Secukinumab Sustains Individual Clinical Responses Over Time in Patients With Psoriatic Arthritis: 2-Year Results From a Phase 3 Trial

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INTRODUCTION

- The assessment of achieving, sustaining, and improving clinical responses and low disease status with biologics in psoriatic arthritis (PsA) are important parts of EULAR and GRAPPA recommendations that aim to optimize treatment goals and improve patient quality of life[1,2]
- Secukinumab, a fully human monoclonal antibody that selectively neutralizes interleukin (IL)-17A, has demonstrated significant efficacy in the treatment of moderate to severe psoriasis[3] and PsA,[4,5] demonstrating a rapid onset of action and sustained responses
- In the phase 3 FUTURE 2 study (NCT01752634), secukinumab provided sustained improvement in the signs and symptoms of active PsA over 104 weeks[6]
- Here, we present results at the individual patient-level on the efficacy of secukinumab at improving, sustaining, or worsening ACR response and disease status (28-joint disease activity score using CRP [DAS28-CRP])-derived criteria from Week 24 to 104 in patients with active PsA in the FUTURE 2 study

METHODS

Study Design and Patients

- FUTURE 2 is an ongoing, Phase 3, double-blind, randomized, placebo-controlled study[4,6]
  - A total of 397 patients were randomized (1:1:1:1) to receive subcutaneous (s.c.) secukinumab (300, 150, or 75 mg) or placebo at Weeks 0, 1, 2, 3, and 4 and once every 4 weeks thereafter. Placebo-treated patients were re-randomized (1:1) to receive s.c. secukinumab (300 or 150 mg) at Week 16 (non-responders) or Week 24 (responders) based on clinical response
- The key inclusion and exclusion criteria have been reported elsewhere[4]

Endpoints and Assessments

- *Post-hoc* analysis of data from patients with PsA who were originally randomized to receive secukinumab 300 and 150 mg and completed the 16-week double-blind treatment period followed by long-term uncontrolled treatment
- Shift analyses were performed on ACR responses between Week 24 (primary endpoint) and Week 104 (sustained effect). The sub-groups based on ACR criteria included:
  - ACR non-responders (ACR NR)
  - ACR20 responders
  - ACR50 responders
  - ACR70 responders
- Shift analyses were performed on DAS28-CRP scores between Week 24 and Week 104. The DAS28-CRP-derived criteria[7] included:
  - High disease activity (HDA; >5.1)
  - Moderate disease activity (MoDA; >3.2 and ≤5.1)
  - Low disease activity (LDA; ≤3.2 and ≥2.6)
  - Remission (REM; <2.6)
- Shift analyses were performed on Psoriasis Area and Severity Index (PASI) responses (PASI non-responder [PASI NR], PASI 75, and PASI 90) and minimal disease activity (MDA) responses (MDA non-responders [MDA NR] and MDA) between Week 24 and Week 104

Statistical Analyses

- Data are presented as observed in patients with data available at Weeks 24 and 104
- The shift analyses were performed on ACR, DAS28-CRP, PASI, and MDA responses between Weeks 24 and 104 for subgroups of secukinumab-treated patients categorized by their highest response criteria at the earlier time point, by evaluating whether these responses were improved, sustained, or worsened at the later time point, using mutually exclusive response categories
- A patient was classified as having achieved MDA upon meeting at least five of the seven pre-defined criteria determining MDA response[8]

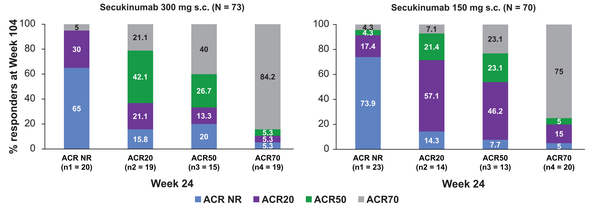
RESULTS

- In total, 86/100 (86%) and 76/100 (76%) patients receiving secukinumab 300 and 150 mg, respectively, completed 104 weeks of treatment[6]
  - Of these, 73/70, 81/75, 34/41, and 83/76 patients in secukinumab 300/150 mg were eligible for ACR, DAS28-CRP, PASI, and MDA shift analyses, respectively, from Week 24 to Week 104
- Patient disposition and baseline characteristics have been reported previously[4]
  - The mean age of patients was 46.9 ± 12.6 and 46.5 ± 11.7 years, mean PASI score was 11.9 ± 8.4 and 16.2 ±14.3, psoriasis body surface area ≥3% was present in 41% and 58% of patients, and mean DAS28-CRP score was 4.8 ± 1.0 and 4.9 ± 1.1 in the secukinumab 300 and 150 mg groups, respectively

Efficacy

- In the secukinumab 300 and 150 mg groups, a majority (84% and 75%) of ACR70 responders and ACR50 responders (67% and 46%), respectively, either maintained or improved their response at Week 104 (**Figure 1**)

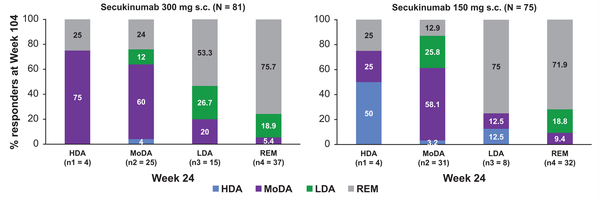
Figure 1. Shift Analysis of ACR Responses From Week 24 to Week 104



N = number of patients who completed Week 104 and had ACR response available at both Weeks 24 and 104; n1 = number of patients with no ACR response at Week 24 who completed Week 104 and had ACR response available; n2–n4 = number of patients with ACR response at Week 24 who completed Week 104 and had ACR response available

- In the secukinumab 300 mg group, 53% of patients with LDA improved to REM and a majority (76%) of patients with REM maintained their status from Week 24 to 104, whereas in the secukinumab 150 mg group, a majority (75% and 72% with LDA and REM, respectively) of patients improved or maintained their status at Week 104 (**Figure 2**)

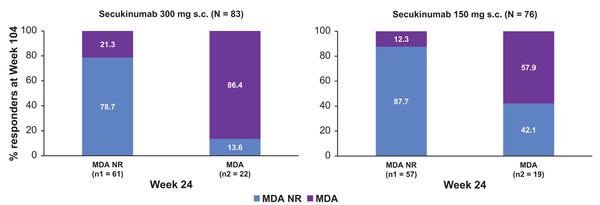
Figure 2. Shift Analysis of DAS28-CRP Status From Week 24 to Week 104



N = number of patients who completed Week 104 and had DAS28-CRP response available at both Weeks 24 and 104; n1 = number of patients with no DAS28-CRP response at Week 24 who completed Week 104 and had DAS28-CRP response available at both time points; n2–n4 = number of patients with DAS28-CRP at Week 24 who completed Week 104 and had DAS28-CRP response available. DAS28-CRP status was calculated with validated cut-offs to indicate HDA (>5.1), MoDA (>3.2 and ≤5.1), LDA (≤3.2 and ≥2.6), and REM (<2.6)[7]

- A majority (86% and 58%) of MDA responders at Week 24 maintained their response at Week 104 in both secukinumab 300 and 150 mg groups, respectively. A total of 21% and 12% of MDA NR at Week 24 developed a response at Week 104 in both secukinumab 300 and 150 mg groups, respectively (**Figure 3**)

Figure 3. Shift Analysis of MDA Response From Week 24 to Week 104



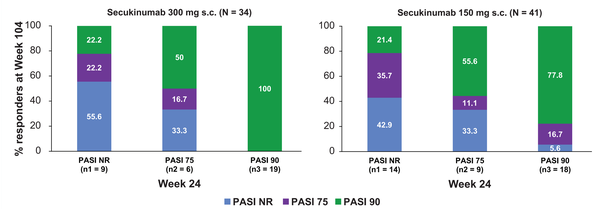
N = number of patients who completed Week 104 and had MDA data available at both Weeks 24 and 104; n1 = number of patients not achieving MDA at Week 24 who completed Week 104 and had MDA data available at both Weeks 24 and 104; n2 = number of patients achieving MDA at Week 24 who completed Week 104 and had MDA data available at both Weeks 24 and 104

- In the secukinumab 300 and 150 mg groups, a majority (100% and 78%, respectively) of PASI 90 responders maintained their status at Week 104, whereas 50% and 56% of PASI 75 responders, respectively, improved their response to PASI 90 at Week 104 (**Figure 4**)

Summary of Results

- Most secukinumab-treated patients who achieved at least an ACR50/70 or PASI response at Week 24 improved or sustained their response at Week 104
- The majority of MDA responders at Week 24 treated with secukinumab 300 mg sustained their response at Week 104
- The majority of patients who were in the MoDA, LDA, or REM status related to DAS28-CRP score at Week 24 sustained or improved their disease status at Week 104

Figure 4. Shift Analysis of PASI Response (psoriasis body surface area ≥3%) From Week 24 to Week 104



N = number of patients who completed Week 104 and had PASI response available at both Weeks 24 and 104; n1 = patients with no PASI score at Week 24 who completed Week 104 and had PASI scores available at both Weeks 24 and 104; n2 and n3 = number of patients achieving PASI 75 and PASI 90, respectively, at Week 24 who completed Week 104 and had PASI score available at both Weeks 24 and 104

CONCLUSIONS

- Improvements in individual ACR and PASI responses and disease status observed with secukinumab at Week 24 were sustained or improved further through 2 years in a majority of patients with PsA
- Sustainability of responses on more stringent efficacy criteria such as ACR70 and MDA were numerically higher with secukinumab 300 mg, extending the results previously reported at group level[4,6]

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DISCLOSURES

P Emery: Consultant for AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCB. **I McInnes:** Consultant for Novartis, Amgen, Janssen, BMS, Pfizer, UCB, AbbVie, Celgene, Lilly. **P Mease:** Grant/research support from AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, UCB; consultant for AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, UCB; speakers' bureau for AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB. **M Schiff:** Consultant for AbbVie, BMS, Lilly, J&J; speakers' bureau for AbbVie. **L Pricop, C Gaillez:** Shareholders and employees of Novartis. **S Shen, Z Wang:** Employees of Novartis.

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