DOI: 10.1111/jdv.18329 JEADV

ORIGINAL ARTICLE

Secukinumab demonstrated sustained retention, effectiveness and safety in a real-world setting in patients with moderate-to-severe plaque psoriasis: long-term results from an interim analysis of the SERENA study

M. Augustin,[1,*] P.G. Sator,[2] R.von Kiedrowski,[3] C. Conrad,[4] D. Rigopoulos,[5] M. Romanelli,[6] P.-D. Ghislain,[7] T. Torres,[8] D. Ioannides,[9] M. Aassi,[10] B. Schulz,[10] P. Jagiello,[10] on behalf of the SERENA study group

[1]Institute for Health Services Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[2]Department of Dermatology, Municipal Hospital Hietzing, Vienna, Austria
[3]Company for Medical Study & Service Selters (CMS3) GmbH, Selters, Germany
[4]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
[5]Dermatology and Venerology, Medical School, National and Kapodistrian University of Athens, Athens, Greece
[6]Dermatology Department, University of Pisa, Pisa, Italy
[7]Dermatology, Cliniques Saint-Luc, Université Catholique de Louvain, Brussels, Belgium
[8]Department of Dermatology, Centro Hospitalar Universitário do Porto, Porto, Portugal
[9]First Department of Dermatology and Venereology, School of Medicine, Aristotle University, Thessaloniki, Greece
[10]Novartis Pharma AG, Basel, Switzerland
*Correspondence: M. Augustin. E-mail: m.augustin@uke.de

Abstract

Background Randomized controlled trials of secukinumab have shown sustained efficacy and a favourable safety profile in multiple manifestations of psoriatic disease.

Objectives To assess the long-term, real-world retention, effectiveness and safety of secukinumab in routine clinical practice for the treatment of moderate-to-severe plaque-type psoriasis (PsO).

Methods SERENA (CAIN457A3403) is a large, ongoing, longitudinal, observational study conducted at 438 sites and 19 countries for an expected duration of up to 5 years in adult patients with moderate-to-severe PsO, psoriatic arthritis and ankylosing spondylitis. Patients received ≥16 weeks of secukinumab treatment before enrolment. This interim analysis presents data from PsO patients, who were enrolled in the study between October-2016 and October-2018 and were observed for ≥2 years.

Results In total, 1756 patients (67.3% male) with a mean age of 48.4 years and body mass index of 28.8 kg/m^2 were included in the analysis. The secukinumab treatment retention rates after 1, 2 and 3 years in the study were 88.0%, 76.4% and 60.5%, respectively. Of the 648 patients who discontinued the study, the most common reasons included lack of efficacy (42.6%), adverse event (17.4%), physician decision (12.2%) and subject decision (11.6%). Mean ± SD absolute PASI was 21.0 ± 13.0 at the start of treatment (n = 1,564). At baseline, the mean ± SD PASI score reduced to 2.6 ± 4.8 and remained low at Year 1 (2.3 ± 4.3), Year 2 (1.9 ± 3.6) and Year 3 (1.9 ± 3.5). The safety profile of secukinumab during the SERENA study was consistent with its known safety profile, with no new safety signals reported. Particularly, low rates of inflammatory bowel disease (0.3%; Incidence Rate [IR]:0.15), candida infections (3.1%; IR:1.43) and MACE (0.9%; IR:0.37) were observed.

Conclusions Secukinumab showed high treatment persistence, sustained effectiveness and a favourable safety profile up to 3 years of follow-up in the real-world population of PsO patients observed in SERENA.

Received: 9 November 2021; Accepted: 29 April 2022

Conflicts of interest

M. Augustin has served as consultant for or has been a paid speaker for clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Eli-Lilly, GSK, Janssen-Cilag, Leo, Medac, Merck, MSD, Novartis, Pfizer, UCB and Xenoport. P.G. Sator has been an advisor and/or received speaker honoraria or travel expense reimbursements and/or received grants and/or

participated in clinical trials for AbbVie, Actelion, Amgen, Almirall, Janssen, Novartis, Leo Pharma, Pfizer, MSD, Celgene, Maruho, ALK, Galderma Abbott, UCB, Gilead and Eli-Lilly. R. von Kiedrowski declares that, through his own company CMS GmbH, he has received honoraria for lectures, consultancy work, and studies from AbbVie, Almirall, Biofrontera, Biogen, Celgene, Dr. Pfleger, Foamix, Janssen-Cilag, Leo, Lilly, Medac, MSD, Novartis, Pfizer, Tigercat and UCB. C. Conrad served as scientific advisor and/or clinical study investigator and/or paid speaker for AbbVie, Actelion, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Galderma, Incyte, Janssen, LEO Pharma, Eli-Lilly, MSD, Novartis, Pfizer, Samsung and UCB. D. Rigopoulos has received consultancy fees, payment for lectures and support for travel to scientific meetings from Celgene, Novartis, Janssen and AbbVie. M. Romanelli has participated in the advisory board of AbbVie, Eli Lilly, Novartis and Urgo. P.-D. Ghislain has received speaker fees, participated in clinical trials and/or advisory boards for Pfizer, MSD, AbbVie, Janssen-Cilag, Merck-Serono, Leo, Novartis, UCB, Amgen, Eli-Lilly, Galderma, BMS, Meda, Maruho, Flen, Menarini, Almirall, PellePharm and Mylan. T. Torres has received speaker fees, participated in clinical trials and/or advisory boards for AbbVie, Almirall, Amgen, Arena Pharmaceuticals, Biocad, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Janssen, LEO Pharma, Eli Lilly, MSD, Mylan, Novartis, Pfizer, Samsung-Bioepis, Sanofi-Genzyme and Sandoz. D. Ioannides has received speaker fees, participated in clinical trials and/or advisory boards for Abbvie, Eli-Lilly, Genesis, Galderma, Janssen, LEO, Novartis, Pfizer and UCB. B. Schulz, M. Aassi and P. Jagiello are employed by Novartis.

Funding sources

This study was funded by Novartis Pharma AG.

Introduction

Psoriatic disease is a systemic inflammatory disorder associated with a wide spectrum of clinical manifestations and comorbidities that can lead to severe impairment on patients' quality of life.[1–8] The development of psoriatic disease manifestations, including psoriasis (PsO), psoriatic arthritis (PsA) and ankylosing spondylitis (AS), is facilitated by a cornerstone cytokine, interleukin-17A (IL-17A). Secukinumab is a fully human monoclonal antibody that selectively neutralizes IL-17A.[9–15]

Randomized controlled trials of secukinumab have shown sustained efficacy and a favourable safety profile in multiple manifestations of psoriatic disease, including nails, scalp, palms, soles and PsA, for up to 5 years of exposure.[9,16–24] A recent meta-analysis of 42 observational studies further supported the clinical effectiveness of secukinumab in patients with moderate-to-severe PsO up to 12 months of treatment.[25] However, there remains a need to collect longer-term effectiveness and safety data for secukinumab, under real-world conditions in the European population. Long-term real-world evidence may help to fully characterize the clinical utility of secukinumab, and its impact on quality of life (QoL), for patients with the aforementioned conditions. It is also important to understand the long-term retention of secukinumab and patterns of use (e.g. dosing, administration and treatment interruptions) in a real-world setting. Finally, data are needed on regain of efficacy response after treatment discontinuation, particularly in light of the recent coronavirus disease 2019 (COVID-19) pandemic.

SERENA is a non-interventional study with an observational period of up to 5 years in patients with moderate-to-severe PsO, PsA and AS treated with secukinumab per routine clinical practice in Europe. This interim analysis of the SERENA study reports data from patients with PsO, who were enrolled in the study between October 2016 and October 2018 and were observed for at least 2 years.

Study objective

The primary objective of this analysis was to assess the long-term retention of secukinumab in routine clinical practice for the treatment of moderate-to-severe plaque-type PsO, and to identify factors affecting the retention of secukinumab.

Additional objectives were to describe the long-term effectiveness and safety of secukinumab in routine clinical practice for the treatment of moderate to severe plaque PsO, and to describe the treatment pattern with secukinumab in terms of dosing, administration intervals and preferred device based on the reported therapy changes.

Patients and methods

Study design

The SERENA study (CAIN457A3403) design was reported previously.[26] Briefly, it is a large, ongoing, longitudinal, observational study with a total intake of more than 2900 patients with moderate-to-severe PsO, PsA, and AS who had received at least 16 weeks of secukinumab treatment before study enrolment. The study was conducted at 438 sites, across 18 European countries (Austria, Belgium, Bulgaria, Croatia, Czech Republic, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Portugal, Russia, Slovenia, Switzerland and the United Kingdom) and Israel.

Patients will participate in the study for a maximum of 5 years (60 months), with individual patients exiting the study if they discontinue secukinumab. Visits are documented every 6 months after enrolment. The study will end either when all enrolled patients complete at least 2 years of follow-up, unless they choose to exit the study, or when the 5-year visit has been documented for approximately 1000 patients (including a representative number of patients for all three indications), whichever occurs later.

Herein, we present the retention, effectiveness and safety data from PsO patients, who were enrolled in the study between October 2016 and October 2018 and were observed for at least 2 years.

Study population

Inclusion and exclusion criteria The full inclusion and exclusion criteria were reported previously.[26] In brief, adult patients with a diagnosis (assessed by the treating physician) of active moderate-to-severe plaque PsO who were receiving secukinumab treatment according to the approved product label were included in the study. All patients received at least 16 weeks of secukinumab treatment before enrolment in the study. After 16 weeks of secukinumab treatment, there was no required response target for enrolment.

Outcomes and assessments

This interim analysis presents safety data from 1835 patients with PsO who were enrolled in the study between October 2016 and October 2018 and were observed for at least 2 years. Due to unfulfilled inclusion/exclusion criteria, 79 patients in the safety set were excluded from the target population (n = 1756) for effectiveness analyses. The most common reasons for exclusion included the following: patient did not receive secukinumab for at least 16 weeks prior to the study; secukinumab was not taken according to approved product information.

Data on primary and additional outcome variables were collected prospectively. As patients included in the study were pretreated with secukinumab, data on effectiveness and safety were also collected retrospectively from the start of treatment. Retention rates of secukinumab were measured after the start of participation in the study, where retention rate is defined as the percentage of patients who have not discontinued secukinumab treatment. Every prior biologic treatment taken for PsO was documented without a time limit, all other prior PsO treatments were documented only if taken within 6 months prior to baseline.

Effectiveness assessments included Psoriasis Area and Severity Index (PASI): assessment of the severity of lesions and the area affected [scored 0 (no psoriasis) to 72 (extremely severe)]; body surface area (BSA): assessed by the percentages of areas affected, including head, trunk, upper limbs and lower limbs; Physician's Global Assessment (PGA) score: assessed by the physician for all patients with plaque-type psoriasis, as part of routine clinical practice; and Dactylitis: of a digit in the foot or hand, counts as 1 tender and swollen joint. QoL was assessed by Dermatology Life Quality Index [DLQI; scored 0 (no impairment) to 30 (maximal impairment).

Treatment interruption

A separate analysis was performed including patients who recorded an interruption in secukinumab treatment lasting >2 months (i.e. 3 months since last injection of secukinumab); shorter treatment interruptions were not included. If a patient recorded >1 treatment interruption, then the interruption with the longest duration was included in the analysis.

Where available, PASI and PGA scores were evaluated before, during and after the treatment interruption. The minimal interval between restarting treatment and data collection was 1 month; the maximum interval was 6 months. The available PASI and PGA assessments closest to 6 months post-treatment interruption were used.

Statistical methods

This interim analysis was mainly based on descriptive statistical methods; no imputations of data analyses were made. Quantitative data (e.g. age) were analysed by the statistical parameters N, mean, standard deviation (SD), and selected quantiles: minimum (0%), lower quartile (25%), median (50%), upper quartile (75%) and maximum (100%). If indicated by the data, an additional frequency distribution was supplied after appropriate grouping of data. Qualitative variables (e.g. binary rating of treatment response) were presented by absolute and relative frequency distributions. Two-sided 95% confidence intervals (CIs) were provided for all binary response rates.

Ethical consent

All patients provided written informed consent before enrolment for their data to be collected for this non-interventional study. The study protocol was approved by the institutional review board of each participating centre according to local regulations. The trial is conducted in accordance with the Guidelines for Good Pharmacoepidemiology Practices (GPP) of the International Society for Pharmacoepidemiology (ISPE 2008), the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, the Declaration of Helsinki and each countries' local regulations.

Results

Patient disposition and baseline characteristics

In total, 1756 patients (67.3% male patients) with a mean age of 48.4 years and body mass index of 28.8 kg/m^2 were included in the efficacy analysis (Table 1). The mean ± SD time since diagnosis of PsO was 17.3 ± 13.2 years. At baseline, 23.1% (406/1754) of patients also had a previous PsA diagnosis. The mean ± SD time since PsA diagnosis at baseline was

10.6 ± 10.1 years. Patients were treated with secukinumab for a mean ± SD duration of 1.1 ± 0.7 years prior to baseline. Treatments taken for PsO prior to secukinumab initiation are displayed in Table 2. Overall, 65.9% (1157/1754) of patients were naive to biologic treatment for either PsO or PsA prior to secukinumab treatment. Of the 599 patients with PsO who were treated with biologics prior to secukinumab treatment, half (48.6%) were treated with one biologic drug only, and a quarter were treated with either 2 (25.4%) or ≥3 biologics (26.0%). During secukinumab treatment, the majority of patients received either no concomitant therapy (56.0%) or concomitant topical treatments only (32.6%); see Table S1 for the full list of psoriasis treatments taken concomitantly to secukinumab.

Efficacy and retention

As all patients received at least 16 weeks of secukinumab treatment before enrolment in the study, treatment start occurred at an earlier timepoint to study baseline. Treatment start data were collected retrospectively and were not available for all patients or for all efficacy parameters.

The secukinumab treatment retention rates after 1, 2 and 3 years in the study were 88.0%, 76.4% and 60.5%, respectively.

Table 1 Patient baseline characteristics and demographics (target population)

Demographic/Baseline characteristic	Psoriasis (*N* = 1756)
Age (years), mean ± SD	48.4 ± 13.5
Gender, male, *n* (%)	1181 (67.3%)
Race, white, *n* (%)	1654 (94.2%)
Body weight (kg), mean ± SD	87.4 ± 20.4
BMI (kg/m^2), mean ± SD	28.8 ± 6.1
Overweight, 25≤BMI<30 (kg/m^2), *n* (%)	506 (37.6%)
Obesity, BMI≥30 (kg/m^2), *n* (%)	477 (35.4%)
Smoking status, *n* (%)	
Current	547 (31.2%)
Former	241 (13.7%)
Never	688 (39.2%)
Time since first diagnosis of plaque psoriasis (years), mean ± SD	17.3 ± 13.2
Duration with any secukinumab treatment prior to inclusion (years), mean ± SD	1.08 ± 0.7
Concomitant PsA at inclusion in the study, *n* (%)	406 (23.1%)*
Time since diagnosis of PsA (years), mean ± SD	10.6 ± 10.1
Clinical characteristics at time of diagnosis	
Medical history term by severity of psoriasis diagnosis	
Severe, *n* (%)	861 (49.0%)
Moderate, *n* (%)	868 (49.4%)

*Data on PsA at inclusion in the study were unavailable for two patients.
Subjects were receiving the secukinumab 300 mg dose.
BMI, body mass index; *N*, total number of patients; *n*, number of patients with non-missing data; PsA, psoriatic arthritis; SD, standard deviation.

Table 2 Percentage of psoriasis patients by treatment type prior to secukinumab initiation

Psoriasis treatments taken prior to secukinumab initiation	Psoriasis (*N* = 1756)
No documented psoriasis treatment, *n* (%)	724 (41.2%)
Topical treatments, *n* (%)	95 (5.4%)
Conventional systemic treatments/phototherapy, *n* (%)	243 (13.8%)
Biologic treatments, *n* (%)	353 (20.1%)
Topical and conventional systemic treatments/phototherapy, *n* (%)	113 (6.4%)
Topical and biologic treatments, *n* (%)	44 (2.5%)
Conventional systemic treatments/phototherapy and biologic treatments, *n* (%)	141 (8.0%)
Topical, conventional systemic treatments/phototherapy and biologic treatments, *n* (%)	43 (2.4%)
Biologic treatments* taken prior to secukinumab initiation	
Biologic naive, *n* (%)	1157 (65.9%)
Previous treatment with a biologic, *n* (%)	599 (34.1%)
1 biologic treatment pre-secukinumab, *n* (%)	291 (48.6%)†
2 biologic treatments pre-secukinumab, *n* (%)	152 (25.4%)†
≥3 biologic treatments pre-secukinumab, *n* (%)	156 (26.0%)†

*Prescribed for the treatment of either psoriasis or psoriatic arthritis.
†Calculated as a percentage of patients previously treated with a biologic (*n* = 599).
The most commonly taken biologics prior to secukinumab initiation were adalimumab (19.6%), ustekinumab (14.5%), etanercept (14.0%) and infliximab (7.3%). *N*, total number of patients; *n*, number of patients with non-missing data.

Time to treatment discontinuation is displayed in Fig. 1. Of the 648 patients who discontinued the study, the most common reasons provided included lack of efficacy (42.6%), adverse event (17.4%), physician decision (12.2%) and subject decision (11.6%; Table 3).

The mean ± SD absolute PASI was 21.0 ± 13.0 at the start of treatment (*n* = 1564). At Baseline, the mean ± SD PASI score reduced to 2.6 ± 4.8 (*n* = 1621) and remained low at Year 1 (2.3 ± 4.3; *n* = 1392), Year 2 (1.9 ± 3.6; *n* = 1056) and Year 3 (1.9 ± 3.5; *n* = 439; Fig. 2). Absolute PASI ≤3/≤2/≤1 responses were 74.2%/64.6%/49.9% at Baseline, 76.5%/68.3%/55.7% at Year 1, 80.1%/70.9%/54.9% at Year 2, and 81.8%/70.4%/58.1% at Year 3, respectively (Fig. 3).

The proportion of patients achieving a PGA score of 0 or 1 (clear or almost clear skin) was 72.0% (527/732), 77.6% (578/745), 81.7% (470/575) and 78.2% (204/261) at Baseline, Year 1, Year 2, and Year 3, respectively (Fig. 4a). PGA score data at treatment start were not available.

The proportion of patients achieving a DLQI score of 0 or 1 (little to no impact on QoL) was 61.0% (929/1523), 63.6% (829/1304), 66.3% (652/984) and 64.5% (274/425) at Baseline, Year 1, Year 2, and Year 3, respectively (Fig. 4b). DLQI score data at treatment start were not available. Total DLQI score showed a correlation with total PASI score at Year 1 (*r* = 0.55), Year 2

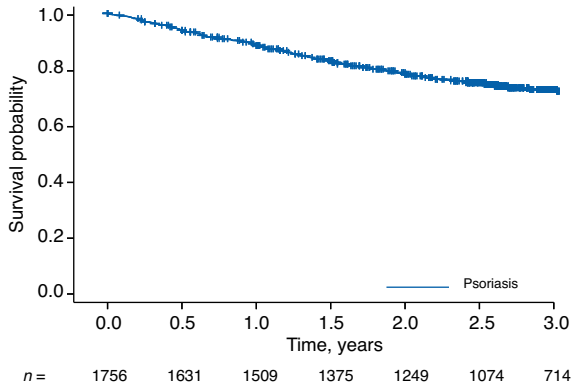

Figure 1 Time to secukinumab treatment discontinuation for psoriasis patients (survival probability)*. *Since enrolment in the study. *n* = number of patients with evaluation (i.e. with non-missing data).

Table 3 Reasons for study discontinuation

Reasons for study discontinuation	Psoriasis (*N* = 1756)
n	648
Lack of efficacy	276 (42.6)
AE	113 (17.4)
Physician decision	79 (12.2)
Subject decision	75 (11.6)
Lost to follow-up	47 (7.3)
Administrative reason	28 (4.3)
Withdrawal of informed consent	14 (2.2)
Death	12 (1.9)
COVID-19 outbreak-related (not an AE)	4 (0.6)

AE, adverse event; COVID-19, coronavirus disease 2019; *N*, total number of patients; *n*, number of patients with non-missing data.

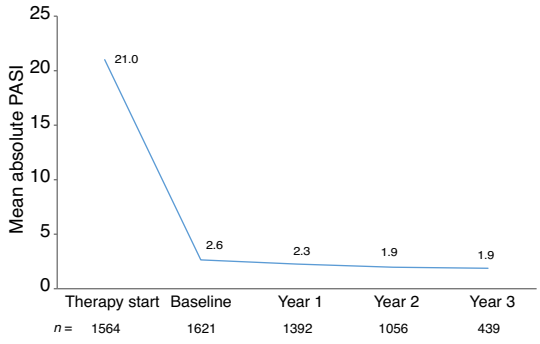

Figure 2 Absolute PASI at secukinumab treatment start and during the study (Therapy start; Baseline; Year 1; Year 2, Year 3). *n* = number of patients with evaluation (i.e. with non-missing data). Patients were treated with secukinumab for a mean ± SD duration of 1.1 ± 0.7 years prior to baseline. PASI, Psoriasis Area and Severity Index.

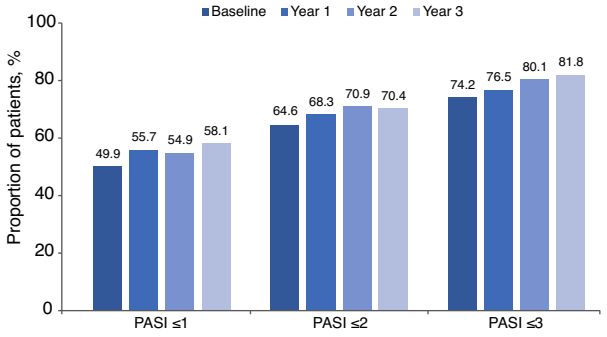

Figure 3 Absolute PASI bands (≤3, ≤2, ≤1) at Baseline, Year 1, Year 2 and Year 3. Total number of patients with evaluation (i.e. with non-missing data) at Baseline, Year 1, Year 2 and Year 3 were 1621, 1392, 1056 and 439 respectively. Mean ± SD absolute PASI score at treatment start was 21.0 ± 13.0, *n* = 1564. Patients were treated with secukinumab for a mean ± SD duration of 1.1 ± 0.7 years prior to baseline. PASI, Psoriasis Area and Severity Index.

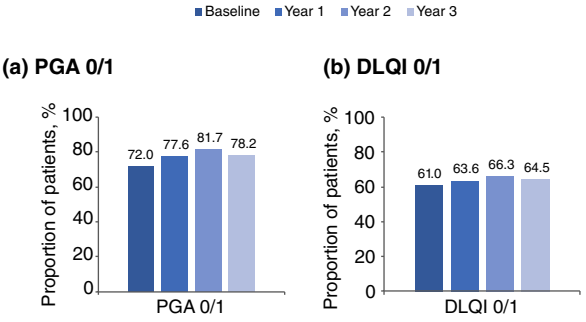

Figure 4 Proportion of patients with PGA 0/1 (a) and DLQI 0/1 (b) responses at Baseline, Year 1, Year 2 and Year 3. Percentages are based on the number of patients with non-missing data. Total number of patients with evaluation at Baseline, Year 1, Year 2 and Year 3 were 732, 745, 575 and 261 for PGA, and 1523, 1304, 984 and 425 for DLQI, respectively. Patients were treated with secukinumab for a mean ± SD duration of 1.1 ± 0.7 years prior to baseline. DLQI, Dermatology Life Quality Index; PGA, Physician's Global Assessment.

(r = 0.55) and Year 3 (r = 0.57), as well as with PGA score at Year 1 (r = 0.56), Year 2 (r = 0.56) and Year 3 (r = 0.54).

The mean ± SD total BSA percentage affected by plaque-type PsO was 4.1 ± 7.3 at Baseline, 3.1 ± 6.3 at Year 1, 2.4 ± 4.3 at Year 2, and 2.5 ± 5.0 at Year 3 (Fig. 5a). The proportion of PsO patients with dactylitis was 2.0% at Baseline, 1.1% at Year 1, 0.9% at Year 2, and 0.6% at Year 3 (Fig. 5b). The proportion of PsO patients with nail involvement was 24.4% at Baseline, 8.4% at Year 1, 7.8% at Year 2, and 8.2% at Year 3 (Fig. 5c). Data at

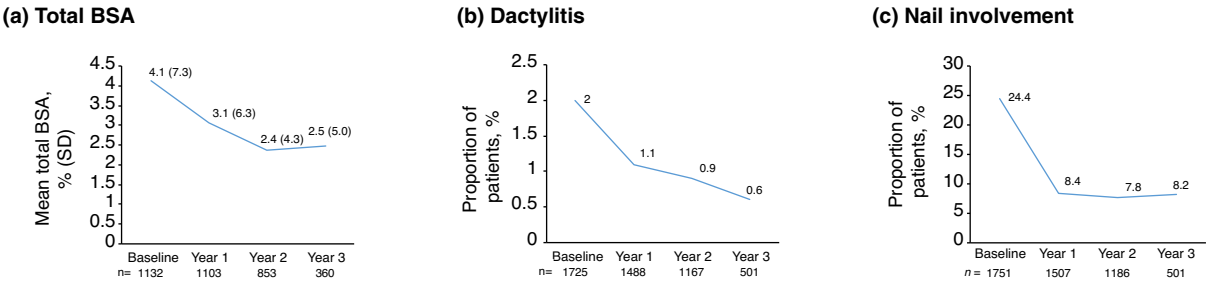

Figure 5 Total BSA (a) and Dactylitis (b) and Nail involvement (c) at Baseline, Year 1, Year 2 and Year 3. *n* = number of patients with evaluation (i.e. with non-missing data); SD, standard deviation. Patients were treated with secukinumab for a mean ± SD duration of 1.1 ± 0.7 years prior to baseline. BSA, body surface area.

treatment start for mean total BSA percentage involvement, and the proportion of patients with dactylitis and nail involvement were not available.

Treatment interruption

In total, 178 patients with PsO had an interruption in secukinumab treatment lasting >2 months since initiation of secukinumab (Table 4). Where available, the reported reasons for treatment interruption were adverse event (AE; 25.3%); subject decision (14.0%); 'other' (7.3%); lack of patient adherence (5.1%); COVID-19 outbreak-related reasons that were not an AE (5.1%); complete remission of clinical signs and symptoms (3.4%); lack of efficacy (2.8%); and treatment change according to approved product information (0.6%). The reason for treatment interruption was not recorded for 36.5% of patients. The median [lower quartile (Q1), upper quartile (Q3)] duration of treatment interruption in the study was 130.5 (90.0, 227.0) days.

After the treatment interruption, 26.4% (47/178) of patients re-started secukinumab treatment with a re-loading phase, while 53.4% (95/178) of patients re-started secukinumab treatment with maintenance dosing; these data were not available for 20.2% (36/178) of patients. The median (Q1, Q3) duration of treatment interruption was greater in patients who restarted treatment with a re-loading phase [193.0 (129.0, 275.0) days, $n = 47$] compared with patients who restarted secukinumab treatment with maintenance dosing [97.0 (75.0, 149.0) days, $n = 95$; Table S2]. Although available assessments were limited, the first available mean ± SD PASI during the treatment interruption was greater in patients who restarted treatment with a re-loading phase (9.4 ± 13.0, $n = 6$) compared with patients who restarted secukinumab treatment with maintenance dosing (3.7 ± 6.1, $n = 25$). Mean ± SD PASI at the assessment closest to 6 months post-treatment interruption was low in both patients who restarted with a loading phase (2.6 ± 2.7, $n = 33$) or with maintenance dosing (2.0 ± 2.8, $n = 72$).

The median (Q1, Q3) duration of secukinumab treatment prior to the treatment interruption was 482.5 (212.0, 910.0) days. After the treatment interruption, the median (Q1, Q3) duration of secukinumab treatment was 670.0 (312.0, 1103.0) days.

Overall, absolute mean ± SD PASI continued to decrease over time from the last assessment prior to treatment interruption (9.0 ± 11.1, $n = 126$), to the first assessment during the treatment interruption (5.5 ± 9.5, $n = 47$), to the assessment closest to 6 months post-treatment interruption (2.2 ± 2.8, $n = 105$).

Mean ± SD PGA score remained stable throughout the last assessment prior to the treatment interruption (1.1 ± 1.2, $n = 43$), to the first assessment during the treatment interruption (1.3 ± 1.4, $n = 19$), to the assessment closest to 6 months post-treatment interruption (1.1 ± 1.3, $n = 33$).

Safety

The safety profile of secukinumab during the SERENA study, based on 4412.0 years of total secukinumab exposure, was consistent with the known secukinumab safety profile, with no new safety signals reported for the duration of the interim analysis (Table 5). This observational study revealed particularly low rates of inflammatory bowel disease (IBD), candida infections and severe infections, confirming the favourable safety profile of secukinumab demonstrated in the development program.

The overall number of AEs reported in the study was 3143, while the total number of patients who experienced at least one AE was 1132 (61.7%). The overall number of serious adverse events (SAEs) reported in the study was 281, and the total number of patients who experienced at least one SAE was 187 (10.2%). The most common SAEs (system organ class, SOC) were infections and infestations, reported by 2.4% of patients [Incidence Rate (IR): 1.21]. The number of patients with AEs leading to death was 15 (0.8%). Causality of death was not

Table 4 Characterization of secukinumab treatment interruption including PASI and PGA score relative a treatment interruption

	Psoriasis (*N* = 1756)
Number of patients reporting a treatment interruption*	178
Duration of treatment interruption (days), median (Q1, Q3)	130.5 (90.0, 227.0)
Treatment phase directly after treatment interruption	
Initiation phase/Re-loading, *n* (%)	47 (26.4)
Maintenance dosing/Non-loading, *n* (%)	95 (53.4)
Missing, *n* (%)	36 (20.2)
Duration of treatment with secukinumab	
Before interruption (days), median (Q1, Q3)	482.5 (212.0, 910.0)
After interruption (days), median (Q1, Q3)	670.0 (312.0, 1103.0)
Most common reasons for treatment interruption†	
Adverse event, *n* (%)	45 (25.3%)
Subject decision, *n* (%)	25 (14.0%)
Other, *n* (%)	13 (7.3%)
Lack of patient adherence, *n* (%)	9 (5.1%)
COVID-19 outbreak related (not an AE), *n* (%)	9 (5.1%)
PASI relative a treatment interruption	
Last assessment prior, mean ± SD, *n*	9.0 ± 11.1, 126
First assessment during, mean ± SD, *n*	5.5 ± 9.5, 47
Assessment closest to 6 months post-, mean ± SD, *n*	2.2 ± 2.8, 105
PGA score relative a treatment interruption	
Last assessment prior, mean ± SD, *n*	1.1 ± 1.2, 43
First assessment during, mean ± SD, *n*	1.3 ± 1.4, 19
Assessment closest to 6 months post-, mean ± SD, *n*	1.1 ± 1.3, 33

*A treatment interruption was defined as lasting longer than 2 months (i.e. 3 months since last injection of secukinumab); shorter treatment interruptions were not included. If a patient had more than one treatment interruption then the interruption with the longest duration was included in the analysis.
†Occurring in more than 5% of the total reported treatment interruptions.
AE, adverse event; COVID-19, coronavirus disease 2019; *N*, total number of patients; *n*, number of patients with non-missing data; PASI, Psoriasis Area and Severity Index; Q1–Q3 interquartile range; PGA, Physician's Global Assessment; SD, standard deviation.

Table 5 Adverse events observed during the total study (Safety set)

Treatment emergent AEs	**Psoriasis patients (*N* = 1835)**	
Total exposure time, years	4412.0	
Mean exposure time, years	2.4	
All AEs	3143	
Number of patients with at least one AE, *n* (%)	1132 (61.7%)	
All SAEs	281	
Number of patients with at least one SAE, *n* (%)	187 (10.2%)	
Number of patients with AEs leading to death, *n* (%)	15 (0.8%)	
Discontinued study treatment due to AE, *n* (%)	384 (20.9%)	
Most common AEs by System Organ Class*	***n* (%)**	**Incidence Rate**
Infections and infestations	510 (27.8)	20.15
Skin and subcutaneous tissue disorders	372 (20.3)	10.54
General disorders and administration site conditions	288 (15.7)	6.96
Musculoskeletal and connective tissue disorders	227 (12.4)	6.88
Gastrointestinal disorders	129 (7.0)	3.86
Injury, poisoning and procedural complications	114 (6.2)	2.95
AEs of special interest by System Organ Class	***n* (%)**	**Incidence rate**
Candida Infections	56 (3.1)	1.43
Candida infection (PT)	19 (1.0)	0.48
Oral candidiasis (PT)	28 (1.5)	0.71
Skin candida (PT)	5 (0.3)	0.11
Serious infections	44 (2.4)	1.21
Malignancy	41 (2.2)	1.06
IBD	6 (0.3)	0.15
MACE	16 (0.9)	0.37
Injection site reaction	8 (0.4)	0.18

*Incidence Rate > 2.
AE, adverse event; IBD, Inflammatory bowel disease; MACE, major adverse cardiovascular event; *N*, total number of patients; *n*, number of patients in group; PT, preferred term; SAE, serious adverse event.

considered to be related to secukinumab treatment in any of these cases. In total, 384 patients (20.9%) discontinued secukinumab treatment due to an AE. The most common AE leading to secukinumab treatment discontinuation was lack of efficacy (11.1% of AEs leading to discontinuation).

Infections and infestations (SOC) were the most commonly reported AEs throughout the study (27.8% of patients; IR: 20.15). Candida infections (SOC) were experienced by 3.1% of patients (IR: 1.43); of these, the most commonly reported preferred terms were: candida infections, experienced by 1% of patients (IR:0.48); oral candidiasis, experienced by 1.5% of patients (IR:0.71), and skin candida, experienced by 0.3% of patients (IR:0.11).

Overall, 2.2% of patients reported any malignancy (IR:1.06), the most common of which was basal cell carcinoma 0.7% of patients (IR:0.31). Major adverse cardiovascular events (MACE) were experienced by 0.9% of patients (IR:0.37). The identified risks of IBD and injection site reaction were reported in 0.3% of patients (IR:0.15) and 0.4% of patients (IR:0.18), respectively.

Discussion

SERENA is the first European observational study to collect real-world data for up to 5 years on the retention, effectiveness, safety, tolerability, treatment pattern and effects on QoL of secukinumab in patients with active moderate-to-severe plaque psoriasis, active PsA and active AS. The secukinumab treatment retention rates after 1, 2 and 3 years in the study were 88.0%, 76.4% and 60.5%, respectively, suggesting high treatment

persistence in the real-world population observed in the SERENA study.

Secukinumab showed sustained effectiveness up to 3 years of follow-up in patients with moderate to severe PsO in real-world settings. Secukinumab also demonstrated improvements in health-related QoL, with the majority of patients (63.6%) seeing no impact of PsO on QoL after one year in the study. No new safety signals were reported at the time of interim analysis and secukinumab was well-tolerated in real-world settings.

There are several limitations to this observational study. In particular, data are only collected from patients who remain on secukinumab treatment for follow-ups, which could lead to patient selection bias. As the inclusion criterion was patients with at least 16 weeks of secukinumab treatment prior to study entry, patients who did not achieve a satisfactory result during the first 16 weeks of treatment and discontinued secukinumab did not enter the study. Only 714 of 1756 and 439 of 1574 patients are evaluated at 3 years for persistence and absolute PASI, respectively, which may reduce the reliability of the results at this timepoint. Finally, there is no control group with which to compare the results against.

As with all observational studies, incompleteness of the data is a limitation; notably, detailed reasons (for example, clinical information) for treatment discontinuation were not always recorded. Lack of efficacy was the most common reason given for study discontinuation (42.6%). However, dose optimization strategies that may improve efficacy and thus help to avoid treatment discontinuation in patients with a higher weight[27], for example, were not yet available at the time of this analysis. Finally, numbers for the treatment interruption analysis were quite low, and the before, during and after treatment interruption PASI and PGA assessments were not available for each patient.

In the treatment interruption analysis, PASI and PGA assessments before treatment interruption were 9.04 ± 11.07 ($n = 126$) and 1.09 ± 1.19 ($n = 43$), respectively. PASI, but not PGA, was unusually high considering the entry criteria of at least 16 weeks of secukinumab treatment before enrolment in the study. This implies that the group of patients with available PASI, but not PGA, assessments prior to the treatment interruption may have had a more severe disease prior to treatment interruption. One further possible explanation is that few patients with high PASI scores prior to treatment interruption are skewing the results. Reasons for treatment interruption included AE (25.3%), lack of patient adherence (5.1%) and lack of efficacy (2.8%), which could all have been associated with an increased PASI score in this patient population. Furthermore, a high proportion of reasons for treatment interruption were not recorded (36.5%).

Reasons for re-initiation of treatment specifically were not collected. Patients who restarted secukinumab treatment with a re-loading phase had a longer duration of treatment interruption and a higher first available PASI during treatment interruption compared with patients who restarted treatment with maintenance dosing. However, mean PASI at 6 months post-treatment interruption was low in both groups of patients. This highlights the importance of tailoring treatment patterns to the individual patient to optimize long-term outcomes. Overall, this analysis implies that the long-term effectiveness of secukinumab is not impacted by treatment interruption.

Aknowledgement

The authors thank Daniella Taylor, MA (Novartis Pharmaceuticals UK Ltd, London, UK) for providing medical writing support/editorial support, which was funded by Novartis Pharma AG, Basel, Switzerland in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Data availability statement

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

References

1 Merola JF, Qureshi A, Husni ME. Underdiagnosed and undertreated psoriasis: Nuances of treating psoriasis affecting the scalp, face, intertriginous areas, genitals, hands, feet, and nails. *Dermatol Ther* 2018; **31** (3): e12589.
2 Mease PJ, Gladman DD, Papp KA *et al*. Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. *J Am Acad Dermatol* 2013; **69**(5): 729–735.
3 Crowley J. Scalp psoriasis: an overview of the disease and available therapies. *J Drugs Dermatol* 2010; **9**(8): 912–918.
4 Richette P, Tubach F, Breban M *et al*. Psoriasis and phenotype of patients with early inflammatory back pain. *Ann Rheum Dis* 2013; **72**(4): 566–571.
5 Baran R. The burden of nail psoriasis: an introduction. *Dermatology* 2010; **221**(Suppl 1): 1–5.
6 Frieder J, Kivelevitch D, Fiore CT, Saad S, Menter A. The impact of biologic agents on health-related quality of life outcomes in patients with psoriasis. *Expert Rev Clin Immunol* 2018; **14**(1): 1–19.
7 Armstrong AW, Schupp C, Wu J, Bebo B. Quality of life and work productivity impairment among psoriasis patients: findings from the National Psoriasis Foundation survey data 2003-2011. *PLoS One* 2012; **7** (12): e52935.
8 Eskin M, Savk E, Uslu M, Küçükaydoğan N. Social problem-solving, perceived stress, negative life events, depression and life satisfaction in psoriasis. *J Eur Acad Dermatol Venereol* 2014; **28**(11): 1553–1559.
9 Thaçi D, Blauvelt A, Reich K *et al*. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol* 2015; **73** (3): 400–409.
10 Res PC, Piskin G, de Boer OJ *et al*. Overrepresentation of IL-17A and IL-22 producing CD8 T cells in lesional skin suggests their involvement in the pathogenesis of psoriasis. *PLoS One* 2010; **5**(11): e14108.
11 Jin W, Dong C. IL-17 cytokines in immunity and inflammation. Emerg. *Microbes Infect* 2013; **2**(9): e60-e.
12 Lynde CW, Poulin Y, Vender R, Bourcier M, Khalil S. Interleukin 17A: toward a new understanding of psoriasis pathogenesis. *J Am Acad Dermatol* 2014; **71**(1): 141–150.

13 Krueger JG, Wharton KA Jr, Schlitt T *et al*. IL-17A inhibition by secukinumab induces early clinical, histopathologic, and molecular resolution of psoriasis. *J Allergy Clin Immunol* 2019; **144**(3): 750–763.
14 McGonagle DG, McInnes IB, Kirkham BW, Sherlock J, Moots R. The role of IL-17A in axial spondyloarthritis and psoriatic arthritis: recent advances and controversies. *Ann Rheum Dis* 2019; **78**(9): 1167–1178.
15 Blauvelt A, Chiricozzi A. The immunologic role of IL-17 in psoriasis and psoriatic arthritis pathogenesis. *Clin Rev Allergy Immunol* 2018; **55**(3): 379–390.
16 Langley RG, Elewski BE, Lebwohl M *et al*. Secukinumab in plaque psoriasis--results of two phase 3 trials. *N Engl J Med* 2014; **371**(4): 326–338.
17 McInnes IB, Mease PJ, Kirkham B *et al*. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2015; **386**(9999): 1137–1146.
18 Bagel J, Duffin KC, Moore A *et al*. The effect of secukinumab on moderate-to-severe scalp psoriasis: Results of a 24-week, randomized, double-blind, placebo-controlled phase 3b study. *J Am Acad Dermatol* 2017; **77**(4): 667–674.
19 Gottlieb A, Sullivan J, van Doorn M *et al*. Secukinumab shows significant efficacy in palmoplantar psoriasis: Results from GESTURE, a randomized controlled trial. *J Am Acad Dermatol* 2017; **76**(1): 70–80.
20 Bissonnette R, Luger T, Thaçi D *et al*. Secukinumab demonstrates high sustained efficacy and a favourable safety profile in patients with moderate-to-severe psoriasis through 5 years of treatment (SCULPTURE Extension Study). *J Eur Acad Dermatol Venereol* 2018; **32**(9): 1507–1514.
21 Reich K, Sullivan J, Arenberger P *et al*. Effect of secukinumab on the clinical activity and disease burden of nail psoriasis: 32-week results from the randomized placebo-controlled TRANSFIGURE trial. *Br J Dermatol* 2019; **181**(5): 954–966.
22 Reich K, Warren RB, Coates LC, Di Comite G. Long-term efficacy and safety of secukinumab in the treatment of the multiple manifestations of psoriatic disease. *J Eur Acad Dermatol Venereol* 2020; **34**(6): 1161–1173.
23 Mease PJ, Kavanaugh A, Reimold A *et al*. Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Psoriatic Arthritis: Final 5-year Results from the Phase 3 FUTURE 1 Study. *ACR Open Rheumatol* 2020; **2**(1): 18–25.
24 Deodhar A, Mease PJ, McInnes IB *et al*. Long-term safety of secukinumab in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis: integrated pooled clinical trial and post-marketing surveillance data. *Arthritis Res Ther* 2019; **21**(1): 111.
25 Augustin M, Jullien D, Martin A, Peralta C. Real-world evidence of secukinumab in psoriasis treatment - a meta-analysis of 43 studies. *J Eur Acad Dermatol Venereol* 2020; **34**(6): 1174–1185.
26 Kiltz U, Sfikakis PP, Gaffney K *et al*. Secukinumab use in patients with moderate to severe psoriasis, psoriatic arthritis and ankylosing spondylitis in real-world setting in europe: baseline data from SERENA Study. *Adv Ther* 2020; **37**(6): 2865–2883.
27 Augustin M, Reich K, Yamauchi P *et al*. Secukinumab dosing every two weeks demonstrated superior efficacy compared with dosing every four weeks in patients with psoriasis weighing 90 kg or more: results of a randomised controlled trial. *Br J Dermatol* 2022; **186**(6): 942–954.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Percentage of psoriasis patients by treatment type taken concomitantly to secukinumab.
Table S2. Duration of secukinumab treatment interruption and PASI score relative a treatment interruption* by patients who reinitiated treatment with re-loading or maintenance dosing.