of loss of HiSCR (1/2)

- An exploratory analysis observed that **~40%** of the total patients treated with secukinumab 300 mg (either Q2W or Q4W) maintained HiSCR at the time of meeting LOR criteria

- **SECQ2W-R-Q2W**:
  - **43.8%** of patients were still maintaining HiSCR at the time of meeting LOR
- **SECQ4W-R-Q4W**:
  - **39.7%** of patients were still maintaining HiSCR at the time of meeting LOR
- Approximately **90%** of patients who did not meet the LOR criteria were achieving HiSCR at Week 104



*If a patient met LOR at the Week 104 visit, they were counted in both LOR and Week 104 groups.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; n, number of patients with event; N, number of patients evaluated; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

The definition of LOR is not the same as the definition of loss of HiSCR (2/2)

Example of a patient's lesion count, HiSCR and LOR status through the core and extension trial:

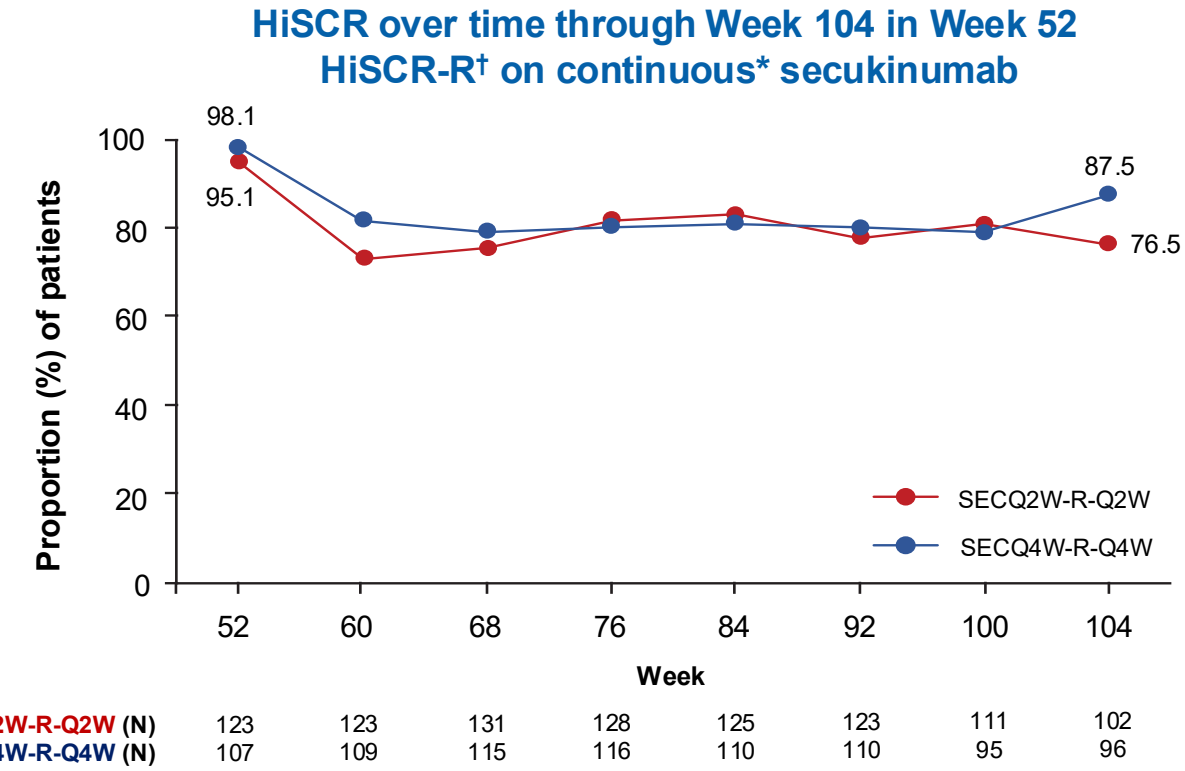
- Patient retained HiSCR status when meeting LOR

	Core Trial				Extension Study
	Baseline	**Week 44**	**Week 48**	**Week 52**	**Week 60**
AN count	14	2	2	2	5
Draining tunnels	0	0	0	0	0
Abscesses	0	0	0	0	0
HiSCR	-	YES	YES	YES	YES
LOR	-	-	-	-	YES

Data on file.
AN, abscess and inflammatory nodule; HiSCR, Hidradenitis Suppurativa Clinical Response; LOR, loss of response.

Post hoc analysis suggested that HiSCR was sustained through Week 104 in patients receiving continuous* secukinumab from Week 52 to Week 104

- **SECQ2W-R-Q2W**:
  - **95.1%** at Week 52† versus **76.5%** at Week 104
- **SECQ4W-R-Q4W**:
  - **98.1%** at Week 52† versus **87.5%** at Week 104
  - This included those who up-titrated to OL SECQ2W upon meeting LOR



*Visits across both randomized withdrawal and open-label periods were considered. †HiSCR responders at Week 52 of core trials did not equal 100% given the difference in definitions between identification of HiSCR responders at Week 52 and calculation of the HiSCR response over time.

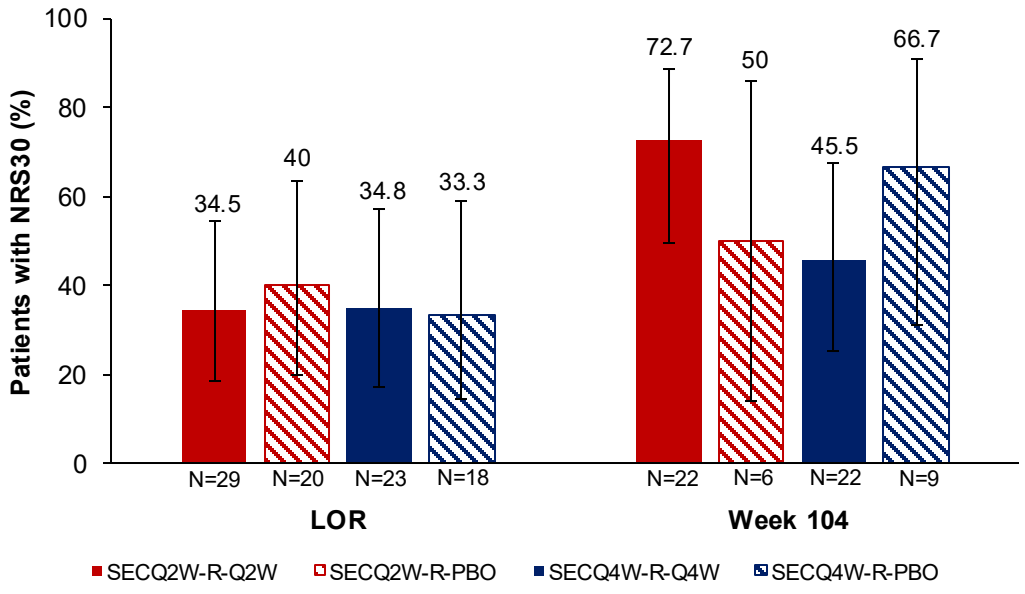
Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

HiSCR, Hidradenitis Suppurativa Clinical Response; OL, open-label; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

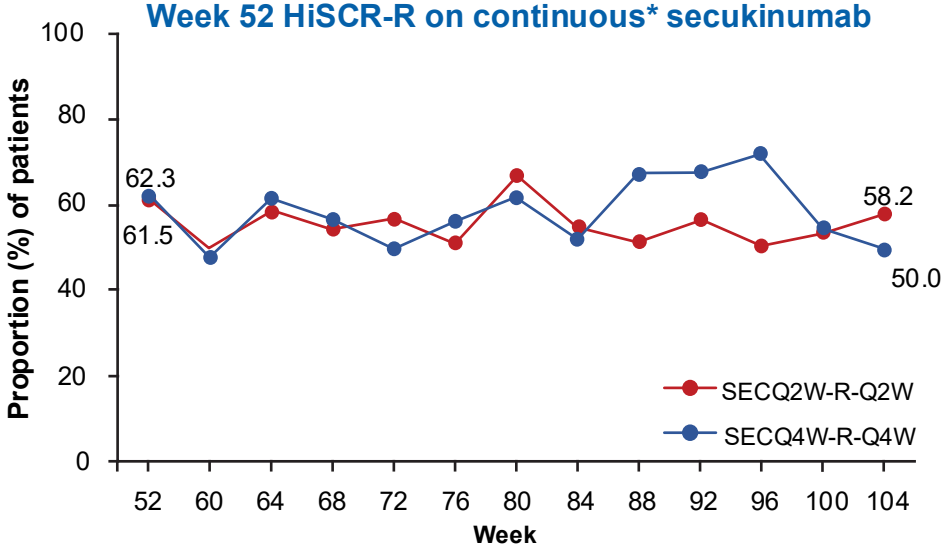
Exploratory and post hoc analysis suggested that secukinumab had a positive effect on skin pain through 104 weeks

- An exploratory analysis observed that ~**34%** of the total patients treated with secukinumab 300 mg (either Q2W or Q4W) maintained NRS30 response at the time of meeting LOR criteria **(A)**
- A post hoc analysis suggested NRS30 was sustained through Week 104 in patients receiving continuous* secukinumab from Week 52 to Week 104 **(B)**

(A) **NRS30 stratified by LOR status†**



(B) **NRS30 over time through Week 104 in Week 52 HiSCR-R on continuous* secukinumab**



SECQ2W-R-Q2W (N)	96	66	70	62	58	66	67	60	60	65	53	65	55
SECQ4W-R-Q4W (N)	77	54	42	51	42	46	45	44	40	50	36	42	44

*Visits across both randomized withdrawal and open-label periods were considered. The SECQ4W-R-Q4W arm included those who up-titrated to open-label SECQ2W upon meeting LOR. †If a patient met LOR at the Week 104 visit, they were counted in both LOR and Week 104 groups.

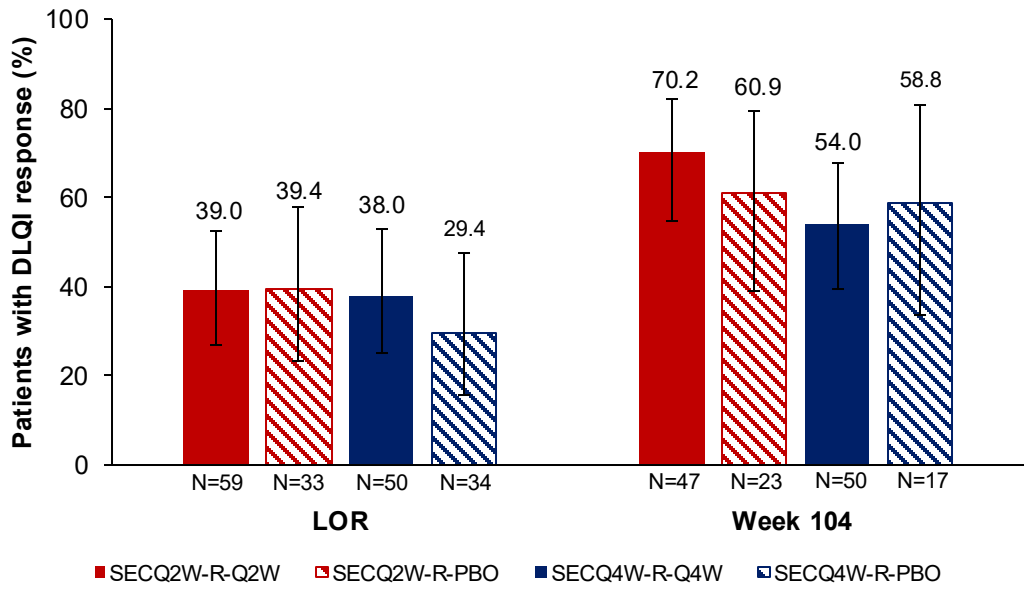
Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; n, number of patients with event; N, number of patients evaluated; NRS, numerical rating scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

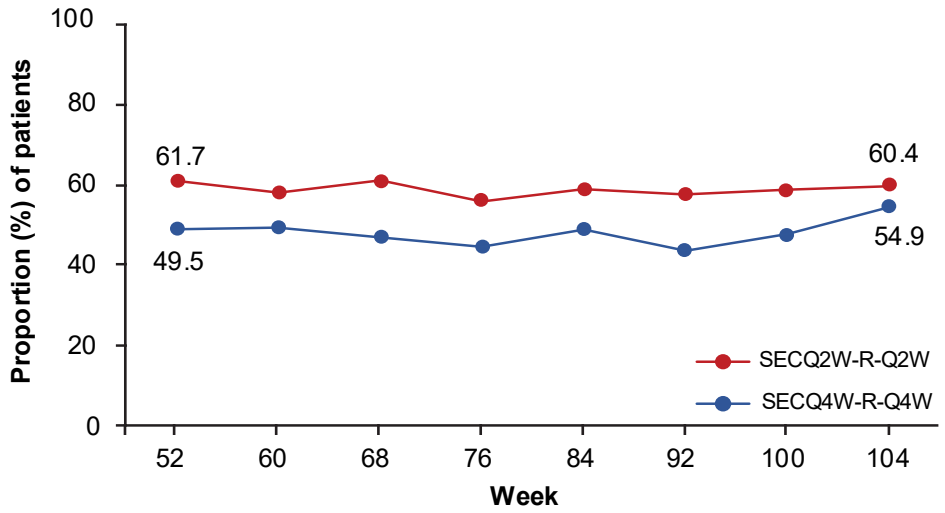
Post hoc analysis suggested that secukinumab had a positive effect on quality of life through 104 weeks

- A post hoc analysis observed that **~40%** of the total patients treated with secukinumab 300 mg (either Q2W or Q4W) maintained DLQI response at the time of meeting LOR criteria **(A)**
- A post hoc analysis suggested **>50%** of patients reported a DLQI response at Week 104 in patients receiving continuous* secukinumab from Week 52 to Week 104 **(B)**

(A) **DLQI response stratified by LOR status†**



(B) **DLQI response over time through Week 52 HiSCR-R on continuous* secukinumab**



SECQ2W-R-Q2W (N)	107	102	112	113	108	108	98	91
SECQ4W-R-Q4W (N)	93	98	101	104	99	99	87	91

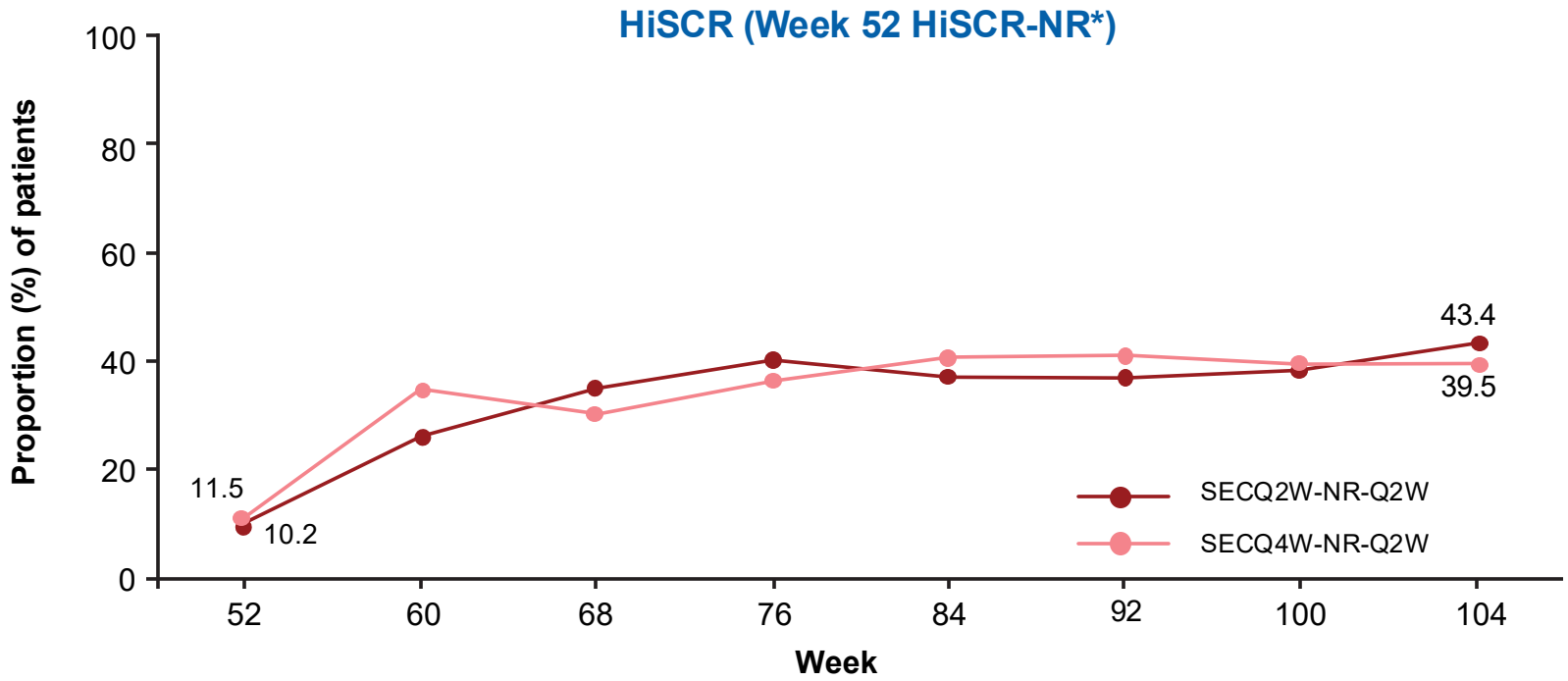
*Visits across both randomized withdrawal and open-label periods were considered. The SECQ4W-R-Q4W arm included those who up-titrated to open-label SECQ2W upon meeting LOR. †If a patient met LOR at the Week 104 visit, they were counted in both LOR and Week 104 groups.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

DLQI, Dermatology Life Quality Index; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; n, number of patients with event; N, number of patients evaluated; Q2W, every 2 weeks; Q4W, every 4 weeks; ; R, Week 52 HiSCR responders; SEC, secukinumab 300 mg.

Patients who were HiSCR non-responders at Week 52 of the core trials received clinical benefits between Weeks 52 and 104 (1/2)

- An exploratory analysis observed that **~40%** of patients continuing SECQ2W or up-titrating from Q4W to Q2W achieved HiSCR by Week 104



SECQ2W-NR-Q2W (N)	128	134	137	134	129	122	112	113
SECQ4W-NR-Q2W (N)	139	141	142	135	133	127	109	114

*Week 52 HiSCR-NR did not equal 0% at the first timepoint, given the difference in definitions for identification of HiSCR at Week 52 and over time.

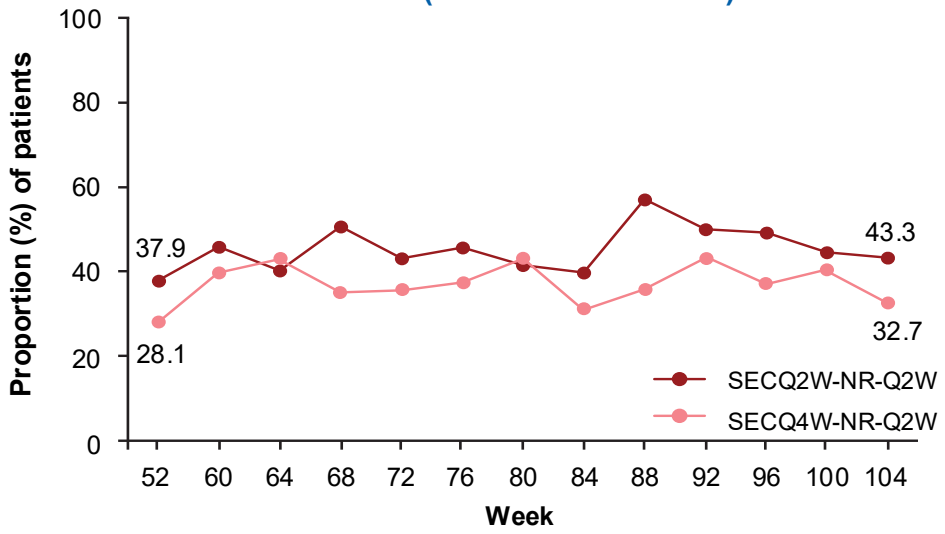
Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; NR, Week 52 HiSCR non-responder; NRS, numeric rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; SEC, secukinumab 300 mg.

Patients who were HiSCR non-responders at Week 52 of the core trials received clinical benefits between Weeks 52 and 104 (2/2)

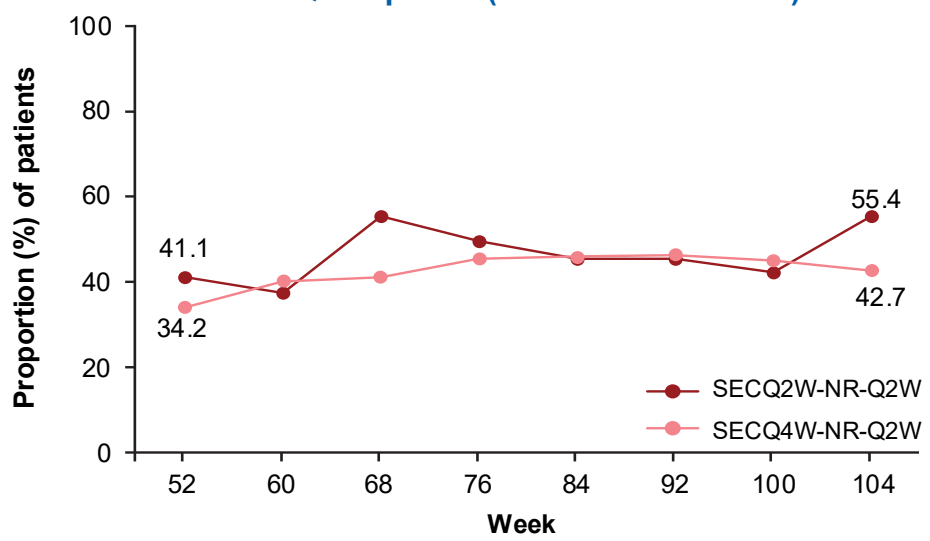
- An exploratory analysis observed that skin pain/NRS30 reductions and improved DLQI responses at week 52 were sustained through Week 104 in both secukinumab dosing regimens, and suggested a trend towards improvement

NRS30 (Week 52 HiSCR-NR)



SECQ2W-NR-Q2W (N)	103	74	72	75	72	79	65	73	56	62	59	65	67
SECQ4W-NR-Q2W (N)	96	58	56	57	56	59	58	61	45	51	46	52	49

DLQI response (Week 52 HiSCR-NR)



SECQ2W-NR-Q2W (N)	107	107	112	113	108	99	97	101
SECQ4W-NR-Q2W (N)	120	120	121	119	116	112	100	103

For skin pain response/NRS30 analyses, only patients with an NRS≥3 at baseline of the core trials were included.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

DLQI, Dermatology Life Quality Index; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; NR, Week 52 HiSCR non-responder; NRS, numeric rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; SEC, secukinumab 300 mg.

Safety outcomes: Summary

Randomized withdrawal period[1]

- AE reporting was balanced between treatment arms with no trend observed between treatment arms or secukinumab dosing regimens
- No deaths were reported, and the rate of discontinuation due to AEs and SAEs was low
- The frequency of safety topics of interest was similar across treatment arms; no IBD cases were reported

Entire study period*[1,2]

- Based on EAIR, no differences in rate of AEs were observed between secukinumab dosing regimens in the entire study period (with the exception of fungal infectious disorders)
  - More patients treated with SECQ2W reported fungal infectious disorders, a finding similar to that reported in the core trials
- There were no deaths reported in the extension trial up to the data cut-off date*. The rate of discontinuation due to AEs and SAEs was low
- In the entire study period, six new-onset cases of IBD were recorded (0.9% [EAIR 0.5/100 PTY])

*Entire study period is Week 52 up to the data cut-off date (26-May-2023).

1. Kimball AB, et al. *Br J Dermatol.* 2024;ljae469. 2. Kimball AB, et al. *Lancet*. 2023;401(10378):747–761.

AE, adverse event; EAIR, exposure adjusted incidence rate; HiSCR, Hidradenitis Suppurativa Clinical Response; IBD, inflammatory bowel disease; PBO, placebo; PTY, patient-treatment-years; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; SAE, serious adverse event; SEC, secukinumab 300 mg.

AE reporting was balanced between treatment arms in the RWP with no trend observed between treatment arms or secukinumab dosing regimens

	Week 52 HiSCR responders (RWP)			
	SECQ2W-R-Q2W (N=137)*	SECQ2W-R-PBO (N=70)	SECQ4W-R-Q4W (N=121)	SECQ4W-R-PBO (N=63)
Any AE(s), n (%), [EAIR/100 PTY]	78 (56.9) [154.1]	41 (58.6) [160.7]	71 (58.7) [143.9]	31 (49.2) [130.8]
Most common treatment emergent AEs by PT (≥5%), n (%), [EAIR/100 PTY]				
COVID-19†	11 (8.0) [13.1]	7 (10.0) [17.3]	11 (9.1) [14.7]	7 (11.1) [20.3]
Hidradenitis	7 (5.1) [8.0]	4 (5.7) [9.7]	5 (4.1) [6.4]	3 (4.8) [8.3]
Nasopharyngitis	5 (3.6) [5.8]	2 (2.9) [4.7]	6 (5.0) [7.6]	2 (3.2) [5.6]
Eczema	3 (2.2) [3.4]	4 (5.7) [9.4]	3 (2.5) [3.9]	1 (1.6) [2.7]
Patients with serious or other significant events, n (%)				
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SAE	2 (1.5)	4 (5.7)	5 (4.1)	5 (7.9)
Discontinued due to AE	2 (1.5)	1 (1.4)	0 (0.0)	1 (1.6)

*A serious GCP violation in the core trial was reported for one patient in this arm, and they were subsequently excluded from the full analysis set/efficacy analyses but were still included in the safety analyses. †The trial was conducted during the COVID-19 pandemic.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AE, adverse event; COVID-19, coronavirus disease 2019; EAIR, exposure adjusted incidence rate; GCP, Good Clinical Practice; HiSCR, Hidradenitis Suppurativa Clinical Response; n, number of patients with event; N, number of patients evaluable; PBO, placebo; PT, preferred term; PTY, patient-treatment years; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; RWP, randomized withdrawal period; SAE, serious adverse event; SEC, secukinumab 300 mg; SMQ, standardized MedDRA query; SOC, system organ class.

The frequency of safety topics of interest was similar across treatment arms in the RWP; no IBD cases were reported

	Week 52 HiSCR responders (RWP)			
	SECQ2W-R-Q2W (N=137)*	SECQ2W-R-PBO (N=70)	SECQ4W-R-Q4W (N=121)	SECQ4W-R-PBO (N=63)
Safety topics of interest, n (%), [EAIR/100 PTY]				
Infections and infestations (SOC)	47 (34.3) [69.7]	20 (28.6) [57.7]	40 (33.1) [61.4]	21 (33.3) [74.9]
Upper respiratory tract infections (HLT)	10 (7.3) [11.9]	3 (4.3) [7.1]	13 (10.7) [17.1]	5 (7.9) [14.5]
Fungal infectious disorders (HLGT)	6 (4.4) [7.0]	4 (5.7) [9.5]	2 (1.7) [2.5]	2 (3.2) [5.4]
Candida infections (HLT)	1 (0.7) [1.1]	3 (4.3) [7.0]	1 (0.8) [1.3]	1 (1.6) [2.7]
Hypersensitivity (SMQ) (narrow)	8 (5.8) [9.3]	6 (8.6) [14.4]	5 (4.1) [6.5]	5 (7.9) [14.0]
Malignant or unspecified tumors (SMQ)	0 (0.0) [0.0]	1 (1.4) [2.3]	0 (0.0) [0.0]	0 (0.0) [0.0]
MACE (NMQ)	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]
IBD (CMQ)	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]
Colitis ulcerative (PT)	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]
Crohn's disease (PT)	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]
IBD (PT)	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]	0 (0.0) [0.0]

*A serious GCP violation in the core trial was reported for one patient in this arm, and they were subsequently excluded from the full analysis set/efficacy analyses but were still included in the safety analyses.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AE, adverse event; CMQ, customized medDRA query; EAIR, exposure adjusted incidence rate; GCP, good clinical practice; HiSCR, Hidradenitis Suppurativa Clinical Response; HLGT, high-level group terms; HLT, high-level term; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular event; n, number of patients with event; N, number of patients evaluable; NMQ, Novartis MedDRA query; PBO, placebo; PT, preferred term; PTY, patient-treatment years; Q2W, every 2 weeks; Q4W, every 4 weeks; R, Week 52 HiSCR responders; RWP, randomized withdrawal period; SEC, secukinumab 300 mg; SMQ, standardized MedDRA query; SOC, system organ class.

Based on EAIR, no differences in rate of AEs was observed between secukinumab dosing regimens in the entire study period*

	Entire trial period		
	Any SECQ2W (N=637)†	Any SECQ4W (N=180)	Any SEC (N=687)*
Any AE(s), n (%), [EAIR/100 PTY]	486 (76.3) [129.3]	102 (56.7) [138.4]	537 (78.2) [126.9]
Most common treatment-emergent AEs by PT (≥5%), n (%), [EAIR/100 PTY]			
COVID-19‡	129 (20.3) [14.1]	19 (10.6) [14.1]	148 (21.5) [14.2]
Hidradenitis	87 (13.7) [9.2]	7 (3.9) [4.8]	92 (13.4) [8.5]
Nasopharyngitis	55 (8.6) [5.5]	8 (4.4) [5.5]	63 (9.2) [5.5]
Headache	32 (5.0) [3.2]	9 (5.0) [6.2]	41 (6.0) [3.6]
Patients with serious or other significant events, n (%)			
Death	0 (0.0)	0 (0.0)	0 (0.0)
SAE	72 (11.3)	11 (6.1)	80 (11.6)
Discontinued due to AE	24 (3.8)	3 (1.7)	27 (3.9)

*Entire study period is Week 52 up to the data cut-off date (26-May-2023). †A serious GCP violation in the core trial was reported for one patient in this arm, and they were subsequently excluded from the full analysis set/efficacy analyses but were still included in the safety analyses. ‡The trial was conducted during the COVID-19 pandemic.

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AE, adverse event; COVID-19, coronavirus disease 2019; EAIR, exposure adjusted incidence rate; GCP, good clinical practice; n, number of patients with event; N, number of patients evaluable; PBO, placebo; PT, preferred term; PTY, patient-treatment years; Q2W, every 2 weeks; Q4W, every 4 weeks; SAE, serious adverse event; SEC, secukinumab 300 mg; SMQ, standardized MedDRA query; SOC, system organ class.

More patients treated with SECQ2W reported fungal infectious disorders in the entire study period*, a finding similar to that reported in the core trials[1,2]

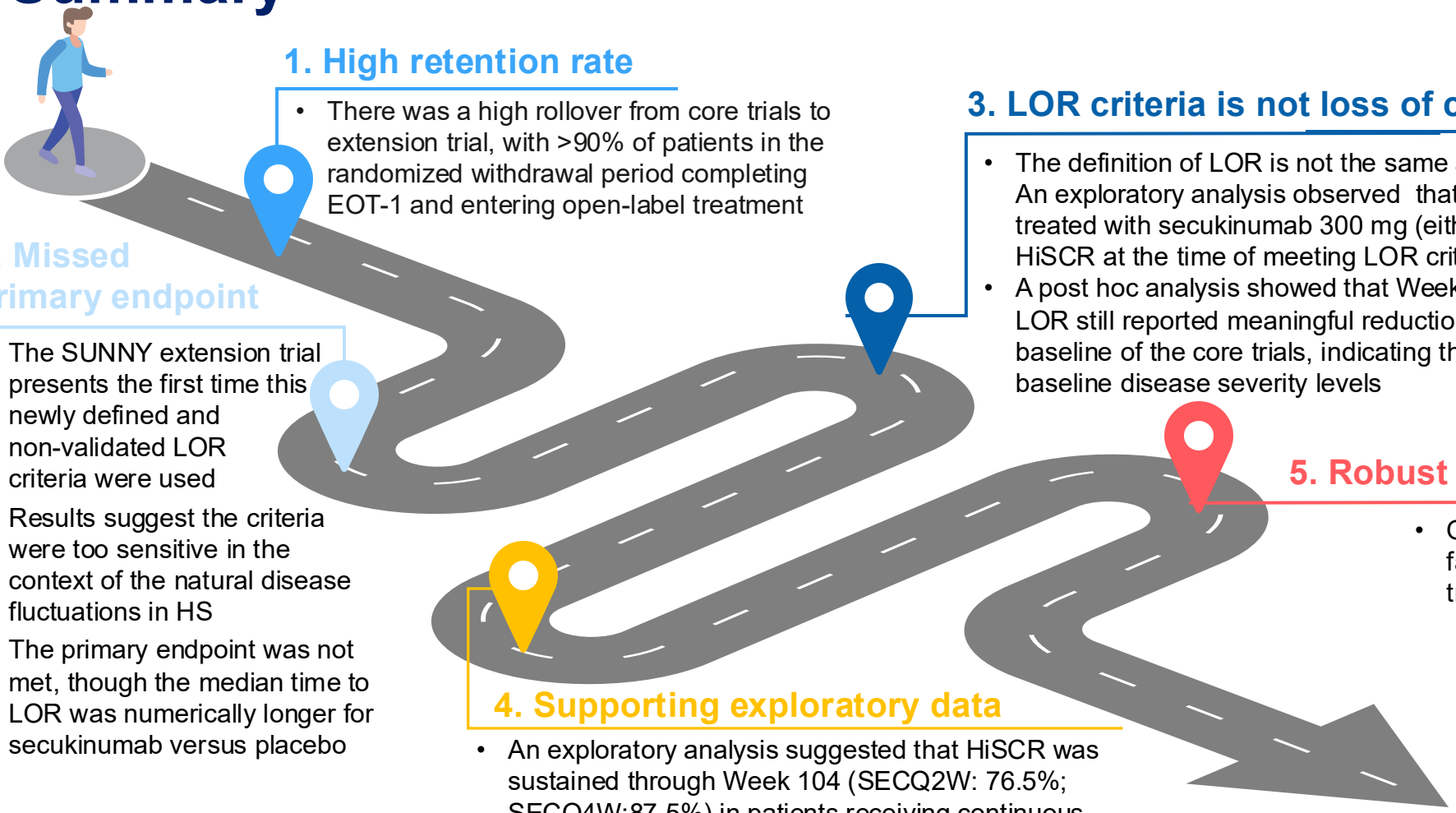
	Entire trial period		
	Any SECQ2W (N=637)†	Any SECQ4W (N=180)	Any SEC (N=687)*
Safety topics of interest, n (%), [EAIR/100 PTY]			
Infections and infestations (SOC)	349 (54.8) [56.3]	60 (33.3) [55.0]	389 (56.6) [54.9]
Upper respiratory tract infections (HLT)	116 (18.2) [12.4]	21 (11.7) [15.0]	136 (19.8) [12.8]
Fungal infectious disorders (HLGT)	52 (8.2) [5.3]	3 (1.7) [2.0]	54 (7.9) [4.8]
Candida infections (HLT)	23 (3.6) [2.3]	2 (1.1) [1.3]	24 (3.5) [2.1]
Hypersensitivity (SMQ) (narrow)	72 (11.3) [7.4]	8 (4.4) [5.7]	80 (11.6) [7.2]
Malignant or unspecified tumors (SMQ)	5 (0.8) [0.5]	1 (0.6) [0.7]	6 (0.9) [0.5]
MACE (NMQ)	2 (0.3) [0.2]	1 (0.6) [0.7]	3 (0.4) [0.3]
IBD (CMQ)	5 (0.8) [0.5]	1 (0.6) [0.7]	6 (0.9) [0.5]
Colitis ulcerative (PT)	1 (0.2) [0.1]	1 (0.6) [0.7]	2 (0.3) [0.2]
Crohn's disease (PT)	3 (0.5) [0.3]	0 (0.0) [0.0]	3 (0.4) [0.3]
IBD (PT)	1 (0.2) [0.1]	0 (0.0) [0.0]	1 (0.1) [0.1]

*Entire study period is Week 52 up to the data cut-off date (26-May-2023). †A serious GCP violation in the core trial was reported for one patient in this arm, and they were subsequently excluded from the full analysis set/efficacy analyses but were stillincluded in the safety analyses.

1. Kimball AB, et al. *Lancet.* 2023;401(10378):747–761. 2. Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AE, adverse event; CMQ, customized medDRA query; EAIR, exposure adjusted incidence rate; GCP, good clinical practice; HLGT, high-level group terms; HLT, high-level term; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular event; n, number of patients with event; N, number of patients evaluable; NMQ, Novartis MedDRA query; PBO, placebo; PT, preferred term; PTY, patient-treatment years; Q2W, every 2 weeks; Q4W, every 4 weeks; SEC, secukinumab 300 mg; SMQ, standardized MedDRA query; SOC, system organ class.

Summary



1. High retention rate

- There was a high rollover from core trials to extension trial, with >90% of patients in the randomized withdrawal period completing EOT-1 and entering open-label treatment

2. Missed primary endpoint

- The SUNNY extension trial presents the first time this newly defined and non-validated LOR criteria were used
- Results suggest the criteria were too sensitive in the context of the natural disease fluctuations in HS
- The primary endpoint was not met, though the median time to LOR was numerically longer for secukinumab versus placebo

3. LOR criteria is not loss of clinical response

- The definition of LOR is not the same as the definition of loss of HiSCR. An exploratory analysis observed that ~40% of the total patients treated with secukinumab 300 mg (either Q2W or Q4W) maintained HiSCR at the time of meeting LOR criteria
- A post hoc analysis showed that Week 52 HiSCR responders meeting LOR still reported meaningful reductions in absolute AN count versus baseline of the core trials, indicating that patients did not revert to baseline disease severity levels

4. Supporting exploratory data

- An exploratory analysis suggested that HiSCR was sustained through Week 104 (SECQ2W: 76.5%; SECQ4W:87.5%) in patients receiving continuous secukinumab from Week 52 to Week 104
- Exploratory and post hoc analyses suggested that secukinumab had a positive effect on skin pain and QoL in patients receiving continuous secukinumab from Week 52 to Week 104

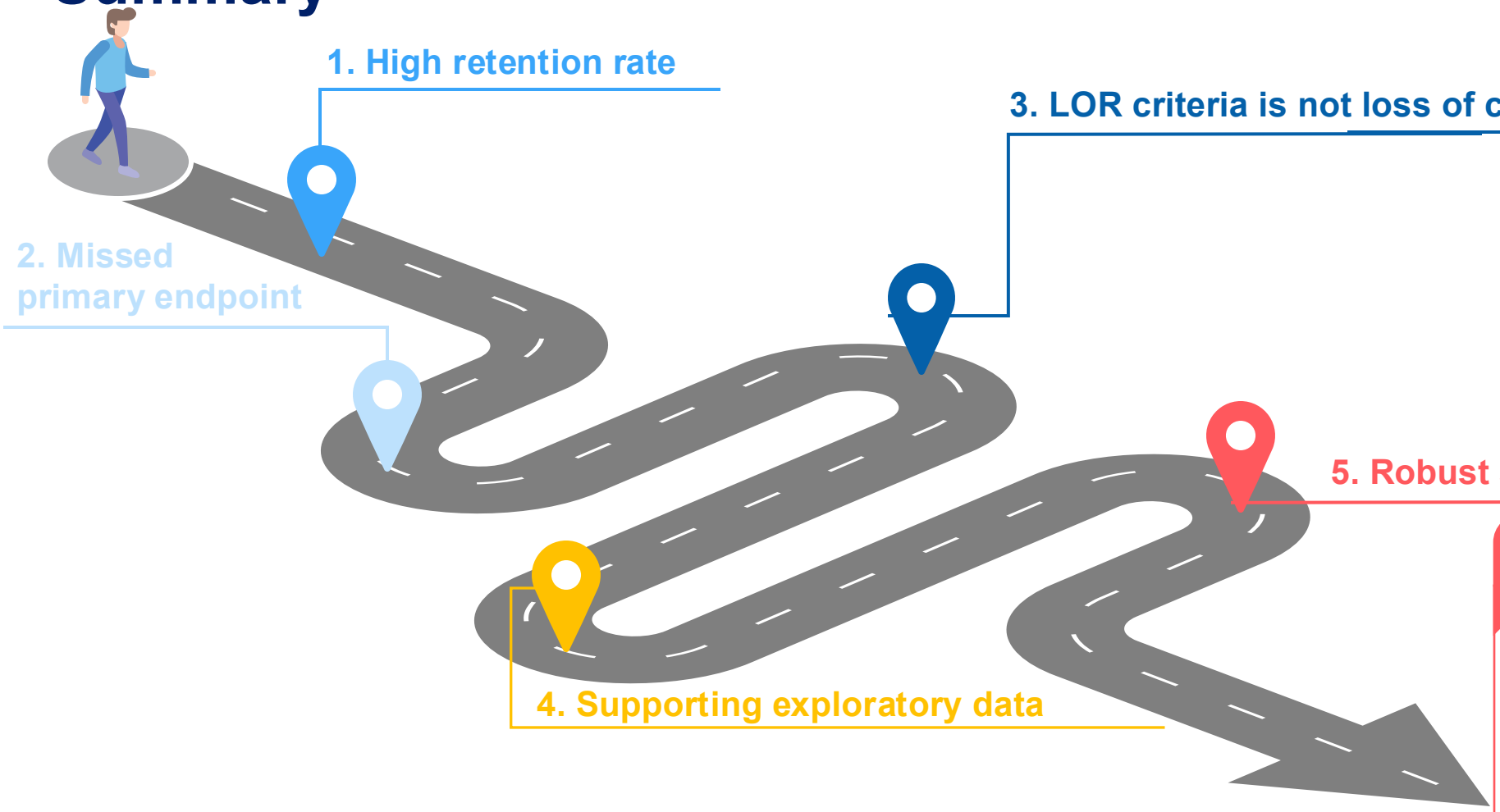
5. Robust safety data

- Overall, safety analyses confirmed the favorable safety profile associated with treatment with secukinumab

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.

AN, abscess and inflammatory nodule; EOT-1, end of treatment period 1; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response; QoL, quality of life; Q2W, every 2 weeks; Q4W, every 4 weeks.

Summary



Summary Narrative

The primary endpoint (time to LOR) of the randomized withdrawal extension of the SUNSHINE and SUNRISE trials was not met, likely due to the high sensitivity of the newly defined, non-validated LOR criteria used and the natural disease fluctuations in HS. However, in an exploratory analysis, sustained HiSCR was observed in patients on continuous secukinumab treatment for up to 2 years

Kimball AB, et al. *Br J Dermatol.* 2024;ljae469.
HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; LOR, loss of response.