Secukinumab in Biologic-Naive PsA

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Secukinumab in US Biologic-Naive Patients With Psoriatic Arthritis: Results From the Randomized, Placebo-Controlled CHOICE Study

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Statement of ethics and consent: The study was approved by a central institutional review board (Chespeake IRB, now Advarra; IRB#00000971) and by the institutional review board or independent ethics committee at each participating institution, and was conducted in accordance with the Declaration of Helsinki. Patients provided written informed consent before starting any study-related procedures.

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ABSTRACT

Objective: To evaluate secukinumab 300 mg and 150 mg vs placebo in a US-only population of biologic-naive patients with psoriatic arthritis (PsA).

Methods: CHOICE was a randomized, double-blind, controlled trial conducted in the United States. Biologic-naive patients with PsA and psoriasis were randomized 2:2:1 to secukinumab 300 mg (n = 103), secukinumab 150 mg (n = 103), or placebo (n = 52). The primary objective was to show superiority of secukinumab 300 mg vs placebo in ACR20 response at week 16. Additional objectives included the effect of secukinumab on dactylitis, enthesitis, psoriasis, and safety.

Results: ACR20 response rates at week 16 were higher with secukinumab 300 mg than with placebo (51.5% vs 23.1%; odds ratio, 3.51 [95% CI: 1.65, 7.45]; *P* = .0011). Secukinumab 300 mg also led to greater ACR50/70 responses and improvements in other variables vs placebo. Responses were generally sustained over time. Patients with inadequate response to secukinumab 150 mg at weeks 16, 28, or 40 who received dose escalation to 300 mg experienced improved clinical response after uptitration. The most common adverse events were upper respiratory tract infections and diarrhea. No inflammatory bowel disease was reported or new safety signals observed.

Conclusion: Secukinumab 300 mg led to rapid and significant improvements over placebo in symptoms of PsA in this heavier population of US-only biologic-naive patients. Findings were consistent with previous studies and suggest that secukinumab 300 mg is a safe and efficacious first-line biologic treatment for patients with PsA.

Trial registration: ClinicalTrials.gov, NCT02798211

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INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease that occurs in up to 30% of patients with psoriasis,[1,2] and is associated with functional disability and reduced quality of life.[3-5] The disease is progressive and, if untreated, can result in destruction of cartilage and bone as well as new bone formation, leading to permanent joint damage.[6,7] Patients can experience peripheral arthritis, dactylitis, enthesitis, axial involvement, and/or skin and nail psoriasis.[8] Additionally, patients with PsA are at an increased risk of several comorbidities, such as obesity and diabetes, which correlate with disease severity.[9]

Secukinumab, a human monoclonal antibody that selectively targets interleukin-17A, has proven to be efficacious and safe for the treatment of PsA,[10-14] with responses to therapy including resolution of enthesitis and dactylitis, and improvement in skin and nail psoriasis and in axial manifestations of PsA,[10-16] as well as prevention of radiographic progression in these patients[14]; response rates were sustained through 5 years.[17] Overall, secukinumab was well tolerated and demonstrated a favorable safety profile.[10-14] However, US patients were a minority of those enrolled in these studies. Additionally, US patients in these studies had a baseline clinical profile indicating harder-to-treat disease than the total study population, including higher body mass index (BMI), higher tender and swollen joint counts, increased prevalence of enthesitis and dactylitis, and more tumor necrosis factor inhibitor (TNFi) experience.[11-14,18]

To gather additional data on the effect of secukinumab in US biologic-naive patients with PsA and psoriatic skin lesions, the CHOICE study evaluated the efficacy and safety of secukinumab 300 mg and 150 mg vs placebo. We report primary findings and 52-week results of the CHOICE study.

PATIENTS AND METHODS

Study Design and Participants

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CHOICE was a multicenter, randomized, double-blind, placebo-controlled, parallel-group, phase 4 trial that evaluated the efficacy and safety of secukinumab vs placebo in treating patients with PsA (**NCT02798211**). The study was conducted from July 20, 2016, to October 1, 2018, in 67 centers in the United States, was approved by a central institutional review board (Chespeake IRB, now Advarra; IRB#00000971) and by the institutional review board or independent ethics committee at each participating institution, and was conducted in accordance with the Declaration of Helsinki. Patients were recruited over a 15-month period beginning July 2016 and provided written informed consent before starting any study-related procedures. Eligible patients had moderate to severe active PsA by the Classification Criteria for Psoriatic Arthritis, with symptoms for ≥ 6 months, the presence of ≥ 3 tender joints of 78 and ≥ 3 swollen joints of 76, and psoriatic skin lesions with a Psoriasis Area and Severity Index (PASI) ≥ 1. Patients with active ongoing inflammatory diseases other than PsA were excluded from this study. Previous treatment with any biologic agent was not permitted, and disease-modifying antirheumatic drugs other than methotrexate were discontinued 4 weeks prior to randomization, (8 weeks for leflunomide). Investigational treatments were prohibited.

Patients were randomized 2:2:1 to receive secukinumab 300 mg, secukinumab 150 mg, or placebo. Patients received treatment every 4 weeks (q4w) to week 16, with a weekly loading phase from baseline to week 4 (treatment period 1). At week 16, patients randomized to secukinumab 300 mg continued receiving the same dose and patients randomized to placebo began receiving secukinumab 300 mg q4w to week 52 (treatment period 2). Patients receiving secukinumab 150 mg who achieved < 20% improvement from baseline in both tender and swollen joint counts (nonresponders) at weeks 16, 28, or 40 started receiving secukinumab 300 mg q4w, while responders continued receiving secukinumab 150 mg q4w to week 52. Patients were allowed concomitant treatment with nonsteroidal anti-inflammatory drugs or corticosteroids (≤ 10 mg/day prednisone or equivalent) up to week 16, or with methotrexate (≤ 25 mg/week) up to week 52, provided the dose was stable.

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Objectives and Outcomes

The primary objective was to show superiority of secukinumab 300 mg vs placebo based on the proportion of patients achieving 20% improvement in the American College of Rheumatology score (ACR20) at week 16. Secondary objectives included the evaluation of efficacy of secukinumab 150 mg vs placebo based on the proportion of patients achieving ACR20 at week 16, and to evaluate the efficacy of secukinumab 300 mg and 150 mg vs placebo based on the proportion of patients achieving ACR50; ACR70; resolution of dactylitis (based on the Leeds Dactylitis Index [LDI]); resolution of enthesitis (based on the combined Leeds Enthesitis Index [LEI] and Spondyloarthritis Research Consortium of Canada Enthesitis Index [SPARCC]); minimal disease activity (MDA); 75%, 90%, or 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI75, 90, and 100, respectively), and change from baseline in Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP); Psoriatic Arthritis Disease Activity Score (PASDAS); and Health Assessment Questionnaire–Disability Index (HAQ-DI). Exploratory objectives included achievement of ACR20/50/70, low-disease activity (DAS28-CRP < 2.6), and HAQ-DI responses through week 52, as well as change from baseline over time in DAS28-CRP, HAQ-DI score, PASDAS, dactylitis count, enthesitis count, and the Multidimensional Health Assessment Questionnaire/Routine Assessment of Patient Index Data 3 (RAPID3). Subgroup analyses evaluating the efficacy of secukinumab by methotrexate use (yes or no), BMI (≤ or > 30 kg/m^2), and number of tender and swollen joints (< 10 or ≥ 10) at baseline were also conducted. Safety and tolerability of secukinumab were assessed during the 52-week study by monitoring adverse events (AEs), serious AEs, laboratory assessments, and vital signs.

Statistical Analysis

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The sample size was calculated based on ACR20 response for the primary comparison. ACR20 response rates of 50% for secukinumab 300 mg and 20% for placebo (odds ratio [OR] of 4) at week 16 were assumed. Using a continuity-corrected chi-squared test, an allocation ratio of 2:1, a 2-sided significance level of .05, and a power of 0.90, approximately 88 patients in the secukinumab 300-mg group and 44 patients in the placebo group were needed. Assuming a loss to follow-up rate of 10% and a 2:2:1 allocation ratio, the total number of randomized patients was approximately 250 (100 receiving secukinumab 300 mg, 100 receiving secukinumab 150 mg, and 50 receiving placebo).

All statistical tests were conducted against a 2-sided alternative hypothesis, using a significance level of .05. Comparative efficacy analyses focused on the first 16 weeks of treatment (placebo-controlled period) and were performed based on the full analysis set. The primary efficacy variable (ACR20 response) was analyzed at week 16 using a logistic regression model with treatment (3 treatment groups), methotrexate use at baseline (yes, no), and body weight (in kg) as explanatory variables; nonresponder imputation was used for missing values. The percentages of patients achieving ACR20 at each time point up to week 16 were also estimated using multiple imputation. This analysis was also performed for binary secondary and exploratory efficacy variables using nonresponder imputation. No adjustment for multiple comparisons was made, and *P* values resulting from analyses addressing the secondary and exploratory objectives should be considered nominal.

The changes from baseline at each time point through week 16 for all continuous secondary and exploratory efficacy variables were assessed using an analysis of covariance model with treatment, baseline, methotrexate use at baseline, and body weight as explanatory variables; missing data were imputed using last observation carried forward. Analyses for dactylitis included patients with an LDI ≥ 1 at baseline, and analyses of enthesitis included patients who had an enthesitis score ≥ 1 when sites from LEI and SPARCC were assessed

together at baseline. Analyses of PASI75/90/100 responses included patients with ≥ 3% of their body surface area affected by psoriatic skin involvement at baseline.

All safety analyses were performed on all patients who received ≥ 1 dose of study medication. Treatment-emergent AEs, serious AEs, and risks based on AEs were summarized.

RESULTS

Patients

A total of 258 patients were randomized to receive secukinumab 300 mg (n = 103), secukinumab 150 mg (n = 103), or placebo (n = 52) (**Figure 1**). At week 52, a higher proportion of patients in the secukinumab 300-mg group completed treatment period 2 (80.6%) compared with patients in the secukinumab 150-mg group (74.8%) and those who were originally randomized to placebo and switched to secukinumab 300 mg after week 16 (76.9%). The main reasons for discontinuation in treatment period 1 were withdrawal of informed consent (300 mg, 1.9%; 150 mg, 6.8%; placebo, 5.8%) and loss to follow-up (300 mg, 1.9%; 150 mg, 1.0%; placebo, 0%). The main reasons for discontinuation in treatment period 2 were withdrawal of informed consent (300 mg, 1.0%; 150 mg, 3.9%; placebo−300 mg, 5.8%) and AEs (300 mg, 4.9%; 150 mg, 1.9%; placebo−300 mg, 0%).

The age of patients at baseline ranged from 19 to 82 years and the mean time since diagnosis of PsA ranged from 3.0 to 3.9 years (**Table 1**). The mean baseline BMI of patients was > 30 kg/m^2 in all treatment groups, indicating an obese population. Most patients (73.3%) had enthesitis, and 48.1% had dactylitis. Approximately one-third of patients were receiving methotrexate at baseline.

Efficacy

The study met its primary objective, with a greater percentage of patients treated with secukinumab 300 mg achieving an ACR20 response at week 16 vs placebo (51.5% vs 23.1%

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using nonresponder imputation); the OR of 3.51 was statistically significant (95% CI: 1.65, 7.45; *P* =.0011) (**Figure 2A**). Secukinumab 150 mg led to a numerically higher ACR20 response rate (36.9%) than placebo, although the OR of 1.92 was not statistically significant (95% CI: 0.89, 4.15; *P* = .0961) (**Figure 2A**). Results were similar when multiple imputation was used (secukinumab 300 mg, 55.0%; secukinumab 150 mg, 38.2%; placebo, 23.1%).

Secukinumab also led to higher ACR50 (**Figure 2B**) and ACR70 (**Figure 2C**) response rates at week 16 than placebo. ACR50 response rates were higher with significant ORs for secukinumab 300 mg (28.2%; OR, 6.30 [95% CI: 1.81, 21.88]; *P* = .0038) and secukinumab 150 mg (24.3%; OR, 4.77 [95% CI: 1.36, 16.77]; *P* = .0149) vs placebo (5.8%) (**Figure 2B**). Both secukinumab doses led to higher ACR70 response rates than placebo, although only secukinumab 300 mg resulted in a significant OR (17.5% vs 1.9%; OR, 10.50 [95% CI: 1.36, 81.30]; *P* = .0243) (**Figure 2C**). Overall, ACR20/50/70 and Disease Activity in PSoriatic Arthritis-based remission or low disease activity response rates with secukinumab at week 16 were higher in patients who had < 10 tender joints and < 10 swollen joints at baseline than in those with more swollen and tender joints (**Supplementary Tables 1, 2**).

When assessed by concomitant methotrexate use at baseline (no methotrexate vs methotrexate), ACR20 response rates at week 16 were comparable in both secukinumab groups; in contrast, patients in the placebo group who received methotrexate had higher response rates than those who received placebo alone (38.9% vs 14.7%) (**Supplementary Figure 1**). No consistent patterns of differences were observed in ACR50 or ACR70 response rates by baseline methotrexate use. A greater percentage of patients treated with secukinumab vs placebo had resolution of enthesitis at week 16 based on the combined LEI and SPARCC, with a significant OR (secukinumab 300 mg, 37.8% vs 17.9%; OR, 2.85 [95% CI: 1.08, 7.50]; *P* = .0341; secukinumab 150 mg, 39.5% vs 17.9%; OR, 2.65 [95% CI: 1.01, 6.93]; *P* = .0469) (**Table 2**). Treatment with secukinumab also resulted in numerically higher rates of resolution of dactylitis than placebo, although the ORs were not significant. Patients treated with

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secukinumab had substantial improvements in psoriasis and achieved higher PASI75/90/100 response rates than patients taking placebo, with significant ORs. Secukinumab also led to improvements in other secondary and exploratory efficacy variables vs placebo, including MDA, DAS28-CRP, and PASDAS (**Table 2**). Patients receiving either dose of secukinumab experienced significant improvements vs those taking placebo as measured by RAPID3 at week 16 (secukinumab 300 mg, least-squares mean [LSM] of treatment difference, −3.80 [95% CI: −5.65, −1.94]; *P* < .0001; secukinumab 150 mg, LSM of treatment difference, −2.89 [95% CI: −4.78, −1.00]; *P* = .0028). Sustained clinical responses in several efficacy variables were seen with continued secukinumab treatment to week 52 (**Figure 2**; **Supplementary Table 3**).

In addition, the proportion of patients achieving ACR responses at any time point between weeks 16 and 52 increased in patients for whom secukinumab was uptitrated from 150 mg to 300 mg (**Figure 3A**). Before uptitration, only 2.4% of patients in the uptitration subset had achieved an ACR20 response; this proportion increased to 65.9% after dose escalation. Additionally, although no patients in the uptitration subset had achieved an ACR50 or ACR70 response before uptitration, 34.1% of patients achieved an ACR50 response following uptitration, and 12.2% achieved an ACR70 response. Improvements were also observed in dactylitis, enthesitis, and MDA in patients with uptitration, with response rates increasing almost 2-fold after uptitration (**Figure 3B-D**). Interestingly, 11.9% of patients with uptitration (those who had not achieved ≥ 20% improvement from baseline in both tender and swollen joint counts) were classified as in MDA at the time of dose escalation; the proportion in MDA increased to 31.0% after uptitration, between weeks 16 and 52. Most patients (83.3%) achieved dactylitis resolution after dose escalation, compared with 44.4% who achieved response prior to uptitration. Similarly, patients initially receiving placebo had increased ACR20/50/70 response rates after switching to secukinumab 300 mg (**Figure 2**).

Efficacy by BMI Subgroups

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Given that the mean BMI at baseline indicated an obese patient population, the efficacy of secukinumab was evaluated in patients with BMI ≤ 30 kg/m^2 and in those with BMI > 30 kg/m^2. Secukinumab led to achievement of ACR20/50/70 responses in both subgroups, regardless of BMI at baseline, and these responses were sustained from week 16 to week 52 (**Supplementary Figure 2**). However, ACR50 and ACR70 response rates at week 52 were numerically lower in patients with BMI > 30 kg/m^2 than those with BMI ≤ 30 kg/m^2. An analysis of PASI response by BMI subgroups was also conducted (**Supplementary Figure 3**). PASI responses, including PASI100 responses, were achieved by patients receiving secukinumab regardless of BMI at baseline, although patients with BMI > 30 kg/m^2 had numerically lower PASI responses at week 16 than those with BMI ≤ 30 kg/m^2.

Safety

The most commonly reported AEs up to week 16 were diarrhea (secukinumab 300 mg, 5.8%; secukinumab 150 mg, 5.8%; placebo, 1.9%), hypertension (300 mg, 4.9%; 150 mg, 3.9%; placebo, 0%), and upper respiratory tract infections (300 mg, 5.8%; 150 mg, 1.9%; placebo, 0%) (**Table 3**). Most AEs were mild (secukinumab 300 mg, 30.1%; secukinumab 150 mg, 35.9%; placebo, 38.5%) or moderate (300 mg, 23.3%; 150 mg, 20.4%; placebo, 11.5%). By week 16, serious AEs were reported in 2 patients in each treatment group (secukinumab 300 mg, 1.9%; secukinumab 150 mg, 1.9%; placebo, 3.8%) (**Table 3** and **Supplementary Table 4**). At week 16, 1 patient in the secukinumab 300-mg group and 1 patient in the secukinumab 150-mg group had discontinued due to psoriasis.

Throughout the 52-week study, the most common AEs in patients receiving secukinumab were upper respiratory tract infection (any secukinumab 300-mg group, 13.7%; any secukinumab 150-mg group, 13.6%) and diarrhea (any secukinumab 300-mg group, 7.6%; any secukinumab 150-mg group, 6.8%) (**Supplementary Table 5**). At week 52, serious AEs were reported in 9.6% of patients in the any secukinumab 300-mg group and in 7.8% of patients

in the any secukinumab 150-mg group (**Supplementary Table 5**). *Candida* infection through week 52 was reported in 0.5% of patients in the secukinumab 300-mg group and 1.9% of patients in the secukinumab 150-mg group. There was 1 report of myocardial infarction in a patient receiving secukinumab 150 mg, and 1 report of ischemic stroke during placebo treatment in a patient included in the Week-52 secukinumab 300-mg group. Transient Common Terminology Criteria for Adverse Events grade 2 neutropenia was reported in 1 patient (secukinumab 300-mg group), during one visit, and was not associated with concomitant infection. One case of breast cancer and 1 case of prostate cancer occurred in patients treated with secukinumab 300 mg (**Supplementary Tables 5** and **6**). No cases of inflammatory bowel disease (Crohn disease or ulcerative colitis), or tuberculosis were reported in any group throughout the study. Among the observed cases of diarrhea, none were hemorrhagic. Serious AEs through Week 52 are listed in **Supplementary Table 6**. The most frequently reported types of serious AEs through Week 52 were infections (any secukinumab 300-mg group, 2.5%; any secukinumab 150-mg group, 1.9%) and nervous system disorders (including syncope, cerebral cyst, ischemic stroke, and seizure; any secukinumab 300-mg group, 2.5%; any secukinumab 150-mg group, 1.0%). Over the entire treatment period, AEs leading to treatment discontinuation were reported in 8 patients (4.1%) receiving any secukinumab 300-mg dose and 1 patient (1.0%) receiving any secukinumab 150-mg dose. One death, due to cardiac arrest, was reported in a patient who received placebo prior to week 16 and who was randomized to but did not yet receive secukinumab 300 mg; no other deaths were reported.

DISCUSSION

In this randomized study of biologic-naive US patients with PsA, secukinumab 300 mg was superior to placebo in achieving rapid and significant improvements in symptoms of PsA, including achievement of stringent binary outcomes such as ACR50, ACR70, PASI90, PASI100, and MDA. Benefits were also observed with secukinumab 150 mg, although responses were

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generally higher with secukinumab 300 mg. An analysis of ACR responses by baseline methotrexate use showed higher response rates with secukinumab 300 mg compared with placebo, regardless of methotrexate use. Differences between patients receiving secukinumab vs placebo in achievement of ACR20, a modest outcome compared with ACR50 or ACR70, were greatest among patients not receiving methotrexate at baseline. Response rates with secukinumab were higher in patients with a tender or swollen joint count < 10 than in patients with more tender or swollen joints, likely reflecting a patient population with a lower baseline disease activity that was more responsive to treatment.

Secukinumab also led to sustained or improved responses over time. Furthermore, uptitrating the dose of patients to secukinumab 300 mg led to improvements in ACR and PASI responses, as well as to a greater percentage of patients achieving response in dactylitis, enthesitis, and MDA. These findings show the benefits of dose escalation in patients whose symptoms are not adequately controlled with secukinumab 150 mg and suggest potential benefit from increasing the dose of secukinumab over the course of treatment. RAPID3 is a patient-reported outcome developed for the assessment of rheumatoid arthritis disease activity.[19] It is commonly used in clinical practice to assess patients with PsA but has not been evaluated in randomized controlled trials of PsA despite having been evaluated in post hoc analyses and cohort studies.[20,21] Here, RAPID3 improvements from either dose of secukinumab at week 16 were significant vs placebo.

Overall, ACR response rates in CHOICE were lower than those seen in the TNFi-naive patient population of the FUTURE studies.[14,22] These findings may have been due to patients in CHOICE having higher disease activity scores at baseline compared with TNFi-naive patients in the FUTURE studies.[23] For instance, patients in CHOICE had a higher mean tender joint count (secukinumab 300 mg, 27.1 vs 17.9; secukinumab 150 mg, 25.6 vs 20.0; placebo, 25.2 vs 19.8) and mean swollen joint count (secukinumab 300 mg, 17.7 vs 9.3; secukinumab 150 mg, 14.4 vs 10.6; placebo, 13.8 vs 10.7) compared with patients in the FUTURE studies. More patients in

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CHOICE had concomitant psoriasis affecting ≥ 3% of their body surface area compared with TNFi-naive patients in the FUTURE studies (secukinumab 300 mg, 76.7% vs 46.8%; secukinumab 150 mg, 80.6% vs 55.1%; placebo, 82.7% vs 50.5%), suggestive of a more difficult-to-treat disease. Additionally, patients in the CHOICE study were more likely to be obese than TNFi-naive patients in the FUTURE studies (mean BMI, secukinumab 300 mg, 32.8 vs 28.7 kg/m^2; secukinumab 150 mg, 30.7 vs 29.2 kg/m^2; placebo, 34.1 vs 29.1 kg/m^2), which is associated with faster clearance of secukinumab [24] and with lower treatment responses.[25,26] In our study, secukinumab led to improvements in symptoms of PsA regardless of BMI, although patients with BMI ≤ 30 kg/m^2 treated with secukinumab had generally higher ACR response rates than those with BMI > 30 kg/m^2. Finally, patients with fibromyalgia or osteoarthritis were not excluded and could contribute to lower response rates observed here based on the potential residual impact of noninflammatory disease not targeted by secukinumab treatment.

The safety profile of secukinumab in CHOICE was consistent with previous reports.[10-14] AEs were generally mild or moderate and led to few discontinuations; no relation to dose was apparent. No deaths in patients treated with secukinumab were reported; 1 patient in the placebo group died due to cardiac arrest. *Candida* infections were more common in patients treated with secukinumab than in those receiving placebo. No cases of inflammatory bowel disease were reported, and no new safety signals were observed.

Overall, the findings from CHOICE were consistent with previous studies and demonstrated that secukinumab provides significant and sustained improvements in signs and symptoms of psoriatic arthritis. Our findings suggest that secukinumab 300 mg is safe and efficacious as a first-line biologic treatment for patients with PsA. Further studies will also help determine the optimal dose of secukinumab for treating overweight patients or those with high disease activity at treatment initiation.

ACKNOWLEDGMENTS

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FIGURE LEGENDS

Figure 1. Patient disposition.

* One patient discontinued treatment period 2 before receiving study drug due to a positive pregnancy test.

† Patients who discontinued study treatment were considered to have withdrawn due to patient decision if other possible underlying causes such as adverse events or lack of efficacy were excluded.

‡ Patients who chose to stop participating in the study and wanted no further visits or assessments and no further study-related contact were considered to have withdrawn consent.

Figure 2. (A) ACR20, **(B)** ACR50, and **(C)** ACR70 response rates through week 52.

ACR = American College of Rheumatology.

† Includes patients with uptitration to secukinumab 300 mg at weeks 16, 28, or 40.

* *P* < .05; statistically significant odds ratio in favor of secukinumab dose vs placebo based on logistic regression using nonresponder imputation.

Figure 3. (A) ACR, **(B)** enthesitis, **(C)** dactylitis, and **(D)** MDA responses at any time point between weeks 16 and 52 following uptitration from secukinumab 150 mg to 300 mg among nonresponders.*

ACR = American College of Rheumatology; LEI = Leeds Enthesitis Index, MDA = minimal disease activity; SPARCC = Spondyloarthritis Research Consortium of Canada Enthesitis Index.

* Patients defined as nonresponders were those who had < 20% improvement from baseline in both tender and swollen joint counts, at weeks 16, 28, or 40. Unless otherwise noted, these analyses included all patients with uptitration from secukinumab 150 mg to 300 mg and completed the study.

† Patients included in the LEI + SPARCC subset were included in this analysis.

‡ Patients included in the dactylitis subset were included in this analysis.

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§ MDA is defined as achievement of ≥ 5 of the following 7 criteria: tender joint count ≤ 1; swollen

joint count ≤ 1; Psoriasis Area and Severity Index ≤ 1 or body surface area ≤ 3; patient pain

visual analog scale ≤ 15; patient global disease activity visual analog scale ≤ 20; Health

Assessment Questionnaire ≤ 0.5; tender entheseal points ≤ 1.

Table 1. Patient characteristics at baseline

Variable	Secukinumab 300 mg (n = 103)	Secukinumab 150 mg (n = 103)	Placebo (n = 52)
Age, years			
Mean (SD)	51.9 (12.6)	51.3 (14.6)	53.1 (12.7)
Median (min, max)	53.0 (29, 82)	52.0 (19, 80)	56.0 (20, 74)
Male, n (%)	53 (51.5)	56 (54.4)	23 (44.2)
Race, n (%)			
White	88 (85.4)	88 (85.4)	45 (86.5)
Black	2 (1.9)	2 (1.9)	3 (5.8)
Asian	9 (8.7)	10 (9.7)	1 (1.9)
Native American	0	1 (1.0)	1 (1.9)
Pacific Islander	1 (1.0)	1 (1.0)	0
Other	2 (1.9)	0	2 (3.8)
Unknown	1 (1.0)	1 (1.0)	0
Weight, mean (SD), kg	93.4 (23.0)	86.9 (23.3)	97.2 (26.5)
Body mass index, mean (SD), kg/m^2	32.8 (8.2)	30.7 (7.6)	34.1 (7.8)
10th percentile	23.7	21.9	24.9
25th percentile	26.4	25.4	27.8
50th percentile	32.4	29.0	32.4
75th percentile	38.1	35.1	40.7
90th percentile	42.8	40.7	44.9

Time since first PsA diagnosis, mean (SD), years	3.0 (4.4)	3.8 (5.6)	3.9 (5.0)
Methotrexate use, n (%)	34 (33.0)	23 (22.3)	18 (34.6)
Dose, mean (SD), mg/week	17.1 (4.6)	16.4 (4.2)	16.3 (6.1)
Corticosteroid use, n (%)	12 (11.7)	11 (10.7)	3 (5.8)
NSAID use, n (%)	33 (32.0)	35 (34.0)	18 (34.6)
Presence of dactylitis (LDI), n (%)	49 (47.6)	52 (50.5)	23 (44.2)
Presence of enthesitis (SPARCC + LEI), n (%)	74 (71.8)	76 (73.8)	39 (75.0)
Tender joint count (78 joints), mean (SD)	27.1 (19.6)	25.6 (18.6)	25.2 (15.0)
Swollen joint count (76 joints), mean (SD)	17.7 (16.4)	14.4 (13.9)	13.8 (11.9)
PASI score, mean (SD)	8.3 (8.0)	9.0 (10.0)	5.9 (5.4)
DAS28-CRP score, mean (SD)	4.9 (1.2)	4.7 (1.3)	5.0 (1.1)
PASDAS score, mean (SD)	6.2 (1.3)	6.0 (1.3)	6.2 (1.3)
SF-12 mental component score, mean (SD)	46.5 (11.0)	45.7 (10.8)	46.0 (11.6)
SF-12 physical component score, mean (SD)	36.9 (10.1)	38.3 (9.7)	35.9 (8.8)
HAQ-DI score, mean (SD)	1.1 (0.6)	1.0 (0.6)	1.3 (0.7)
RAPID3 score, mean (SD)	14.6 (5.6)	13.9 (5.7)	15.6 (5.7)

DAS28-CRP = Disease Activity Score in 28 joints using C-reactive protein; HAQ-DI = Health

Assessment Questionnaire–Disability Index; LDI = Leeds Dactylitis Index; LEI = Leeds

Enthesitis Index; NSAID = nonsteroidal anti-inflammatory drug; PASI = Psoriasis Area and

Severity Index; PASDAS = Psoriatic Arthritis Disease Activity Score; PsA = psoriatic arthritis;

RAPID3 = Routine Assessment of Patient Index Data 3; SD = standard deviation; SF-12 = Short

Form 12-question Health Survey; SPARCC = Spondyloarthritis Research Consortium of

Canada Enthesitis Index.

Table 2. Summary of primary and key secondary and exploratory efficacy results at week 16*

Outcome	Placebo, n/N (%) (n = 52)	SEC 300 mg, n/N (%) (n = 103)	OR (95% CI)	P value	SEC 150 mg, n/N (%) (n = 103)	OR (95% CI)	P value
Primary efficacy variable							
ACR20	12/52 (23.1)	53/103 (51.5)	3.51 (1.65, 7.45)	.0011	38/103 (36.9)	1.92 (0.89, 4.15)	.0961
Secondary binary efficacy variables							
ACR50	3/52 (5.8)	29/103 (28.2)	6.30 (1.81, 21.88)	.0038	25/103 (24.3)	4.77 (1.36, 16.77)	.0149
ACR70	1/52 (1.9)	18/103 (17.5)	10.50 (1.36, 81.30)	.0243	11/103 (10.7)	5.42 (0.67, 43.64)	.1120
Resolution of enthesitis (LEI + SPARCC)[†]	7/39 (17.9)	28/74 (37.8)	2.85 (1.08, 7.50)	.0341	30/76 (39.5)	2.65 (1.01, 6.93)	.0469
Resolution of dactylitis[‡]	4/23 (17.4)	20/49 (40.8)	3.27 (0.96, 11.20)	.0587	20/52 (38.5)	3.40 (0.98, 11.76)	.0529
PASI75[§]	7/43 (16.3)	51/79 (64.6)	9.49 (3.73, 24.16)	< .0001	45/83 (54.2)	6.38 (2.51, 16.24)	.0001
PASI90[§]	4/43 (9.3)	39/79 (49.4)	9.86 (3.19, 30.45)	< .0001	30/83 (36.1)	5.21 (1.68, 16.21)	.0043

	Placebo LSM (n = 52)	SEC 300 mg LSM (n = 103)	LSM of treatment difference (SE)¶ [95% CI]	P value	SEC 150 mg LSM (n = 103)	LSM of treatment difference (SE)¶ [95% CI]	P value
PASI100§	1/43 (2.3)	20/79 (25.3)	14.38 (1.86, 111.53)	.0107	15/83 (18.1)	9.82 (1.24, 77.90)	.0307
MDA	2/52 (3.8)	27/103 (26.2)	8.75 (1.99, 38.45)	.0041	27/103 (26.2)	8.34 (1.89, 36.85)	.0051
Secondary and exploratory continuous efficacy variables#							
Change from baseline in DAS28-CRP	−0.35	−1.39	−1.05 (0.203) [−1.45, −0.65]	< .0001	−1.18	−0.83 (0.207) [−1.24, −0.43]	< .0001
Change from baseline in PASDAS	−0.36	−1.04	−0.68 (0.085) [−0.85, −0.52]	< .0001	−0.92	−0.57 (0.086) [−0.74, −0.40]	< .0001
Change from baseline in SF-12 mental component score	1.54	3.05	1.51 (1.334) [−1.12, 4.14]	.2579	1.77	0.23 (1.353) [−2.43, 2.90]	.8621

Change from baseline in SF-12 physical component score	−0.63	4.82	5.45 (1.363) [2.76, 8.13]	< .0001	4.32	4.94 (1.385) [2.22, 7.67]	.0004
Change from baseline in HAQ-DI	−0.11	−0.32	−0.21 (0.081) [−0.37, −0.05]	.0107	−0.24	−0.13 (0.083) [−0.30, 0.03]	.1109
Change from baseline in RAPID3	−0.78	−4.57	−3.80 (0.941) [−5.65, −1.94]	< .0001	−3.67	−2.89 (0.960) [−4.78, −1.00]	.0028

ACR = American College of Rheumatology; ANCOVA = analysis of covariance; DAS28-CRP = Disease Activity Score in 28 joints using C-reactive protein; HAQ-DI = Health Assessment Questionnaire – Disability Index; LEI = Leeds Enthesitis Index; LSM = least-squares mean; SE = standard error; MDA = minimal disease activity; OR = odds ratio; PASDAS = Psoriatic Arthritis Disease Activity Score; PASI = Psoriasis Area and Severity Index; RAPID3 = Routine Assessment of Patient Index Data 3; SEC = secukinumab; SF-12 = Short Form 12-question Health Survey; SPARCC = Spondyloarthritis Research Consortium of Canada Enthesitis Index.

* ORs, 95% CIs, and *P* values are based on logistic regression using nonresponder imputation.

† Results are from the combined LEI and SPARCC subset. Enthesitis was determined in patients who had an enthesitis score ≥ 1 when sites from LEI and SPARCC were assessed together at baseline: secukinumab 300 mg, n = 74; secukinumab 150 mg, n = 76; placebo, n = 39.

‡ Dactylitis was determined in patients who had a Leeds Dactylitis Index ≥ 1 at baseline: secukinumab 300 mg, n = 49; secukinumab 150 mg, n = 52; placebo, n = 23.

§ Results are from patients having psoriatic skin involvement in ≥ 3% of their body surface area at baseline: secukinumab 300 mg, n = 79; secukinumab 150 mg, n = 83; placebo, n = 43.

¶ LSM of the treatment difference vs placebo.

LSM, LSM of treatment differences, 95% CI, and *P* values are based on an ANCOVA model; missing data were imputed using last observation carried forward.

Table 3. Safety profile of secukinumab until week 16 (placebo-controlled period)

Patients with AEs, n (%)	Secukinumab 300 mg (n = 103)	Secukinumab 150 mg (n = 103)	Placebo (n = 52)
Any AE	59 (57.3)	61 (59.2)	27 (51.9)
Serious AEs	2 (1.9)	2 (1.9)	2 (3.8)
Death	0	0	1 (1.9)
Discontinuation due to AEs	1 (1.0)	1 (1.0)	0
Common AEs (≥ 3% in any treatment group)			
Diarrhea	6 (5.8)	6 (5.8)	1 (1.9)
Upper respiratory tract infection	6 (5.8)	2 (1.9)	0
Hypertension	5 (4.9)	4 (3.9)	0
Sinus congestion	4 (3.9)	0	0
Fatigue	3 (2.9)	5 (4.9)	0
Headache	3 (2.9)	4 (3.9)	2 (3.8)
Nasopharyngitis	3 (2.9)	4 (3.9)	1 (1.9)
Abdominal pain	2 (1.9)	2 (1.9)	2 (3.8)
Musculoskeletal pain	2 (1.9)	1 (1.0)	3 (5.8)
Sinusitis	2 (1.9)	1 (1.0)	2 (3.8)
Arthralgia	1 (1.0)	2 (1.9)	4 (7.7)
Back pain	1 (1.0)	4 (3.9)	0
Pain in extremity	1 (1.0)	3 (2.9)	3 (5.8)
Peripheral oedema	1 (1.0)	0	2 (3.8)
Psoriasis	1 (1.0)	4 (3.9)	0

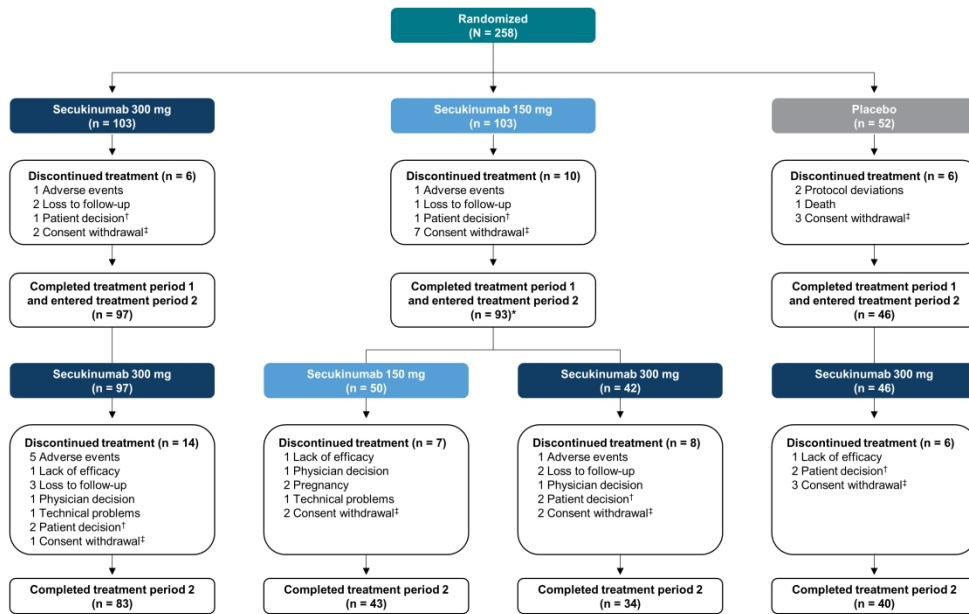|			
Psoriatic arthropathy	1 (1.0)	4 (3.9)	0
Respiratory tract congestion	0	0	2 (3.8)
Selected AEs of interest			
Candidiasis			
Candida infection	1 (1.0)	2 (1.9)	0
Skin *Candida*	0	1 (1.0)	0
Major adverse cardiac events			
Myocardial infarction	0	1 (1.0)	0
Ischemic stroke	0	0	1 (1.9)
Neutropenia	1 (1.0)	0	0

AE = adverse event.

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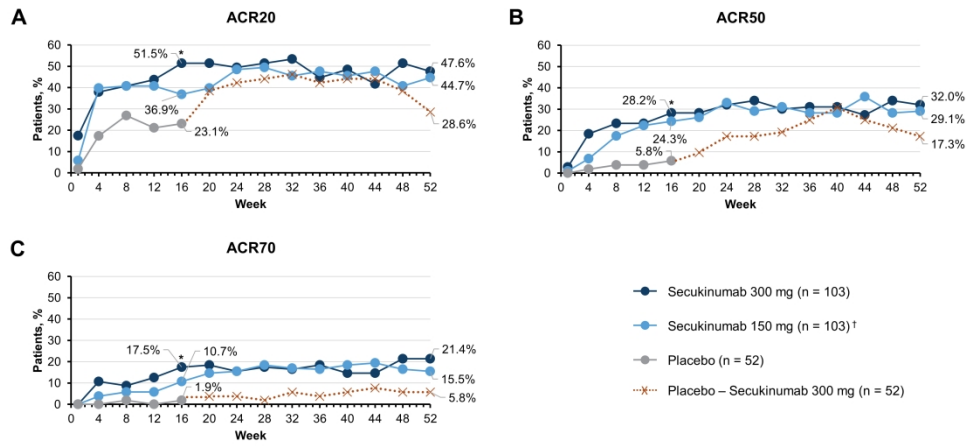
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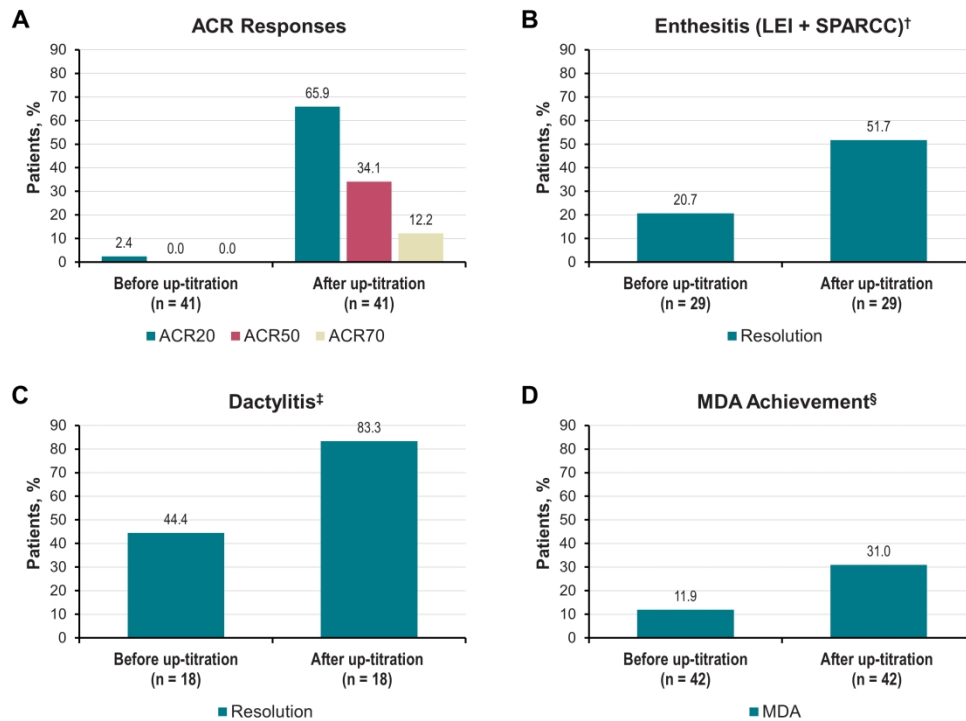regression using nonresponder imputation.

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