Secukinumab Exhibits Sustained and Stable Response in Patients with Moderate-to-Severe Psoriasis: Results from the SUPREME Study

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Secukinumab, a fully human monoclonal antibody, neutralizes interleukin-17A, a cornerstone cytokine driving the multiple manifestations of psoriasis. This post-hoc analysis of the SUPREME study was performed to determine the sustainability of response to secukinumab in terms of Psoriasis Area and Severity Index (PASI) 90 in patients with moderate-to-severe plaque psoriasis. Based on PASI 90 response at week 16, patients were stratified as PASI 90 responders (PASI90R, *n* = 337) or non-responders (PASI90NR, *n* = 72). At week 20, 94.2% (*n* = 295/313) achieved PASI 90/100 response in PASI90R, with response maintained through week 48 (89.6%, *n* = 189/211). An increased proportion of patients achieved PASI 90/100 response in PASI90NR (week 20: 29.9%, *n* = 20/67; week 48: 57.1%, *n* = 20/35). Overall, 64.4% patients achieved absolute PASI score = 0 at week 24 with response sustained to week 48 (66.9%). Secukinumab showed sustained and stable efficacy in maintaining PASI 90 response in patients with moderate-to-severe plaque psoriasis up to week 48.

Key words: interleukin-17A; psoriasis; PASI 90; secukinumab.

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SIGNIFICANCE

Secukinumab, a fully human monoclonal antibody, neutralizes interleukin-17A, a cornerstone cytokine driving the multiple manifestations of psoriatic disease. Secondary loss of response over time has been observed with biologic therapies for psoriasis. This *post-hoc* analysis of the SUPREME study was performed to determine the sustainability of response to secukinumab in patients with moderate-to-severe plaque psoriasis. After 24 weeks of treatment with secukinumab, the majority of patients achieved complete clearance and response was sustained to week 48, demonstrating the sustainability of response to secukinumab in patients with moderate-to-severe plaque psoriasis.

Psoriasis (PsO) is a chronic, immune-mediated inflammatory disease with a reported prevalence of between 1.8% and 3.1% in the total population in Italy (1). PsO typically manifests as erythematous squamous plaques that occur most commonly on the elbows and knees, but can affect any area, including the palms, soles, nails and scalp (2–5). Interleukin (IL)-17A) is a key cytokine in the pathogenesis of psoriasis driving skin inflammation and, in some instances, joint inflammation (6). The advent of anti-IL-17 therapy in the treatment of psoriasis delivered the first Psoriasis Area and Severity Index (PASI) 100 end point, beginning an era of "treat to clear" with biologic monotherapy (7).

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Secukinumab is a fully human monoclonal antibody that selectively neutralizes IL-17A, a cornerstone driving the multiple manifestations of psoriatic disease. Secukinumab has shown long-lasting efficacy and safety in the various domains of psoriatic disease, including nails, scalp, palms and soles, and psoriatic arthritis (PsA) (2, 8–13). A high proportion of patients treated with secukinumab achieve a 90% reduction in Psoriasis Area and Severity Index (PASI) 90 within 16 weeks, (10, 14) and long-term data from patients treated over 5 years in the SCULPTURE study show that high levels of efficacy are sustained (15).

Secondary loss of response over time has been observed with biologic therapies for psoriasis (16–20). Conventional response analyses present aggregate data for a population at single time-point, potentially masking late responders and patients with reduced or variable efficacy (21). The Phase 3b SUPREME study (NCT02394561) demonstrated the efficacy of secukinumab in patients with moderate-to-severe plaque-type psoriasis, irrespective of HLA-Cw6 allele status at week 24 (22). PASI 75 responders at the end of the core phase (24 weeks) were eligible to enter the extension phase up to 72 weeks (23). In this analysis, PASI 90 response at week 16 (of the core phase) and its sustainability up to week 48, with secukinumab 300 mg every 4 weeks (q4w) in patients enrolled in the SUPREME study, is reported.

MATERIALS AND METHODS

Study design

This is a *post-hoc* analysis of response data from the SUPREME study (NCT02394561). The design and population of the SUPREME study have been reported in detail previously (22, 23). Briefly, the SUPREME core study was a 24-week, phase 3b, multicentre, prospective study conducted across 50 centres in Italy, with a variable extension phase up to 72 weeks. As per study design, after completing the core phase (24 weeks) patients entered a 48-week extension phase. Commercial secukinumab was available in Italy in June 2016 and at different time-points in regional study centres; much later than the time the study was initiated. Hence, patients had variable extension periods, and could complete the study based on the availability of commercial secukinumab. In the core phase, all patients received subcutaneous secukinumab, 300 mg/week for the first 5 weeks, followed by 300 mg every 4 weeks (q4w) until week 24. Patients entering the extension phase self-administered 300 mg q4w until week 72. Male or female patients aged ≥18 years diagnosed with moderate-to-severe chronic plaque-type psoriasis for at least 6 months (including patients with concomitant nail, scalp, or PsA according to Classification Criteria for Psoriatic Arthritis (CASPAR)) were included in the study. Moderate-to-severe plaque-type psoriasis was defined at enrolment by: PASI score ≥10 or PASI score >5 but <10 and Dermatology Life Quality Index (DLQI) ≥10.

Assessments

The severity of psoriasis was measured using PASI, which combines the assessment of the severity of lesions and the area affected into a single score with a range of 0 (no disease) to 72 (maximal disease) (24). PASI 50, PASI 75 and PASI 90 were defined as the achievement of ≥50%, ≥75%, and ≥90% improvement (reduction) in PASI score compared with baseline, respectively. PASI 100 was defined as the achievement of complete clearing of psoriasis (PASI=0). The IGA mod 2011 scale was used to assess overall psoriatic disease on a 5-point scale ranging from 0 (no disease, "clear") to 4 ("very severe") (25).

Objectives

The objectives of these post-hoc analyses were: (*i*) to evaluate PASI 90 response at week 16 (of the core phase) and its sustainability up to week 48, (*ii*) to describe and understand the determinant to lack of PASI 90 response at week 16, (*iii*) to describe the faster responder patients defined as patients with PASI 90 at week 4, and (*iv*) to understand the determinant to faster PASI 90 response at week 4.

Analysis

The safety set included all enrolled patients who were given at least one dose of the study drug with available baseline PASI assessment ($n=433$). Patients were divided into 2 cohorts based on PASI 90 response at week 16 of the core phase. PASI 90 responders (PASI90R) were defined as all patients in the safety set who were responders at week 16 in terms of PASI 90. PASI 90 non-responders (PASI90NR) were defined as all patients in the safety set who were not responders at week 16 in terms of PASI 90.

Patients were also analysed based on fast response at week 4 in terms of PASI 90 and were divided into 2 cohorts. PASI 90 fast responders (PASI90FR) were defined as patients who were responders at week 4 in terms of PASI 90, while PASI 90 non-fast responders (PASI90NFR) were those who did not achieve PASI 90 by week 4.

Both analyses were performed at week 4 and 16 separately for evaluable population with objective of identifying fast-responders (at week 4) and PASI 90 response (at week 16). Data were analysed as observed. Differences between cohorts were tested on all baseline demographics and anamnestic variables. Categorical variables were analysed by χ^2 test, while continuous variables were analysed by means of *t*-test or Wilcoxon test, based on data distribution. In order to understand the determinant to PASI 90 non-response, applying the stepwise methodology, a multivariate logistic regression model was fitted.

RESULTS

Patient demographics and disease characteristics

In total, 433 patients were included in the safety population and 409 patients were evaluable at week 16 for PASI 90 (i.e. have a baseline and week 16 PASI score). Based on PASI 90 response at week 16, 337 (82.4%) and 72 (17.6%) patients were included in PASI90R and PASI90NR cohort, respectively (Fig. S1[1]). In PASI90R cohort, 331 (98.2%) patients completed the CORE phase, 318 (94.4%) patients entered the extension phase, of whom 305 (95.9%) completed the extension phase. In PASI90NR cohort, 63 (87.5%) patients completed the core phase, 59 (81.9%) patients entered the extension phase and 48 (81.4%) patients completed the extension phase.

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PASI90R patients were significantly younger than PASI90NR (mean ± standard deviation (SD) age: 43.80 ± 13.10 vs 51.28 ± 11.86 years, $p<0.001$) and leaner (body weight: $p<0.001$; body mass index (BMI): $p<0.001$) with lower waist circumference ($p<0.001$). The proportion of patients with a BMI ≥25 in PASI90R vs PASI90NR was 59.64% vs 80.56% ($p<0.001$), respectively (Table SI[1]). There were no differences in terms of sex and smoking status. Considering baseline characteristics, there was no difference in terms of psoriasis localization and time since first diagnosis of psoriasis (mean ± SD duration: 18.12 ± 11.99 vs 19.74 ± 12.02 years, $p=0.28$) between cohorts, but PASI90R patients were younger than PASI90NR at diagnosis (mean ± SD age: 26.25 ± 13.76 vs 32.07 ± 14.08 years, $p=0.002$). PASI90R patients were affected less frequently by concomitant PsA (16.02% vs 34.72%, $p<0.001$) and metabolic syndrome (13.35% vs 29.17%; $p<0.001$). There was no difference between the cohorts in terms of PASI score ($p=0.25$) and Investigator's Global Assessment (IGA) response ($p=0.43$). At baseline, PASI90R patients had a lower DLQI total score compared with PASI90NR (mean ± SD: 10.04 ± 6.85 vs 12.14 ± 7.49, respectively; $p=0.04$). No difference in terms of Cw6 assessment was present. A significantly higher proportion of patients in PASI90NR cohort received prior biologic therapy (41.67%) compared with PASI90R (26.71%, $p=0.01$). Moreover, 48.10% of patients with concomitant PsA had a prior biologic therapy vs 23.64% of the patients without concomitant PsA ($p<0.001$).

Psoriasis Area and Severity Index status over time

At week 20, 94.2% ($n=295/313$) patients maintained PASI 90/100 response in PASI90R cohort (**Fig. 1**a) and 29.9% ($n=20/67$) patients achieved PASI 90/100 response in PASI90NR cohort (Fig. 1b). PASI 90/100 response was maintained in PASI90R cohort at week 24 (94.0%, $n=313/333$) through to week 48 (89.6%, $n=189/211$; Fig. 1a). There was an increase in proportion of patients achieving PASI 90/100 response in PASI90NR cohort (week 24: 46.3%, $n=31/67$; week 48: 57.1%, $n=20/35$; Fig. 1b).

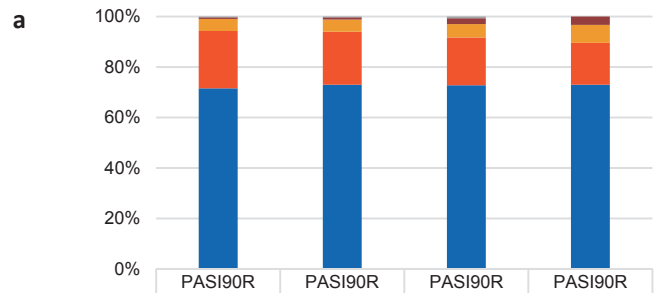
Overall, 17/337 (5%) PASI90R became partial responders (50% to <75% improvement in PASI score compared with baseline) between week 16 and week 48. Demographics and disease characteristics of these 17 patients are presented in Table SII[1]. They had a significantly higher BMI ($p<0.001$) and waist circumference ($p<0.001$) compared with patients who maintained PASI response until Week 48. In total, 6/337 (1.8%) patients became non-responders (PASI <50% compared with baseline) between week 16 and week 48. Patient-level PASI status over time (weeks 16–48) in PASI90R and PASI90NR is shown in Fig. S2[1].

Determinants of Psoriasis Area and Severity Index 90 non-response to secukinumab at week 16

Considering the univariate model, the following covariates were statistically significant: age, weight, BMI, waist circumference, smoking status (former vs never), presence of metabolic syndrome, prior biologic therapy, and presence of PsA. No difference was observed in patients with nails and scalp involvement (**Table I**). Considering the stepwise approach in the multivariate regression model, the following 3 factors were significant: age, waist circumference, and concomitant PsA (Table I).

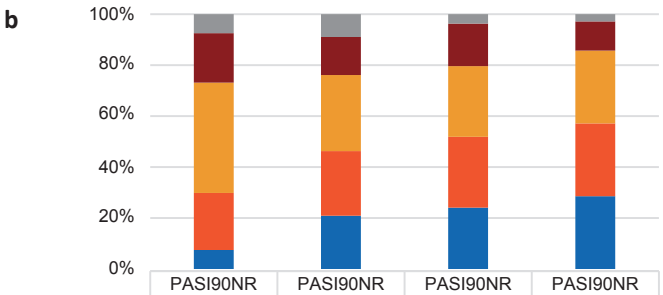
Proportion of patients with absolute Psoriasis Area and Severity Index score 0, ≤1, ≤2 or ≤3 in the overall population

At week 24, 64.4% of patients had an absolute PASI score of 0 (i.e. PASI 100), which was slightly higher compared



	PASI90R (Week 20)	PASI90R (Week 24)	PASI90R (Week 36)	PASI90R (Week 48)
PASI <50	1	1	2	0
75 <PASI ≤50	2	3	7	7
90 < PASI ≤ 75	15	16	16	15
100 < PASI ≤ 90	71	70	57	35
PASI 100	224	243	219	154
Missing*	24	4	36	126

PASI90R, N=337



	PASI90NR (Week 20)	PASI90NR (Week 24)	PASI90NR (Week 36)	PASI90NR (Week 48)
PASI <50	5	6	2	1
75 <PASI ≤50	13	10	9	4
90 < PASI ≤ 75	29	20	15	10
100 < PASI ≤ 90	15	17	15	10
PASI 100	5	14	13	10
Missing*	5	5	18	37

PASI90NR, N=72

Fig. 1. Psoriasis Area and Severity Index (PASI) status over time in (a) PASI 90 responders (PASI90R) (b) PASI 90 (PASI90NR) non-responders at week 16. *Missing values represent patients who completed extension treatment between week 24 and week 48. As per study design, after completing the core phase (24 weeks) patients entered a 48-week extension phase and could complete the study at any time during this period.

Table I. Univariate and multivariate logistic regression model for identifying determinants that may predict lack of response to secukinumab (PASI90NR)

Univariate logistic regression	Odds ratio (95% CI)	Beta	*p*-value
Age, years	1.05 (1.02–1.07)	0.05	**<0.001**
Sex: female vs. male	1.27 (0.73–2.20)	0.24	0.40
Weight, kg	1.03 (1.01–1.04)	0.03	**<0.001**
Body mass index, kg/m^2	1.10 (1.05–1.15)	0.10	**<0.001**
Waist circumference, cm	1.04 (1.02–1.06)	0.04	**<0.001**
Smoke			
Current vs never	1.23 (0.69–2.19)	0.20	0.49
Former vs never	2.13 (1.04–4.40)	0.76	**0.04**
Nail psoriasis: present vs absent	1.31 (0.78–2.18)	0.27	0.31
Scalp psoriasis: present vs absent	0.83 (0.46–1.50)	−0.19	0.54
Time since diagnosis of psoriasis, years	1.01 (0.99–1.03)	0.01	0.30
Baseline PASI score	0.98 (0.95–1.01)	−0.02	0.25
Metabolic syndrome: yes vs no	2.67 (1.47–4.86)	0.98	**0.001**
Previous biologic systemic-therapy: yes vs no	1.94 (1.14–3.29)	0.67	**0.015**
Presence of psoriatic arthritis: yes vs no	2.79 (1.58–4.91)	1.03	**<0.001**

Multivariate logistic regression	Odds ratio, point estimate (95% CI)	Beta	Wald χ^2	*p*-value
Age, years	1.03 (1.01, 1.05)	0.03	6.55	**0.01**
Waist circumference, cm	1.03 (1.01, 1.05)	0.03	11.43	**<0.001**
Presence of psoriatic arthritis	2.06 (1.13, 3.78)	0.72	5.49	**0.02**

CI: confidence interval; PASI: Psoriasis Area and Severity Index; PASI90NR: PASI 90 non-responders at week 16. Those values that are statistically significant are highlighted in bold.

with week 16 (57.5%; **Fig. 2**). The proportion of patients achieving an absolute PASI score of ≤1 was 71.6% and 78.5% at weeks 16 and 24, respectively. Similarly, there was an increase in proportion of patients achieving PASI score of ≤2 from week 16 (83.4%) to week 24 (86.6%). Proportion of patients reaching a PASI score of ≤3, was 88.5% and 90.7% of patients at weeks 16 and 24, respectively. These results remained stable also at week 48.

Patient demographics and disease characteristics of Psoriasis Area and Severity Index 90 fast responders

In total, 421 patients were evaluable at week 4 and based on PASI 90 response, 103 (24.5%) patients were identified as PASI 90 fast responders (PASI90FR) (Figs S3 and S4[1]).

PASI90FR patients were significantly younger than PASI90NFR (mean ± SD age: 42.72 ± 13.76 vs 45.86 ± 12.86 years, $p=0.03$) and leaner (mean ± SD weight: 77.76 ± 16.52 vs 82.13 ± 16.89 kg, $p=0.02$; mean ± SD BMI: 26.41 ± 5.10 vs 27.63 ± 5.26, $p=0.04$). Demographics and disease characteristics of these patients are shown in Table SIII[1]. The proportion of patients with a BMI ≥25 kg/m^2 in PASI90FR vs PASI90NFR was 56.31% vs 66.04% ($p=0.07$), respectively. There were no differences in terms of sex, height, waist circumference and smoking status. Considering baseline characteristics, there was no difference in terms of psoriasis localization and time since first diagnosis of psoriasis (mean ± SD duration: 18.88 ± 12.48 vs 18.27 ± 11.66 years, $p=0.77$) between cohorts (Table SIII[1]), but PASI90FR patients were younger at diagnosis (mean ± SD age: 24.41 ± 14.37 vs 28.17 ± 13.57 years, $p=0.007$). Proportion of patients with concomitant PsA (14.56% vs 21.38%, $p=0.13$) and metabolic syndrome (14.56% vs 17.61%; $p=0.47$) were similar in PASI90FR and PASI90NFR cohorts, respectively. There was no difference between the cohorts in terms of PASI ($p=0.30$) and IGA response ($p=0.08$). A higher proportion of patients in the PASI90FR cohort (92.42%) sustained the PASI90 response vs the PASI90NFR patients (82.42%) at week 48. However, this difference was not statistically significant ($p=0.051$). A significantly higher proportion of patients in PASI90NFR cohort received prior biologic therapy (31.45%) compared with PASI90FR (19.42%, $p=0.02$).

Considering the univariate models, the following characteristics were statistically significant: age, weight, BMI, and prior biologic therapy. No difference was observed in patients with nails and scalp involvement or in baseline PASI score (**Table II**). Considering the multivariate approach with stepwise selection, only weight remains as determinant of faster response (Table II).

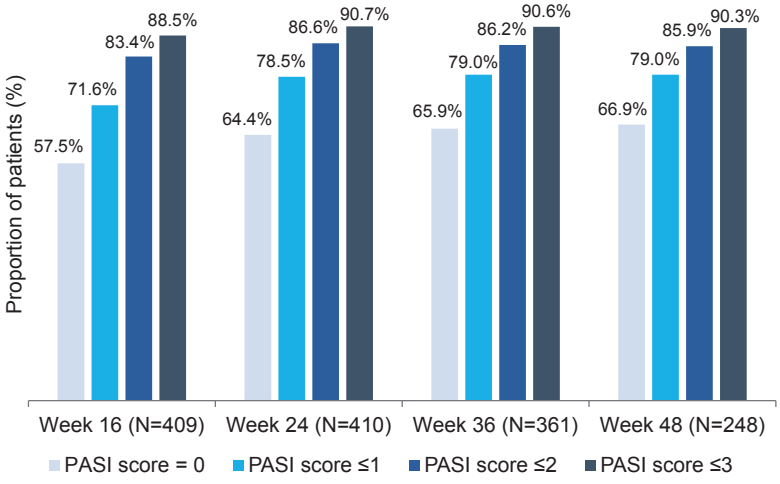


Fig. 2. Proportion of patients with Psoriasis Area and Severity Index (PASI) score 0, ≤1, ≤2 or ≤3 at weeks 16, 24, 36 and 48 (overall population). PASI scores reported for overall population (PASI 90 responder at week 16 (PASI90R) and PASI 90 non-responder at week 16 (PASI90NR)). Proportion of patients available at each assessment varied due to missing values representing patients who completed extension treatment between week 24 and week 48. As per study design, after completing the core phase (24 weeks) patients entered a 48-week extension phase and could complete the study at any time during this period.

Table II. Univariate and multivariate logistic regression model for identifying determinants that may predict non-fast response to secukinumab (PASI90NFR)

Univariate logistic regression	Odds ratio (95% CI)	Beta	*p*-value
Age, years	0.98 (0.97–1.00)	−0.02	**0.04**
Sex: female vs male	1.40 (0.86–2.26)	0.33	0.17
Weight, kg	0.98 (0.97–1.00)	−0.02	**0.02**
BMI, kg/m^2	0.95 (0.91–1.00)	−0.05	**0.04**
Waist circumference, cm	0.99 (0.97–1.00)	−0.01	0.13
Smoke			
Current vs never	1.10 (0.68–1.79)	0.10	0.69
Former vs never	1.06 (0.54–2.11)	0.06	0.86
Nail psoriasis: present vs absent	0.70 (0.44–1.12)	−0.35	0.14
Scalp psoriasis: present vs absent	0.75 (0.44–1.26)	−0.29	0.27
Time since diagnosis of psoriasis, years	1.00 (0.99–1.02)	0.00	0.65
Baseline PASI score	1.01 (0.99–1.03)	0.01	0.30
Metabolic syndrome: yes vs no	0.80 (0.43–1.48)	−0.23	0.47
Previous biologic systemic-therapy: yes vs no	0.53 (0.31–0.90)	−0.64	**0.02**
Presence of psoriatic arthritis: yes vs no	0.63 (0.34–1.15)	−0.47	0.13

Multivariate logistic regression	Odds ratio, point estimate (95% CI)	Beta	Wald χ^2	*p*-value
Weight, kg	0.99 (0.97–1.00)	−0.01	4.33	**0.04**

BMI: body mass index; PASI: Psoriasis Area and Severity Index; PASI90NFR: PASI 90 non-fast responders at week 4.

DISCUSSION

Achievement of clear or almost clear skin has become a treatment goal for the majority of patients with psoriasis, particularly with the advent of biological therapies for the treatment of psoriatic disease (26, 27). A 90% improvement from baseline PASI score is now defined as the threshold of treatment success per the European Medicines Agency and a "measure of optimal response" by the American Academy of Dermatology (28, 29). There is emerging interest in the evaluation of reduction of absolute PASI score as a better indicator of therapeutic response and the higher clinical relevance of the remaining absolute PASI score as therapeutic target (i.e. PASI score 0–1, PASI score ≤2, PASI score ≤3, and PASI ≤5) (30). Secondary loss of response may be experienced by a minority of patients treated with secukinumab, as with other biologics, but the extent of this and the stability of response is not well understood. Previous studies reporting the stability of response with secukinumab are limited by the small number of patients (31).

Since psoriasis is a chronic disease, treatment requires long-term stability of response for the benefit of patients. In the present study, secukinumab showed stable efficacy in the majority of the patients over 48 weeks of treatment. These results are in agreement with a recent study in which efficacy with secukinumab was stable over 52 weeks of treatment (21). In the ERASURE-FIXTURE and SCULPTURE Extension studies, PASI 75/90/100 responders at week 52 demonstrated sustained clinical response up to year 5 with secukinumab 300 mg (15, 32).

There were significant differences in baseline demographic and disease characteristics between the 2 cohorts (PASI90R and PASI90NR) defined at week 16. PASI90R had a moderate effect on quality of life (QoL) as assessed by DLQI, whereas PASI90NR reported very large effect on QoL. Approximately 95% of PASI90R achieved PASI 90/100 response at week 20 and response was maintained up to week 48 (90%). There was also an increase in the proportion of patients maintaining PASI 90/100 response in PASI90NR cohort (week 24: 46.3%; week 48: 57.1%). A small proportion of patients (5%) who became partial responders between week 16 and week 48 had a significantly higher BMI and waist circumference compared with patients who maintained PASI response after week 16, implying the association of body weight with loss or reduction of efficacy. Patient-related factors associated with the lack of PASI 90 response to secukinumab at week 16 were analysed using multivariate logistic regression model. Patients with concomitant PsA were more likely to be PASI90NR at week 16, as well as patients of older age or those with higher waist circumference. However, these results are limited by low numbers of patients in the PASI90NR cohort. In the present analysis, the proportion of patients with psoriasis with concomitant PsA was twice as high in the PASI90NR vs PASI90R cohort (35% vs 16%, respectively). In all, a significantly higher proportion of patients with PASI 90 non-response to secukinumab at week 16 (PASI90NR, 41.7%) received prior biologic therapy for psoriasis compared with 26.7% patients in PASI90R cohort. Exposure to previous biologics for the treatment of psoriasis influences achievement of PASI 75/90/100 response (33). These clinical factors are consistent with a recent study in which bio-naïve condition was identified as a factor determining favoured secukinumab response (30). Secukinumab has shown rapid improvement of skin lesions, particularly in younger patients (33). Younger patients maintain response for a longer period than elderly patients, possibly due to alterations in drug pharmacokinetics and pharmacodynamics with age (33, 34). In previous studies, obesity was associated with reduction of efficacy of anti-tumour necrosis factor (anti-TNF) agents and ustekinumab (35, 36). Measures of abdominal adiposity, such as waist circumference and waist-hip ratio, are considered as good indicators of metabolic abnormalities and cardiovascular disease (37). Previous studies have found higher risk of psoriasis in patients with higher waist circumference and waist-hip ratio (38, 39). Central obesity may play a role in psoriasis; adipose tissue, especially visceral fat, produces adipokines, which have a role in chronic inflammation (40, 41).

At week 24, the majority of patients (64.4%) achieved an absolute PASI score of 0 (complete clearance), the response was sustained to week 48 (66.9%). Overall, during the study, only 1.8% of patients with PASI 90 at week

16 became non-responder (PASI < 50%) until week 48. Considering the CORE study, a single PASI90R became non-responder (PASI < 50%) at week 24; 3 patients with PASI 90 became partial responders (PASI 50 to < 75%) after week 16.

Another objective of this post-hoc analysis was to study demographics and disease characteristics of fast responders (PASI 90 response at week 4) and determine factors affecting achievement of a faster PASI 90 response. PASI90FR patients were significantly younger and leaner than PASI90NFR. A significantly higher proportion of patients in the PASI90NFR cohort received prior biologic therapy (31.5%) compared with PASI90FR (19.4%). Younger patients, patients with lower BMI or biologically naïve patients are more likely to achieve a faster response to secukinumab in terms of PASI 90. Body weight was the determinant factor for achieving PASI response at week 4, an increment of 0.01 unit in weight could lead to a lower probability of being a fast responder. Among limitations, this study was a *post-hoc* analysis; hence, no formal sample size was drawn. The *p*-value should be considered as nominal.

In conclusion, secukinumab showed a sustained and stable response, in terms of maintenance of PASI 90 response, in the majority of patients with moderate-to-severe plaque psoriasis over 48 weeks.

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Conflicts of interest. AC acted as a speaker and consultant for AbbVie, Eli Lilly, Novartis, Almirall, Celgene, Sanofi, Janssen and Pfizer. LS has acted as a speaker and consultant for AbbVie, Eli Lilly, Novartis, Almirall, Celgene, Sanofi and Janssen. LZ acted as a speaker for AbbVie, Eli Lilly and Novartis. MP reports personal fees for advisory board from Janssen-Cilag, outside of the present work. AC has acted as a consultant for AbbVie, Abbott, Amgen, Celgene, Eli Lilly, Janssen Cilag, Leo Pharma, MSD, Novartis, Sandoz, Schering Plough, UCB Pharma, Wyeth. AC served as advisory board member and consultant, and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Biogen, Fresenius Kabi, Leo Pharma, Lilly, Janssen, Novartis, Sanofi Genzyme and UCB-Pharma. FMG has been a consultant and has participated in clinical trials for Abbvie, Eli Lilly, Novartis, Leo Pharma. CM has been a consultant and/or speaker for AbbVie, Celgene, Janssen, Leo-pharma, Eli Lilly, Novartis and Amgen. MLM served as consultant/investigator for AbbVie, Eli Lilly, Janssen-Cilag, Novartis and Biogen. PG has been a consultant and/or speaker for AbbVie, Almirall, Celgene, Janssen, Leo-pharma, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Sandoz, UCB. GP has been speaker and consultant for Novartis and AbbVie. KP reports grants and personal fees from Almirall and AbbVie and personal fees for advisory board from Biogen, Lilly, Celgene, Galderma, Leo Pharma, Novartis, Pierre Fabre, Sanofi, Sandoz, Sun Pharma and Janssen, outside of the present work. AO acted as a speaker and consultant for AbbVie, Eli Lilly, Novartis, Celgene, Sanofi, Galderma, Leo Pharma, Pierre Fabre, outside of the present work. FP reports personal fees for advisory board from AbbVie, Biogen, Eli Lilly, Celgene, Leo Pharma, Novartis, Sanofi and Janssen-Cilag, outside of the present work. FR, CP, MG, MV, FL, VL, RS, LDC, MB, SP, PD, FC, SRM and ST report no conflict of interest. MB, GO, EA and RO are employed by Novartis.

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