Efficacy of Secukinumab in Managing Axial Manifestations and Nail Psoriasis in Patients with Psoriatic Arthritis: Results from the MAXIMISE Trial

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INTRODUCTION

- Psoriatic arthritis (PsA) affects approximately 20–30% of patients with psoriasis, 25–70% of whom may have axial disease
- Up to 80% of patients have nail lesions,[1–3] which are considered as potential predictor of PsA among patients with psoriasis[4]
- We report efficacy results through Week 52 from the MAXIMISE trial (NCT02721966), the first randomized controlled trial evaluating the efficacy of a biologic in the treatment of axial manifestations in PsA

METHODS

Study Design

- MAXIMISE is a Phase IIIb double-blind, placebo-controlled, multicentre 52-weeks trial that included 498 patients
- Patients were randomized (1:1:1) to subcutaneous secukinumab (300 or 150 mg) or placebo weekly for 4 weeks and every 4 weeks thereafter
  - At Week 12, placebo patients were re-randomized (1:1) to subcutaneous secukinumab 300 or 150 mg
- Patients aged ≥18 years diagnosed with PsA and classified by CASPAR criteria, with active spinal disease defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; range 0–10) ≥4 and spinal pain Visual Analog Scale (VAS) ≥40/100 and inadequate response to at least 2 Non-steroidal anti-inflammatory drugs were included
- Details of study design, inclusion and exclusion criteria are previously reported[5]

Study outcomes and Assessments

- The primary and key secondary endpoint was ASAS20 response with secukinumab 300 mg and 150 mg respectively, at Week 12. ASAS20 response was defined as an improvement of ≥20% and ≥1 unit on a scale of 10 in at least three of the four ASAS domains (PtGA of disease activity and inflammatory back pain, BASFI, and average of the last two questions on the six-question BASDAI)
- Other secondary endpoints included assessments of ASAS40 response, mean change from Baseline in spinal pain measured by VAS
- Bone marrow edema of the entire spine and sacroiliac joints were assessed centrally with Berlin magnetic resonance imaging (MRI) scores at Baseline and Weeks 12 and 52. Measurement of inflammation, bone marrow edema and erosion was analyzed centrally using Berlin MRI score
- Modified nail psoriasis severity index (mNAPSI) score at Weeks 12 and 52 was an exploratory endpoint

Statistical Analyses

- Missing data for binary variables were handled using multiple imputation and for continuous variables a mixed-effects model repeated measures approach was followed up to Week 12
- All other data after Week 12 through Week 52 were reported as observed

RESULTS

- Out of 498 randomized patients, 425 (85%) patients completed the study through Week 52. The retention rates at Week 52 were 83% (138/167; secukinumab 300 mg), 86% (142/165; secukinumab 150 mg), 89% (72/81; placebo-secukinumab 300 mg) and 91% (73/80; placebo-secukinumab 150 mg)
- Demographic and baseline disease characteristics were comparable across groups (**Table 1**)

Table 1. Baseline demographic and disease characteristics

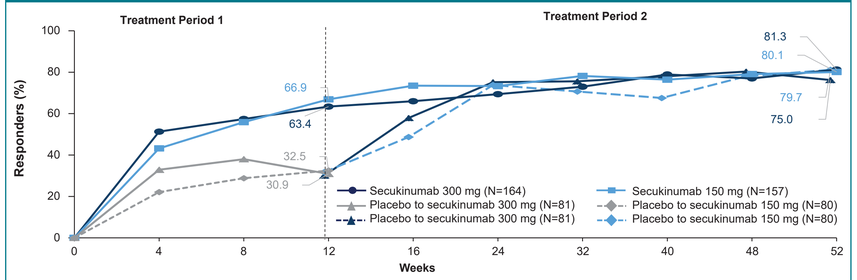
Variables, Mean (SD) unless specified	Secukinumab 300 mg s.c. (N=167)	Secukinumab 150 mg s.c. (N=165)	Placebo (N=166)
Age (years)	46.2 (12.3)	46.9 (11.5)	46.6 (11.5)
Male, n (%)	77 (46.1)	81 (49.1)	88 (53.0)
Body mass index (kg/m²)	27.3 (4.8)	29.0 (6.4)	28.3 (5.5)
Smoking status (tobacco), n (%)			
Current	47 (28.1)	39 (23.6)	39 (23.5)
Former	20 (12.0)	34 (20.6)	25 (15.1)
Total spinal pain score, VAS, mean (SD)	72.5 (13.8)	73.6 (15.4)	74.0 (13.7)
Inflammatory back pain 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 2nd 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)

NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; VAS, visual analog scale; N, total number of randomized patients; n, number of evaluable patients.

Efficacy

- The primary and key secondary endpoints were met; ASAS20 responder rates at Week 12 were 62.9% (secukinumab 300 mg; p<0.0001) and 66.3% (150 mg; p<0.0001) versus 31.2% (Placebo); and at Week 52 ASAS20 responder rates for secukinumab 300 mg and 150 mg groups were 81.3% and 80.1%, respectively (**Figure 1**)

Figure 1. Secukinumab sustained ASAS20 response through Week 52



Full Analysis Set, as observed
ASAS, Assessment of SpondyloArthritis international Society; N, total number of patients in the full analysis set.

- At Week 12, significant improvements were demonstrated for secukinumab versus placebo in other secondary and exploratory endpoints with improvements sustained through Week 52 as shown in **Table 2**

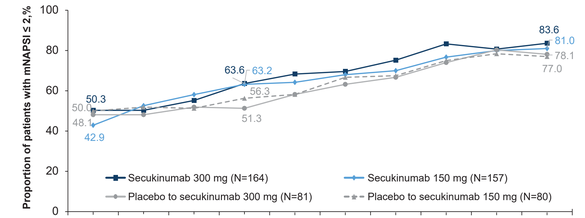
Table 2. Clinical efficacy with secukinumab at Weeks 12 and 52

	Secukinumab 300 mg s.c. (N=164)	Secukinumab 150 mg s.c. (N=157)	Placebo (N=164)
Treatment period 1 (Week 12)			
ASAS20 response, % Responders	62.9%	66.3%	31.2%
OR versus placebo (95% CI)	3.8 (2.4, 6.1)*	4.4 (2.7, 7.0)*	–
ASAS40 response, % Responders	43.6%	39.5%	12.2%
OR versus placebo (95% CI)	5.6 (3.2, 9.8)*	4.7 (2.7, 8.3)*	–
Change from baseline in Spinal pain VAS (any time)	–26.5	–28.5	–13.6
LSM difference with placebo	–12.9 (–18.0, –7.8)*	–14.9 (–20.0, –9.7)*	–
mNAPSI score, LS mean	–4.8	–3.5	–1.4
LSM difference with placebo	–3.3 (–4.7, –2.0)*	–2.1 (–3.4, –0.7)§	–
Change from baseline in Berlin MRI score for Entire Spine	–0.4	–0.4	0.0
LSM difference with placebo	–0.4 (–0.7, –0.2)§	– 0.4 (–0.7, –0.1)§	–
Change from baseline in Berlin MRI score for SIJ	–0.6	–0.6	–0.1
LSM difference with placebo	–0.5 (–0.9, –0.2)§	–0.5 (–0.9, –0.1)§	–
Entire treatment period (Week 52)			
	Secukinumab 300 mg s.c. (N=164)	**Secukinumab 150 mg s.c. (N=157)**	**Placebo to Secukinumab 300 mg s.c. (N=81)** / **Placebo to Secukinumab 150 mg s.c. (N=80)**
ASAS20, n/M % responders	113/139(81.3%)	113/141(80.1%)	54/72(75.0%)	59/74(79.7%)
ASAS40, n/M % responders	96/139(69.1%)	91/141(64.5%)	45/72(62.5%)	40/74(54.1%)
Spinal pain (VAS), mean change from baseline (SD), n	–42.4(27.0),140	–43.8(26.2),142	–43.1(25.0),72	–36.4(25.2),74
mNAPSI score, mean change from baseline (SD), n	–8.5(14.7),137	–7.7(12.9),142	–8.6(16.0),73	–6.2(8.8),74
Berlin MRI score Entire Spine, mean change from baseline (SD), n	–0.6(2.3),121	–0.3(1.3),124	–0.8(2.7),63	–0.4(1.3),60
Berlin MRI score SIJ, mean change from baseline (SD), n	–0.7(2.2),122	–0.5(1.7),122	–0.9(2.4),63	–1.0(2.7),59

*P<0.0001; †P<0.01 versus placebo. For binary efficacy variables, OR, 95% CI and P values using logistic regression with treatment and concomitant MTX intake status as factors after applying multiple imputation to handle missing values. For continuous Berlin MRI variables, LSM treatment difference and P values versus placebo using an ANCOVA model with treatment group and concomitant MTX intake status as factors and baseline score as continuous covariate.
For remaining efficacy variables, LSM treatment difference and P values versus placebo using an MMRM model with treatment group, visit and concomitant MTX intake status as factors, baseline score as continuous covariate and visit by treatment and visit by baseline score as interactions.
ASAS, Assessment of SpondyloArthritis international Society; mNAPSI, modified nail psoriasis severity index; MRI, magnetic resonance imaging; MTX, methotrexate; LSM, least squares mean; M, number of patients with evaluation; N, total number of randomized patients; n, number of subjects satisfying the criterion; OR, Odds Ratio; s.c., subcutaneous; SD, standard deviation; SIJ, sacroiliac joints; VAS, visual analog scale.

- The proportion of patients achieving mNAPSI score ≤2 with secukinumab increased through Week 52 (**Figure 2**)

Figure 2. Clearance of nail psoriasis with secukinumab through Week 52



Treatment group, n	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24	Week 32	Week 40	Week 48	Week 52
Secukinumab 300 mg	81	82	90	103	110	110	115	120	109	117
Secukinumab 150 mg	67	81	90	96	97	104	105	112	112	115
Placebo to Secukinumab 300 mg	39	38	41	41	46	48	52	57	61	57
Placebo to Secukinumab 150 mg	40	41	41	45	46	52	52	57	58	57

Data reported as observed
mNAPSI, modified nail psoriasis severity index; N, number of patients in this analysis; n, the number of patients with NAPSI/mNAPSI score ≤2.

CONCLUSIONS

- Secukinumab 300 and 150 mg provided significant improvements in signs and symptoms and nail psoriasis in PsA patients with axial manifestations at Week 12 and improvements were sustained through Week 52
- Secukinumab also provided significant improvement in inflammatory MRI lesions in the spine and sacroiliac joints
- Results of the MAXIMISE trial provide valuable data that will deepen the understanding of the axial PsA phenotype

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