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# Long-term efficacy and safety of secukinumab in patients with psoriatic arthritis: 5-year (end-of-study) results from the phase III FUTURE 2 study

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| **Abstract:** | Background: Secukinumab is an interleukin (IL)-17A inhibitor used in the treatment of patients with active psoriatic arthritis (PsA). In the phase III FUTURE 2 trial, secukinumab demonstrated sustained improvement in clinical outcomes over 2 years. Herein we report the 5-year (end-of-study) efficacy and safety of secukinumab across doses and dose escalation from the trial.<br>Methods : Patients with active PsA aged ≥18 years were randomised to either secukinumab (300, 150, or 75 mg) or placebo weekly from baseline and then every 4 weeks from Week 4. Secukinumab dose was escalated from 150 to 300 mg and 75 to 150 or 300 mg starting at Week 128, if active signs of disease were observed in patients based on the physician's assessment; the escalated dose was maintained thereafter. Results are presented for key efficacy endpoints at Week 260 (5 years) for secukinumab 300 and 150 mg. Data are reported as observed. This study was registered with ClinicalTrials.gov, number NCT01752634.<br>Findings : At randomisation, 65% of patients were tumour necrosis factor inhibitor-naïve and 47% were receiving concomitant methotrexate. Of 397 patients randomised, 248 (62·5%) completed 5 years of treatment. Overall, 52·5% of patients required dose escalation during the study. American College of Rheumatology (ACR) 20/50/70 responses at 5 years were 74·0%/52·1%/32·3% in thesecukinumab 300 mg group and 69·8%/42·7%/29·2% in the secukinumab 150 mg group.Following dose escalation, the proportions of ACR and PASI non-responders decreased, while, the proportions of ACR and PASI responders increased. No new or unexpected safety signals were reported.<br>Interpretation: Secukinumab 300 and 150 mg provide sustained improvement in the signs and symptoms of PsA with consistent safety over 5 years. This study confirms the clinical benefit and safety of long-term treatment with secukinumab in PsA. |

**Title:** Secukinumab sustains improvement in signs and symptoms of psoriatic arthritis: long-term 5-year (end-of-study) results from the phase III FUTURE 2 study

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**Abstract:**

**Background:** Secukinumab is an interleukin (IL)-17A inhibitor used in the treatment of patients with active psoriatic arthritis (PsA). Herein we evaluated the 5-year (end-of-study) efficacy and safety of secukinumab across doses and dose escalation from the phase III FUTURE 2 trial.

**Methods**: Patients with active PsA aged ≥18 years were randomised to either secukinumab (300, 150, or 75 mg) or placebo weekly from baseline and then every 4 weeks from Week 4. Secukinumab dose was escalated from 150 to 300 mg and 75 to 150 or 300 mg starting at Week 128, if active signs of disease were observed in patients based on the physician's assessment; the escalated dose was maintained thereafter. Results are presented for key efficacy endpoints at Week 260 (5 years) for secukinumab 300 and 150 mg. Data are reported as observed. This study was registered with ClinicalTrials.gov, number NCT01752634.

**Findings**: At randomisation, 65% of patients were tumour necrosis factor inhibitor-naïve and 47% were receiving concomitant methotrexate. Of 397 patients randomised, 248 (62·5%) completed 5 years of treatment. Overall, 52·5% of patients required dose escalation during the study. American College of Rheumatology (ACR) 20/50/70 responses at 5 years were 74·0%/52·1%/32·3% in the secukinumab 300 mg group and 69·8%/42·7%/29·2% in the secukinumab 150 mg group. In patients who dose escalated, the proportions of patients achieving ACR and Psoriasis Area and Severity Index (PASI) responses were increased. No new or unexpected safety signals were reported.

**Interpretation:** Secukinumab 300 and 150 mg provide sustained improvement in the signs and symptoms of PsA over 5 years. ACR and PASI responses were improved in patients who had dose escalation. Secukinumab was well tolerated over 5 years with no unexpected safety signals.

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## Research in context

### Evidence before this study

Interleukin (IL)-17 plays a crucial role in the pathogenesis of psoriasis and psoriatic arthritis (PsA). Secukinumab, a human monoclonal antibody that directly inhibits IL-17A, has demonstrated sustained efficacy and consistent safety in patients with PsA across phase III FUTURE studies. In the FUTURE 2 study, secukinumab 300 and 150 mg demonstrated sustained improvement in multiple clinical domains and consistent safety over 2 years. The scientific literature in the English language were reviewed in PubMed using the search terms "PsA", "IL-17", "biological disease-modifying anti-rheumatic drug (bDMARD)", and "tumour necrosis factor inhibitors (TNFi)" published up to August 31, 2019, with no limitation or restriction for year of publication or article type.

### Added value of this study

The data presented here are the first long-term (5-year) efficacy and safety outcomes in PsA patients treated with subcutaneous loading and maintenance dosing of secukinumab 300 and 150 mg.

### Implications of all the available evidence

This study confirms the clinical benefit and consistent safety of long-term treatment with secukinumab (IL-17A inhibition) in the treatment of patients with active PsA, further expanding on previous reports from the FUTURE studies.

## Introduction

Psoriatic arthritis (PsA) is an immune-mediated chronic inflammatory arthropathy, which is characterised by peripheral articular and axial manifestations, dactylitis, and enthesitis. PsA has an estimated prevalence of up to 30% in patients with psoriasis, comprising 1–3% of the general population.[1-5] PsA is a lifelong condition requiring access to durable therapeutic agents. Early diagnosis and assessment of disease severity is important for timely treatment initiation, leading to sustained long-term therapeutic benefit and quality of life (QoL).[6-8]

The interleukin (IL)-17 pathway plays a crucial role in the pathogenesis of psoriasis and PsA.[9] According to the European League Against Rheumatism (EULAR) 2015 and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2015 recommendations, IL-17A inhibitors are the proposed treatment options to manage the major clinical manifestations of PsA.[10, 11] In the 2018 update of the American College of Rheumatology (ACR) and National Psoriasis Foundation guideline, IL-17 inhibitors are recommended for the treatment of PsA patients with severe psoriasis or contraindications to first-line treatment with tumour necrosis factor inhibitors (TNFi).[12]

Secukinumab, a human monoclonal antibody that directly inhibits IL-17A, demonstrated sustained clinical responses with a consistent safety profile for the treatment of patients with PsA across the phase III FUTURE study programme.[13-18] In particular, in the FUTURE 2 study, secukinumab 300 and 150 mg provided sustained improvements in multiple clinical domains and consistent safety in patients with PsA over 2 years.[19] Secukinumab, administered at 300 and 150 mg subcutaneous (s.c.) doses, is an approved biological disease-modifying anti-rheumatic drug (bDMARD) for PsA, together with TNFi and IL-12/23 inhibitors. Given that there are relatively limited data on the long-term treatment of PsA, our aim was to evaluate and describe the 5-year

(end-of-study) efficacy and safety results from the FUTURE 2 study. We also took this opportunity to assess efficacy in patients who required dose escalation during the course of the study.

## Methods

### Study design and patients

The study design with detailed inclusion and exclusion criteria has been reported previously.[13] In brief, FUTURE 2 was a phase III, double-blind, placebo-controlled trial conducted in 76 centres across the globe. Patients aged ≥18 years with active PsA who met the ClASsification criteria for Psoriatic ARthritis (CASPAR) were randomised to receive s.c. secukinumab (300, 150, or 75 mg) or placebo at baseline, Weeks 1, 2, 3 and 4, followed by every 4 weeks (q4w) starting at Week 4. Placebo patients were re-randomised to s.c. secukinumab 300 or 150 mg (referred to as placebo-switchers hereafter) q4w either at Week 16 (non-responders) or 24 (responders) depending upon ACR20 response. After the Week 52 analysis was conducted, site personnel and patients were unblinded to the treatment regimen. Randomisation was stratified, as pre-specified, by TNFi status (TNFi-naïve and inadequate response or intolerance to these agents [IR]) with ~40% of randomised patients planned to be TNFi-IR.

Following a protocol amendment, patients were escalated from secukinumab 150 to 300 mg and from 75 to 150 or 300 mg starting at Week 128, if active signs of disease were observed based on the physician's judgement, with the escalated dose maintained thereafter; patients were not allowed to switch to a lower dose once dose escalation occurred. Patients continued to receive the same active dose of secukinumab in an open-label fashion until Week 256.

The study was conducted in accordance with the principles of the Declaration of Helsinki[20], International Conference of Harmonisation – Good Clinical Practice guidelines, and

all applicable laws and regulations. All centres received approval from an independent ethics committee or institutional review board. Written informed consent was obtained from all enrolled patients. Data were collected in accordance with Good Clinical Practice guidelines by the study investigators and were analysed by the sponsor.

**Outcomes**

Efficacy assessments at Week 260 (5 years) included the proportion of patients with ACR20, 50 and 70 responses, and Psoriasis Area and Severity Index (PASI) 75 and 90 responses; mean change from baseline in the Short Form-36 Physical Component Summary (SF-36 PCS), 28-joint Disease Activity Score using C-Reactive Protein (DAS28-CRP), Health Assessment Questionnaire-Disability Index (HAQ-DI), and Psoriatic Arthritis Disease Activity Score (PASDAS); and the proportion of patients with resolution of dactylitis and enthesitis, and Minimal Disease Activity (MDA).

Long-term safety and tolerability of secukinumab were assessed by monitoring the frequency of treatment-emergent adverse events (AEs) and serious AEs (SAEs), injection site reactions, immunogenicity, abnormal laboratory findings, electrocardiograms, physical examinations, vital signs, and clinical laboratory variables over time up to 84 days after the last administration of treatment.

**Statistical analysis**

The details of the sample size calculation and statistical analysis have been reported previously.[13] The ACR20 and 50 responses are reported for patients originally randomised to secukinumab 300 and 150 mg to show the full 5-year efficacy, and separately for all patients in the secukinumab 300 and 150 mg treatment doses (i.e. including patients originally randomised to secukinumab and placebo-switchers). Efficacy results are reported as observed data (summary

statistics for binary and continuous variables). Summary statistics for binary variables included absolute and relative frequencies and for continuous variables included total number (N), mean, and standard deviation (SD). Pre-defined subgroup analyses were carried out on the basis of previous TNFi therapy and concomitant methotrexate (MTX) treatment and reported using observed data. For patients who discontinued during a study treatment period, the end of treatment visit was considered as the last week of the period.

The dose escalation analysis included all patients from the overall population who received at least one dose of the escalated dose. 'Before escalation' is defined as the last assessment done on or before the patient took the escalated dose. The bar chart with Sankey-style overlay presented for ACR and PASI responses corresponds to all patients (including placebo-switchers) who escalated from secukinumab 150 to 300 mg. Each ACR20, 50, and 70 responses and PASI 75 and 90 responses were categorised in mutually exclusive response categories. Patients (originally randomised to secukinumab and placebo-switchers) with non-missing assessment values at all the corresponding time points are included.

The safety analysis included all patients who received ≥1 dose of secukinumab. Data are presented as exposure-adjusted incidence rates (EAIR) per 100 patient-years over the entire treatment period, which referred as cumulative treatment period including (i.e. started after the first dose of secukinumab and within 84 days after the last dose of secukinumab). The AEs reported were based on the actual treatment received; therefore, patients that experienced any AEs after the dose escalation are summarised under the higher dose. AEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) version 21·0 preferred terms (PTs). All analyses were computed with SAS version 9·4. This study is registered with ClinicalTrials.gov, NCT01752634.

**Role of the funding source**

A scientific steering committee and the funder designed the study. The statisticians employed by the funder performed the data and statistical analyses. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis, and participated in the decision to publish. The corresponding author, with approval from the co-authors, made the final decision to submit for publication.

## Results

At baseline, demographics and disease characteristics were similar across groups[13]; approximately 65% of patients were TNFi-naïve and 47% were receiving concomitant MTX. Of the 397 patients randomised, 248 (62·5%) completed 5 years of treatment overall; 64 (64%) patients in the original secukinumab 300 mg group, 65 (65%) in the 150 mg group, 59 (59·6%) in the 75 mg group, and 60 (61·2%) in the placebo group completed 260 weeks of treatment (Figure 1). At Week 260, treatment had been discontinued by 7/100 (7·0%) patients in the secukinumab 300 mg group, 10/100 (10·0%) in the 150 mg group, and 17/99 (17·2%) in the 75 mg group due to lack of efficacy, which was the most common cause of discontinuation. In the secukinumab 300 mg group, 10/100 (10·0%) patients discontinued due to an AE, while 8/100 (8·0%) did so in the 150 mg, and 7/99 (7·1%) did in the 75 mg group. Patient disposition through to Week 260 is presented in Figure 1.

In patients originally randomised to secukinumab 300 mg and 150 mg, ACR20 and 50 responses at 5 years were 73·8% and 47·7% and 79·2% and 45·8%, respectively (Figure 2). Improvements in ACR20 and 50 responses were sustained in both TNFi-naïve and TNFi-IR patients, with generally higher responses observed in TNFi-naïve patients. ACR20 and 50 responses through 5 years were similar regardless of baseline concomitant MTX use (Table 1).

In the overall groups of patients originally randomised to secukinumab, including those who switched to secukinumab at Week 16 or 24 (placebo-switchers), efficacy was sustained through 5 years (Table 2). Efficacy results stratified by prior TNFi status at Week 260 are presented in Supplementary Table 1 and showed a sustained improvement regardless of prior TNFi status.

Dose escalation at least once occurred in 127 of the 242 (52·5%) patients in the secukinumab 75 and 150 mg groups: in 21/99 patients from 75 mg to 150 mg; in 35/99 patients from 75 mg to 150 mg or 300 mg; and in 71/100 patients from 150 mg to 300 mg. The ACR20 and 50 responses increased or were sustained in patients who escalated from secukinumab 150 mg to 300 mg (Figure 2). Following dose escalation, the proportions of ACR and PASI non-responders decreased, while, the proportions of ACR and PASI responders increased. The proportion of ACR responders increased from 59% to 69% at 24 to 32 weeks after dose escalation. Similarly, the proportion of PASI responders increased from 70% to 82% at 24 to 32 weeks after dose escalation. The ACR and PASI responses from 24 to 32 weeks and from 48 to 84 weeks after dose escalation from 150 mg to 300 mg are presented in the Sankey-style overlay (Figure 3).

The mean duration of exposure to study treatment for the entire treatment period was 1434·3 days (1519·7 patient-years) in the Any secukinumab group. The overall incidence of AEs leading to discontinuation did not show dose dependence across the secukinumab dose groups (Any 75 mg group: n=5, 5·1%; Any 150 mg: n=11, 5·7%; Any 300 mg: n=16, 6·4%). The EAIR of AEs observed in the Any secukinumab group are shown in Table 3. The most commonly reported treatment-emergent AEs were upper respiratory tract infection and nasopharyngitis. The overall incidence of SAEs did not show dose dependence across the secukinumab dose groups (Any 75 mg group: n=17, 17·2%; Any 150 mg: n=28, 14·5%; Any 300 mg: n=42, 16·7%).

During the entire treatment period, the most frequent treatment-emergent SAE was infections (1·7) in the Any secukinumab group. One case each of new onset Crohn's disease and unspecified inflammatory bowel disease (IBD; preferred term) were reported with secukinumab 300 mg. Two cases of ulcerative colitis were reported (one each in the secukinumab 300 and 150 mg groups), one was a flare in a patient with prior history and the other was new onset. There were two cases (0·1) adjudicated as major adverse cardiovascular events (MACE); one case of myocardial infarction on Day 290 in a 61-year old female patient receiving the secukinumab 75 mg dose escalated to 150 mg, and another case of haemorrhagic stroke in a 59-year old male patient receiving secukinumab 300 mg. Treatment-emergent anti-drug antibodies were detected in three patients (one in the placebo-150 mg and two in the 150 mg groups); of which only one patient revealed a generalized pruritus but not considered as a SAE. During the entire treatment period, one death was reported; a 66-year old male patient died due to sepsis secondary to acute pancreatitis in the secukinumab 150 mg group on Day 1169 of treatment.

## Discussion

This is the first 5-year phase III study in PsA patients with s.c. loading and maintenance dosing of secukinumab. Considering the chronic nature of PsA, the evaluation of long-term efficacy, safety, and tolerability of biologics is important in guiding treatment decisions.[21] TNFi are widely used for the treatment of PsA; however, some patients experience inadequate response or intolerance to these agents.[2, 3, 12, 21-25] In the previous published results of the FUTURE 2 study, secukinumab 300 and 150 mg offered sustained and clinically meaningful improvements in joint and skin symptoms, physical function, and QoL in patients with active PsA over 2 years.[13, 19]

Patients treated with secukinumab also achieved higher rates of MDA response and PASDAS remission/low disease activity at Week 16 versus placebo, with sustained responses/states over 2 years in FUTURE 2 study.[26, 27] The results from the present study demonstrate that in those patients who continued in the study, sustained improvements were observed for clinical outcomes across multiple clinical domains of PsA. These include joint and skin components, resolution of enthesitis and dactylitis, MDA response rates, and mean change in PASDAS, DAS28-CRP, HAQ-DI, SF-36 PCS scores through 5 years. with In these patients we also observed a consistent and satisfactory safety profile.

The retention rate of the patients randomized to secukinumab 150 or 300 mg was 65%, with a 35% treatment discontinuation rate observed over 5 years. This is similar to the discontinuation rate reported in other randomized controlled trials in PsA e.g. 31% in GO-REVEAL with golimumab over 5 years, and 29-43% (depending on usage of DMARD at baseline) in RAPID-PsA with certolizumab-pegol over 4 years.[28, 29] Our study demonstrates that in those patients who continue to receive secukinumab, robust efficacy benefits accrue with an acceptable safety profile over 5 years.

According to EULAR, GRAPPA, and ACR and National Psoriasis Foundation treatment guidelines and recommendations, IL-17A inhibitors have been proposed as a treatment option for PsA patients.[10-12] In the current study, sustained clinical improvements were observed through 5 years in patients treated with secukinumab regardless of prior TNFi therapy status. The TNFi-naïve patients responded at a higher rate to IL-17A inhibitor and therefore the latter deserve consideration for earlier use in the paradigm. An optional dose escalation was possible during the study starting at Week 128 if active signs of disease were observed, based on the physician's judgement. Based on the Sankey-style overlay analysis, more patients showed improvements in their ACR and PASI responses after dose escalation highlighting the potential benefit of dose escalation from 150 to 300 mg in patients with a suboptimal response on secukinumab 150 mg.

The safety profile of secukinumab in this study was based on accumulated exposure of 1519·7 patient-years in the Any secukinumab dose group. The type, incidence, and severity of AEs over the 5-year treatment period were consistent with those reported previously.[13, 19] The overall EAIR of AEs did not show any dose dependence. The rates of *Candida* infections, MACE, IBD, and malignancies were low through the 5-year treatment period and consistent with the results of a retrospective safety analysis of 21 secukinumab clinical trials across different indications.[30] The safety profile of secukinumab showed no new or unexpected safety signals through 5 years of treatment.

A limitation of the study is that the investigator and patients were unblinded to the treatment after the 52-week analysis and there was no active comparator. A head-to-head trial comparing the efficacy of secukinumab versus adalimumab in patients with PsA at Week 52 will be reported in the future (NCT02745080). In addition, the results are reported as observed which does not account for dropouts or missing data, and therefore limit interpretation of results with the risk that proportional improvements may

increase as a reflection of changes in the denominator.[31] Another limitation is that dose escalation during the study was based on physician's judgement and not on specifically outlined efficacy criteria.

In conclusion, the results of this long-term study confirm the clinical benefit of IL-17A inhibition, with secukinumab 300 and 150 mg providing sustained improvement in the signs and symptoms of PsA with a consistent safety profile through 5 years of treatment.

## Contributors

All authors were involved in the drafting and critical review of the manuscript and approved the final version for submission. IBM, PJM, AJK, PN, PR, JR, PGC, BK and SN were involved in the acquisition of clinical data and participated as investigators in the clinical study from which data are reported in the manuscript. IBM and PJM were members of steering committee and contributed to the design of the study. LP was involved with the conception or design of the work. EMD was involved with the analysis of the data in the manuscript. All authors were involved with the interpretation of data in the manuscript. All authors agreed to be accountable for all aspects of the work and attest to the accuracy and integrity of the work.

## Declaration of interests

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**Data sharing statement**

The datasets generated during and/or analysed during the current study are not publicly available. 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 the basis of scientific merit. All data provided is anonymised to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations. The data may be requested from the corresponding author of the manuscript.

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**Figure legends:**

**Figure 1. Patient disposition through 5 years**

Placebo patients were re-randomised to secukinumab 300 or 150 mg s.c.: placebo non-responders received active treatment starting at Week 16 and placebo responders at Week 24. [1]10 patients were not re-randomised to secukinumab; [2]Includes 49 patients escalated to secukinumab 300 mg; [3]Includes 21 patients escalated to secukinumab 150 mg, 6 patients escalated to 300 mg and 29 patients escalated first to secukinumab 150 mg and then to 300 mg; [4]Includes 22 patients escalated to secukinumab 300 mg; N, number of randomised patients

**Figure 2. ACR20 and 50 responses through 5 years**

Data shown are as observed in patients originally randomised to secukinumab 300 and 150 mg and patients escalated from 150 to 300 mg through Week 260. Patients who were escalated to 300 mg are counted only at the originally randomised treatment group. The Secukinumab 150-300 mg group (dotted line from Week 128 to 260) included 49 patients who were originally randomised to secukinumab 150 mg escalated 300 mg starting at Week 128 or later following protocol amendment. Data are presented in the secukinumab 150 mg arm from Week 140 to 260 for patients who continued the 150 mg dose. ACR, American College of Rheumatology; N, total number of patients; n, number of evaluable patients

**Figure 3. ACR and PASI responses after dose escalation from 150 to 300 mg**

The number of patients evaluated was 54 and 33 for ACR and PASI responses, respectively. Patients with data available in all three time periods are presented. For secukinumab 150 to 300 mg, the first escalation was observed at study Week 128. ACR, American College of Rheumatology; PASI, Psoriasis Area and Severity Index

**Table 1. ACR20 and 50 responses by prior TNFi status and concomitant MTX use through 5 years**

| | | TNFi-naïve | | TNFi-IR | |
|---|---|---|---|---|---|
| | | Secukinumab 300 mg | Secukinumab 150 mg group | Secukinumab 300 mg | Secukinumab 150 mg group |
| **Efficacy endpoints** | **Week** | **N=67** | **N=63[1]** | **N=33** | **N=37[1]** |
| **ACR20, n/M (%)** | **156** | 46/54 (85·2) | 39/51 (76·5) | 15/27 (55·6) | 12/22 (54·5) |
| | **208** | 40/53 (75·5) | 39/51 (76·5) | 12/20 (60·0) | 15/21 (71·4) |
| | **260** | 39/49 (79·6) | 37/48 (77·1) | 9/16 (56·3) | 12/18 (66·7) |
| **ACR50, n/M (%)** | **156** | 36/54 (66·7) | 22/51 (43·1) | 8/27 (29·6) | 6/22 (27·3) |
| | **208** | 29/53 (54·7) | 28/51 (54·9) | 5/20 (25·0) | 9/21 (42·9) |
| | **260** | 26/49 (53·1) | 21/48 (43·8) | 5/16 (31·3) | 7/18 (38·9) |
| | | **Concomitant MTX use: Yes** | | **Concomitant MTX use: No** | |

| | | N=45 | N=47[2] | N=55 | N=53[2] |
|---|---|---|---|---|---|
| **ACR20, n/M (%)** | **156** | 27/37 (73·0) | 28/36 (77·8) | 34/44 (77·3) | 23/37 (62·2) |
| | **208** | 23/34 (67·6) | 28/36 (77·8) | 29/39 (74·4) | 26/36 (72·2) |
| | **260** | 20/32 (62·5) | 25/34 (73·5) | 28/33 (84·8) | 24/32 (75·0) |
| **ACR50, n/M (%)** | **156** | 22/37 (59·5) | 15/36 (41·7) | 22/44 (50·0) | 13/37 (35·1) |
| | **208** | 15/34 (44·1) | 18/36 (50·0) | 19/39 (48·7) | 19/36 (52·8) |
| | **260** | 12/32 (37·5) | 16/34 (47·1) | 19/33 (57·6) | 12/32 (37·5) |

Data shown are as observed in patients originally randomised to the respective treatment groups.

[1]Secukinumab 150 mg group included 29 patients in TNFi-naïve and 20 patients in the -IR subgroups who originally randomised to 150 mg escalated to 300 mg starting at Week 128 or later following protocol amendment

[2] Secukinumab 150 mg group included 23 patients in MTX use: Yes and 26 patients in MTX use: No subgroups who originally randomised to 150 mg escalated to 300 mg starting at Week 128 or later following protocol amendment

ACR, American College of Rheumatology; IR, inadequate responder; M, number of evaluable patients; MTX, methotrexate; N, total number of randomised patients; n, number of responders; TNFi, tumour necrosis factor inhibitors

**Table 2. Summary of efficacy results through 5 years**

| Efficacy endpoints | Week | Secukinumab 300 mg group N=145[1] | Secukinumab 150 mg group N=143[1,2] | Secukinumab 150-300 mg group N=71[3] |
|---|---|---|---|---|
| **ACR20, n/M (%)** | **156** | 83/116 (71·6) | 76/111 (68·5) | 26/44 (59·1) |
| | **208** | 77/106 (72·6) | 75/106 (70·8) | 47/67 (70·1) |
| | **260** | 71/96 (74·0) | 67/96 (69·8) | 41/61 (67·2) |
| **ACR50, n/M (%)** | **156** | 61/116 (52·6) | 38/111 (34·2) | 15/44 (34·1) |
| | **208** | 52/106 (49·1) | 53/106 (50·0) | 35/67 (52·2) |
| | **260** | 50/96 (52·1) | 41/96 (42·7) | 24/61 (39·3) |
| **ACR70, n/M (%)** | **156** | 37/116 (31·9) | 21/111 (18·9) | 10/44 (22·7) |
| | **208** | 39/106 (36·8) | 22/106 (20·8) | 14/67 (20·9) |

| | | | | |
|---|---|---|---|---|
| | **260** | 31/96 (32·3) | 28/96 (29·2) | 17/61 (27·9) |
| **PASI 75[3], n/M (%)** | **156** | 37/48 (77·1) | 49/60 (81·7) | 17/22 (77·3) |
| | **208** | 33/43 (76·7) | 48/58 (82·8) | 28/36 (77·8) |
| | **260** | 31/39 (79·5) | 45/57 (78·9) | 28/38 (73·7) |
| **PASI 90[3], n/M (%)** | **156** | 29/48 (60·4) | 33/60 (55·0) | 10/22 (45·5) |
| | **208** | 26/43 (60·5) | 39/58 (67·2) | 22/36 (61·1) |
| | **260** | 25/39 (64·1) | 38/57 (66·7) | 23/38 (60·5) |
| **Resolution of enthesitis[4], n/M (%)** | **156** | 44/64 (68·7) | 49/75(65·3) | 17/29 (58·6) |
| | **208** | 41/59 (69·5) | 50/71 (70·4) | 32/45 (71·1) |
| | **260** | 39/51 (76·5) | 48/64 (75·0) | 30/40 (75·0) |
| **Resolution of dactylitis[5], n/M (%)** | **156** | 44/51 (86·3) | 26/31 (83·9) | 11/14 (78·6) |
| | **208** | 40/45 (88·9) | 27/30 (90·0) | 18/20 (90·0) |

| | | | | |
|---|---|---|---|---|
| | **260** | 35/40 (87·5) | 23/28 (82·1) | 16/20 (80·0) |
| **MDA, n/M (%)** | **156** | 41/118 (34·7) | 25/112 (22·3) | 8/44 (18·2) |
| | **208** | 40/108 (37·0) | 31/106 (29·2) | 19/67 (28·4) |
| | **260** | 35/97 (36·1) | 30/99 (30·3) | 19/64 (29·7) |
| **DAS28-CRP, mean change (SD)** | **156** | -1·99 (1·16) | -1·70 (1·20) | -1·74 (1·48) |
| | | [M=116] | [M=110] | [M=44] |
| | **208** | -1·92 (1·15) | -1·89 (1·18) | -2·05 (1·25) |
| | | [M=105] | [M=106] | [M=67] |
| | **260** | -1·95 (1·15) | -1·98 (1·16) | -2·07 (1·23) |
| | | [M=95] | [M=94] | [M=60] |
| **HAQ-DI, mean change (SD)** | **156** | -0·55 (0·61) | -0·44 (0·47) | -0·51 (0·52) |
| | | [M=117] | [M=112] | [M=44] |
| | **208** | -0·55 (0·61) | -0·46 (0·52) | -0·51 (0·53) |

| | | | | |
|---|---|---|---|---|
| | | [M=106] | [M=106] | [M=67] |
| | **260** | -0·56 (0·59) | -0·42 (0·54) | -0·48 (0·54) |
| | | [M=96] | [M=98] | [M=63] |
| **SF-36 PCS, mean change (SD)** | **156** | 6·96 (8·90) | 5·98 (7·92) | 6·43 (9·09) |
| | | [M=117] | [M=112] | [M=44] |
| | **208** | 6·93 (8·41) | 7·0 (7·51) | 7·51 (7·63) |
| | | [M=107] | [M=106] | [M=67] |
| | **260** | 6·42 (9·34) | 6·97 (7·49) | 7·85 (8·09) |
| | | [M=96] | [M=97] | [M=62] |
| **PASDAS, mean change (SD)** | **156** | -2·70 (1·62) | -2·41 (1·17) | -2·42 (1·40) |
| | | [M=115] | [M=108] | [M=43] |
| | **208** | -2·70 (1·67) | -2·57 (1·40) | -2·72 (1·56) |
| | | [M=101] | [M=105] | [M=66] |
| | **260** | -2·80 (1·53) | -2·74 (1·26) | -2·89 (1·36) |

| | | | |
|---|---|---|---|
| | [M=91] | [M=94] | [M=60] |

Data shown are as observed.

[1]Total number of patients included originally randomised to secukinumab and placebo-switchers

[2]Secukinumab 150 mg group included 71 patients who escalated to 300 mg starting at Week 128 or later following protocol amendment

[3]Secukinumab 150-300 mg group presented 71 patients (originally randomised to 150 mg and placebo-switchers) escalated to 300 mg starting at Week 128 or later following protocol amendment

[4]Assessed in patients (n=58 and 77 in the 300 and 150 mg groups, respectively) with psoriasis affecting ≥3% body surface area at baseline (psoriasis subset)

[5]Assessed in patients (n=82 and 94 in the 300 and 150 mg groups, respectively) with this symptom at baseline

[6]Assessed in patients (n=63 and 40 in the 300 and 150 mg groups, respectively) with this symptom at baseline

ACR, American College of Rheumatology; DAS28-CRP, 28-joint Disease Activity Score using C-Reactive Protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; M, number of evaluable patients; MDA, Minimal Disease Activity; N, total number of patients; n, number of responders; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; SD, standard deviation; SF-36 PCS, Short form-36 physical component summary

**Table 3. Summary of safety through the entire treatment period (5 years)**

| | Any secukinumab group N=387[1] |
|---|---|
| Exposure to treatment, days, mean (SD) | 1434·3 (620·67) |
| Death, n (%)[2] | 1 (0·3) |
| Discontinuation due to AEs, n (%) | 32 (8·3) |
| **EAIR (n; 95% CI)** | |
| Any AEs | 140·5 (357; 126·3, 155·9) |
| Any SAEs | 6·1 (83; 4·9, 7·6) |
| **Most common AEs[3]** | |
| Upper respiratory tract infection | 9·1 (109; 7·4, 10·9) |
| Nasopharyngitis | 8·6 (102; 7·0, 10·4) |
| **AEs of special interest** | |
| Serious infections | 1·7 (25; 1·1, 2·5) |
| *Candida* infection (HLT) | 1·5 (22; 0·9, 2·3) |
| Oral candidiasis | 0·8 (12; 0·4, 1·4) |
| Crohn's disease | 0·1 (1; 0·0, 0·4) |
| IBD (PT)[4] | 0·1 (1; 0·0, 0·4) |
| Ulcerative colitis | 0·1 (2; 0·0, 0·5) |
| Malignancy | 1·2 (18; 0·7, 1·9) |
| MACE | 0·1 (2; 0·0, 0·5) |
| Neutropenia | 0·1 (2; 0·0, 0·5) |

[1]Includes all patients who were administered with at least one dose of secukinumab during the entire treatment period

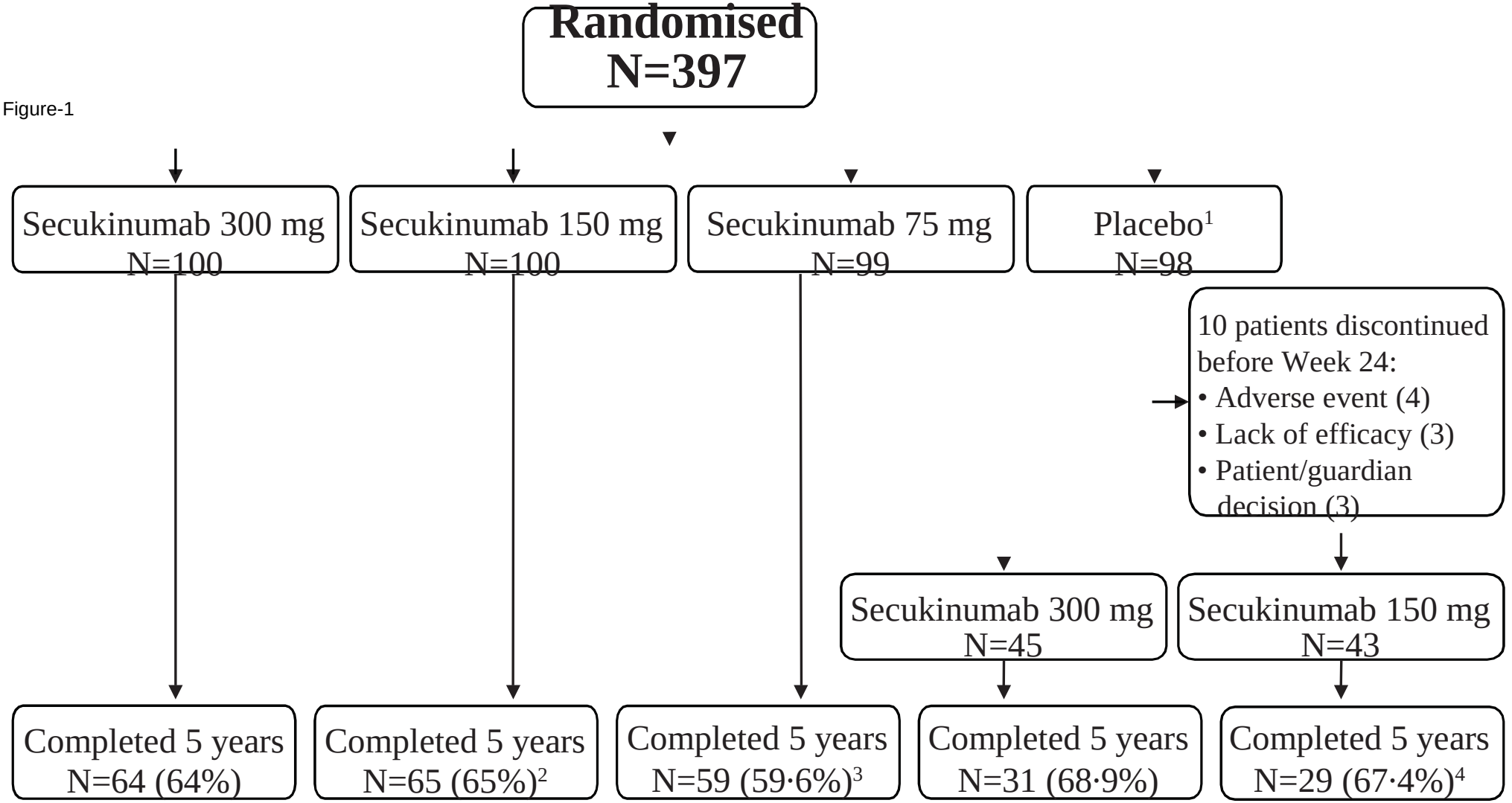
[2]One death due to sepsis secondary to severe acute pancreatitis was reported in the secukinumab 150 mg group on Day 1169 of treatment

[3]Events that had an incidence rate of at least 5·0 cases per 100 patient-years in the combined secukinumab groups (Any secukinumab) during the entire treatment period

[4]This was unspecified IBD

AEs, adverse events; CI, confidence interval; EAIR, Exposure-adjusted incidence rate; HLT, high-level term; IBD, Inflammatory bowel disease; MACE, major adverse cardiovascular events; N, total number of patients analyzed; PT, preferred term; SAEs, serious adverse events; SD, standard deviation

Figure-1


Randomised
N=397
Secukinumab 300 mg
N=100
Secukinumab 150 mg
N=100
Secukinumab 75 mg
N=99
Placebo[1]
N=98
10 patients discontinued before Week 24:
• Adverse event (4)
• Lack of efficacy (3)
• Patient/guardian decision (3)
Secukinumab 300 mg
N=45
Secukinumab 150 mg
N=43
Completed 5 years
N=64 (64%)
Completed 5 years
N=65 (65%)[2]
Completed 5 years
N=59 (59·6%)[3]
Completed 5 years
N=31 (68·9%)
Completed 5 years
N=29 (67·4%)[4]

Discontinued (n=36):
- Adverse event (10)
- Lack of efficacy (7)
- Lost to follow-up (3)
- Non-compliance with study treatment (1)
- Physician decision (4)
- Pregnancy (1)
- Patient/guardian decision (10)

Discontinued (n=35):
- Adverse event (8)
- Lack of efficacy (10)
- Lost to follow-up (2)
- Physician decision (3)
- Patient/guardian decision (11)
- Death (1)

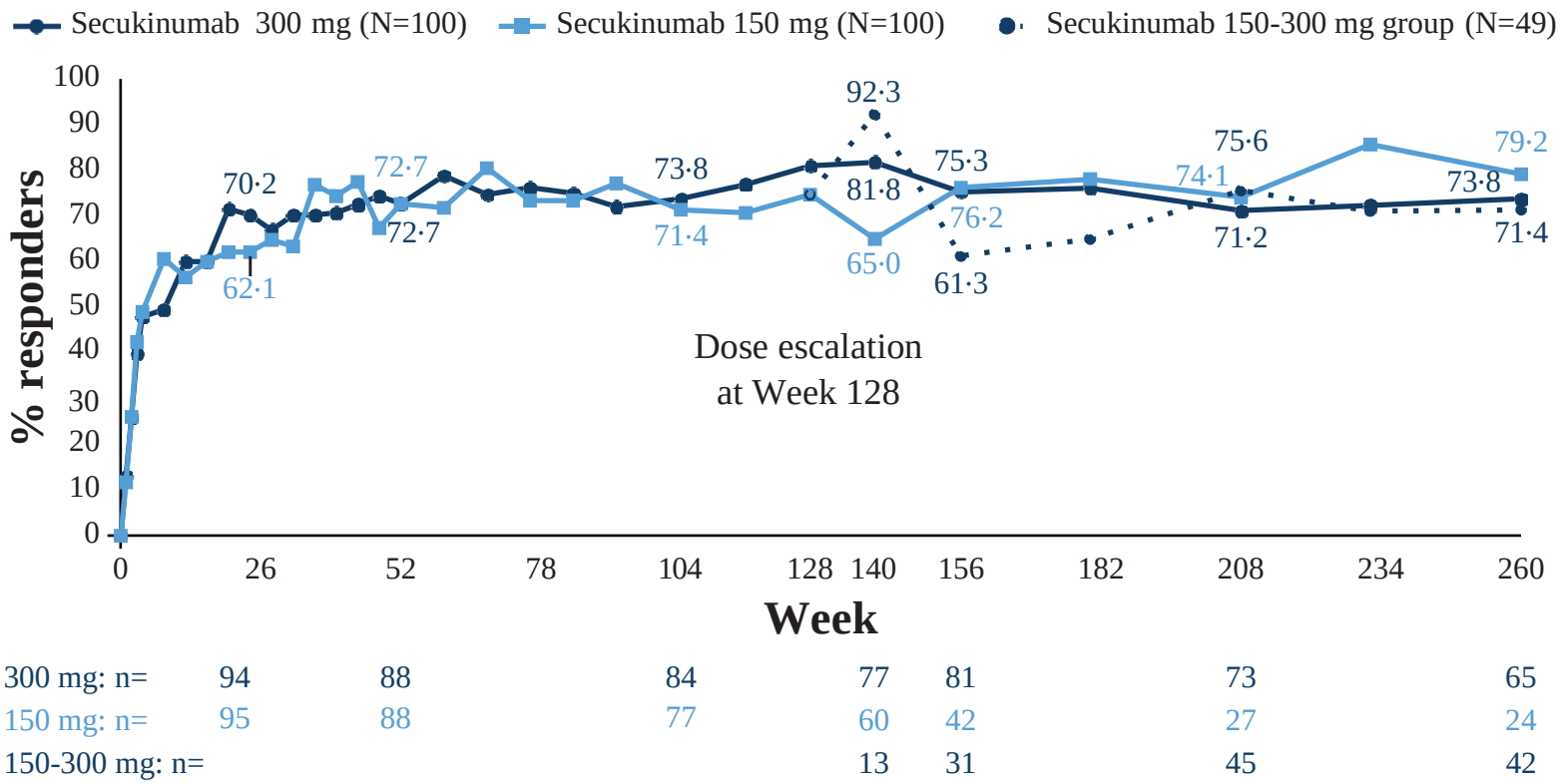
Discontinued (n=40):
- Adverse event (7)
- Lack of efficacy (17)
- Lost to follow-up (2)
- Physician decision (1)
- Patient/guardian decision (13)

Discontinued (n=14):
- Adverse event (2)
- Lack of efficacy (4)
- Lost to follow-up (2)
- Physician decision (1)
- Patient/guardian decision (5)

Discontinued (n=14):
- Adverse event (4)
- Lack of efficacy (3)
- Physician decision (2)
- Patient/guardian decision (5)

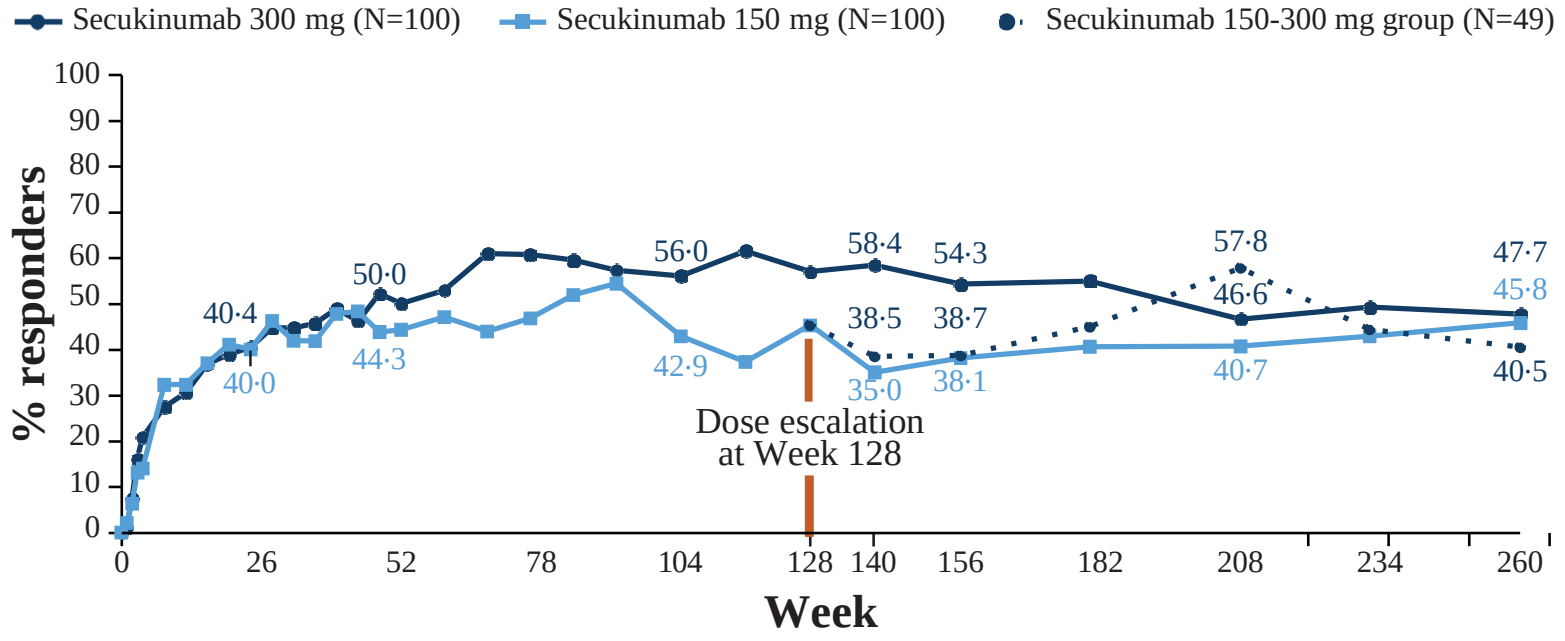
Figure-2

# A) ACR20 response




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 300 mg: n= | 94 | 88 | 84 | 77 | 81 | 73 | 65 |
| 150 mg: n= | 95 | 88 | 77 | 60 | 42 | 27 | 24 |
| 150-300 mg: n= | | | | 13 | 31 | 45 | 42 |

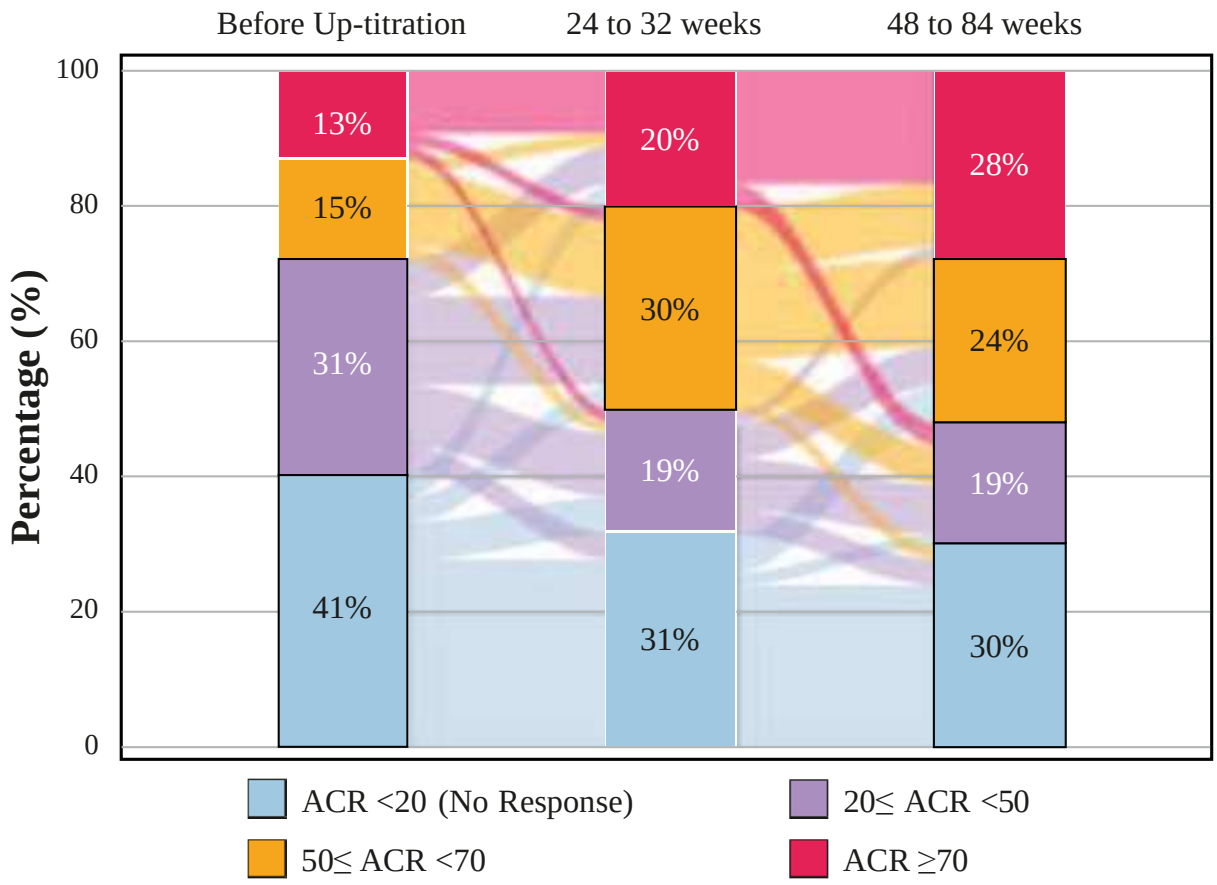
# B) ACR50 response



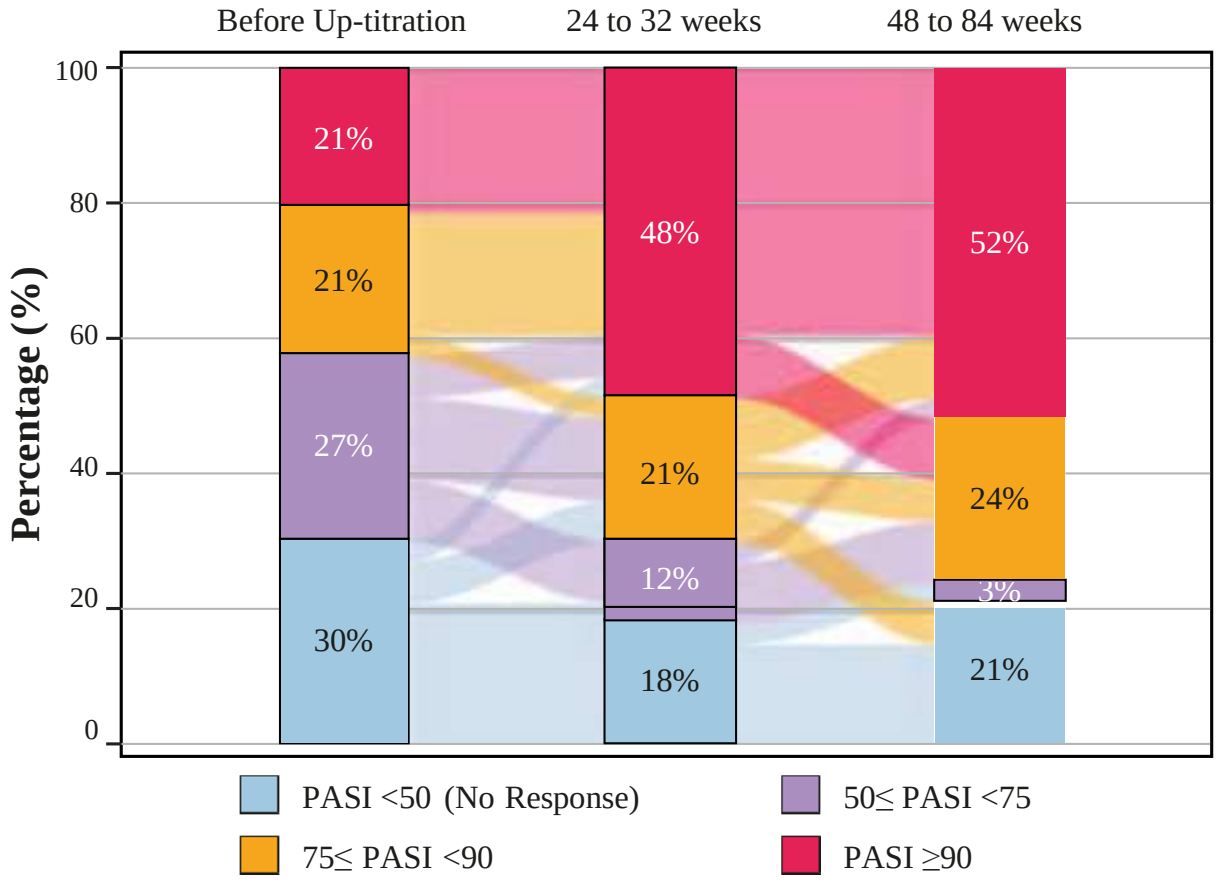

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 300 mg: n= | 94 | 88 | 84 | 77 | 81 | 73 | 65 |
| 150 mg: n= | 95 | 88 | 77 | 60 | 42 | 27 | 24 |
| 150-300 mg: n= | | | | 13 | 31 | 45 | 42 |

Figure-3

## A) ACR response




## B) PASI response



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3. Kavanaugh A, et al. Clinical efficacy, radiographic and safety findings through 5 years of subcutaneous golimumab treatment in patients with active psoriatic arthritis: results from a long-term extension of a randomised, placebo-controlled trial (the GO-REVEAL study). Ann Rheum Dis. 2014 Sep;73(9):1689–94.
4. Walsh JA, et al. Efficacy of certolizumab pegol with and without concomitant use of disease-modifying anti-rheumatic drugs over 4 years in psoriatic arthritis patients: results from the RAPID-PsA randomized controlled trial. Clinical Rheumatology 2018;37:3285–96.