Secukinumab Improves Clinical and Imaging Outcomes in Patients With Psoriatic Arthritis and Axial Manifestations With Inadequate Response to NSAIDs: Week 52 Results From the MAXIMISE Trial

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BACKGROUND

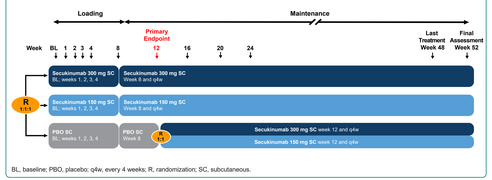
- Secukinumab, a fully human monoclonal antibody that directly inhibits interleukin (IL) 17A, has provided clinically significant and sustained improvement in the signs and symptoms of active psoriatic arthritis (PsA) and ankylosing spondylitis[1,2]
- We present data on the efficacy and safety of secukinumab 300 mg and 150 mg at weeks 12 and 52 in the MAXIMISE trial (NCT02721966), which assessed outcomes of axial manifestations in patients with PsA with an inadequate response to nonsteroidal anti-inflammatory drugs (NSAIDs)

METHODS

Study Design

- This phase 3b, double-blind, placebo-controlled, multicenter 52-week trial included patients aged ≥ 18 years with a diagnosis of PsA according to the Classification Criteria for Psoriatic Arthritis (CASPAR) who had a spinal pain visual analog scale (VAS) score of ≥ 40/100 and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of ≥ 4 despite use of ≥ 2 NSAIDs over a 4-week period
  - Key exclusion criteria included history of exposure to previous biologic disease-modifying antirheumatic drugs (DMARDs) including tumor necrosis factor inhibitors, ustekinumab, and IL-17 or IL-23 inhibitors; active ongoing inflammatory conditions other than PsA; current treatment with DMARDs other than methotrexate; and use of high-potency opioid analgesics
- Eligible patients were randomized to receive secukinumab 300 mg or secukinumab 150 mg or placebo at baseline and weeks 1, 2, and 3, followed by every 4 weeks starting at week 4 (**Figure 1**)
  - At week 12, patients receiving placebo were re-randomized to secukinumab 300 mg or 150 mg

Figure 1. Study Design



BL, baseline; PBO, placebo; q4w, every 4 weeks; R, randomization; SC, subcutaneous.

Outcomes and Assessments

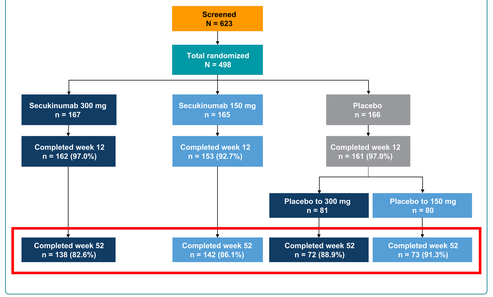
- The primary endpoint was achievement of Assessment of SpondyloArthritis international Society 20% response criteria (ASAS20) with secukinumab 300 mg at week 12
- The key secondary endpoint was ASAS20 response with secukinumab 150 mg at week 12
- Week 52 data are presented as observed
- Bone marrow edema of the entire spine and sacroiliac joints were assessed centrally with Berlin magnetic resonance imaging (MRI) scores at baseline, week 12, and week 52

RESULTS

Patient Population and Baseline Characteristics

- Overall, 623 patients were screened and 498 patients were randomized to secukinumab 300 mg (n = 167), secukinumab 150 mg (n = 165), or placebo (n = 166) (**Figure 2**)
- Completion rates were high, varying between 83% and 91%

Figure 2. Patient Disposition



- Baseline characteristics were comparable across groups (**Table 1**)
- Overall, the vast majority of patients showed ≥ 1 feature of inflammatory back pain; > 90% of patients reported back pain worsening with rest, and > 80% reported awakening in the second half of the night due to back pain

Table 1. Baseline Demographics and Disease Characteristics

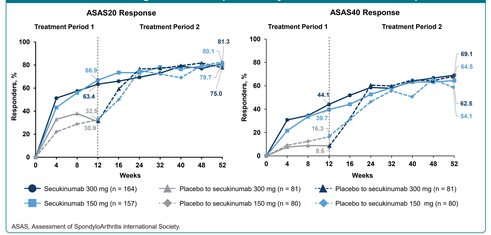
Variables	Secukinumab 300 mg SC (n = 167)	Secukinumab 150 mg SC (n = 165)	Placebo (n = 166)
Age, mean (SD), years	46.2 (12.3)	46.9 (11.5)	46.6 (11.5)
Male, n (%)	77 (46.1)	81 (49.1)	88 (53.0)
BMI, mean (SD), kg/m²	27.3 (4.8)	29.0 (6.4)	28.3 (5.5)
Smoking status (tobacco), n (%)			
Current	47 (28.1)	39 (23.6)	39 (23.5)
Former	20 (12.0)	34 (20.6)	25 (15.1)
Total spinal pain score, mean (SD), VAS	72.5 (13.8)	73.6 (15.4)	74.0 (13.7)
IBP parameters, n (%)			
Onset of back pain is insidious	150 (89.8)	147 (89.1)	152 (91.6)
Back pain improving with exercise	148 (88.6)	139 (84.2)	146 (88.0)
Back pain worsening with rest	152 (91.0)	151 (91.5)	157 (94.6)
Night pain with improvement upon getting up	147 (88.0)	147 (89.1)	143 (86.1)
Awakening due to back pain in second half of night	143 (85.6)	145 (87.9)	137 (82.5)
Alternating buttock pain	102 (61.1)	98 (59.4)	101 (60.8)
Back pain improved after NSAID intake in past	136 (81.4)	134 (81.2)	138 (83.1)

BMI, body mass index; IBP, inflammatory back pain; NSAID, nonsteroidal anti-inflammatory drug; SC, subcutaneous; VAS, visual analog scale.

Efficacy With Secukinumab Through Week 52

- Patients receiving secukinumab 300 mg or 150 mg showed higher response rates than patients receiving placebo at week 12, which were sustained through week 52 (**Figure 3**)
- Patients in the placebo arm were re-randomized to secukinumab 300 mg or 150 mg at week 12 and showed response rates similar to those shown in the originally randomized patients through week 52

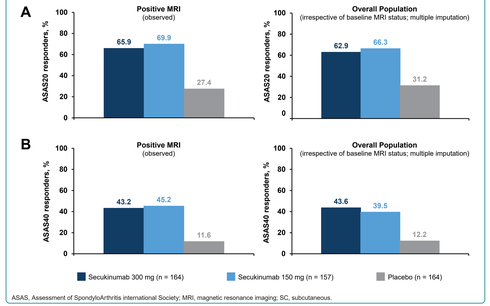
Figure 3. Sustained ASAS20 and ASAS40 Responses With Secukinumab Through Week 52 (full analysis set, as observed)



ASAS, Assessment of SpondyloArthritis international Society.

- Among the MRI-positive patients, higher ASAS20 response rates were observed in the secukinumab 300-mg and 150-mg groups than in the placebo group at week 12; similar observations were made in the overall population (**Figure 4A**)
- Higher ASAS40 response rates were also observed with secukinumab 300 mg and 150 mg than with placebo among MRI-positive patients, which was similar to the overall population (**Figure 4B**)

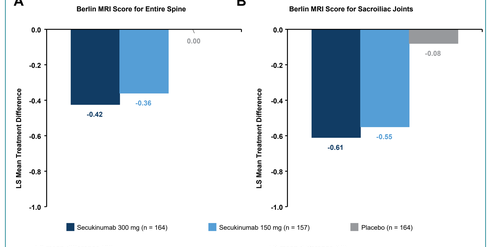
Figure 4. (A) ASAS20 Response and (B) ASAS40 Response at Week 12 Based on Baseline MRI



ASAS, Assessment of SpondyloArthritis international Society; MRI, magnetic resonance imaging; SC, subcutaneous.

- The Berlin MRI scores were significantly lower at week 12 for the entire spine and the sacroiliac joints in patients receiving secukinumab 300 mg and 150 mg than in patients receiving placebo (**Figure 5**)

Figure 5. Berlin MRI Scores at Week 12 for the (A) Entire Spine and (B) Sacroiliac Joints (full analysis set)



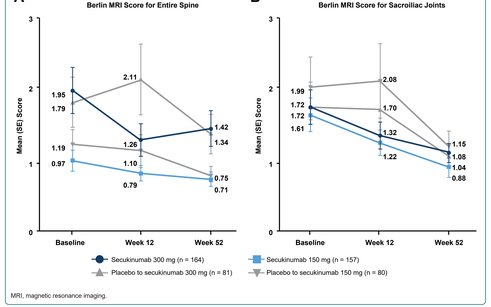
LS mean difference (CI)
Secukinumab 300 mg vs placebo: −0.4 (−0.7 to −0.1); ***P* = .0031**
Secukinumab 150 mg vs placebo: −0.4 (−0.6 to −0.1); ***P* = .0127**

LS mean difference (CI)
Secukinumab 300 mg vs placebo: −0.5 (−0.9 to −0.2); ***P* = .0034**
Secukinumab 150 mg vs placebo: −0.5 (−0.8 to −0.1); ***P* = .0091**

LS, least squares; MRI, magnetic resonance imaging; SC, subcutaneous.

- Furthermore, the Berlin MRI score reductions at week 12 were sustained at week 52 (**Figure 6**)
- Patients in the placebo group who were re-randomized to secukinumab at week 12 also showed lower mean Berlin scores at week 52

Figure 6. Total Berlin MRI Scores Through Week 52 for the (A) Entire Spine and (B) Sacroiliac Joints (full analysis set)



MRI, magnetic resonance imaging.

Safety at Week 52

- There were no new or unexpected safety findings (**Table 2**)

Table 2. Summary of Secukinumab Safety Through Week 52

	Week 12			Week 52	
	Secukinumab 300 mg SC (n = 167)	Secukinumab 150 mg SC (n = 165)	Placebo (n = 166)	Any Secukinumab 300 mg SC (n = 248)	Any Secukinumab 150 mg SC (n = 245)
Duration of exposure, mean (SD), days	84.6 (7.1)	84.9 (7.6)	84.9 (7.4)	—	—
Any AE, n (%)	67 (40.1)	61 (37.0)	80 (48.2)	169 (68.1)	158 (64.5)
Any SAE, n (%)	4 (2.4)	1 (0.6)	4 (2.4)	13 (5.2)	14 (5.7)
AEs leading to study treatment discontinuation, n (%)	2 (1.2)	3 (1.8)	1 (0.6)	9 (3.6)	6 (2.4)
Death, n (%)	0	0	0	1 (0.4)	0
Common AEs[a]	**n (%)**			**EAIR**	
Nasopharyngitis	9 (5.4)	4 (2.4)	11 (6.6)	14.8	9.4
URTI	3 (1.8)	5 (3.0)	5 (3.0)	4.9	5.9
Diarrhea	4 (2.4)	2 (1.2)	4 (2.4)	6.7	2.9
AEs of special interest	**n (%)**			**EAIR**	
Candida infection	3 (1.8)	2 (1.2)	1 (0.6)	2.0	1.2
Crohn disease	0	0	0	0.0	0.4
MACE	1 (0.6)	0	0	0.8	0.4
Malignancy[b]	0	0	0	0.8	0.4

AE, adverse event; EAIR, exposure-adjusted incidence rate per 100 patient-years; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SC, subcutaneous; URTI, upper respiratory tract infection.
[a] AEs with an EAIR ≥ 5 in either of the secukinumab treatment groups over the entire treatment period.
[b] Rates reported are for standardized MedDRA query term malignant or unspecified tumors excluding basal cell carcinoma and squamous cell carcinoma.

CONCLUSIONS

- Secukinumab provided significant improvement in the signs and symptoms and objective signs of inflammation of axial disease in patients with PsA with axial manifestations and inadequate response to NSAIDs
- Results of the MAXIMISE trial provide valuable data that will support ASAS/GRAPPA efforts to deepen the clinical understanding of axial PsA
- The safety profile of secukinumab was consistent with previous reports[3,4]

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DISCLOSURES

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