Secukinumab Immunogenicity in Patients With Psoriatic Arthritis and Ankylosing Spondylitis During a 52-Week Treatment Period

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INTRODUCTION

- Secukinumab, a fully human monoclonal antibody that directly inhibits Interleukin IL-17A, has shown significant efficacy in the treatment of moderate to severe plaque psoriasis, psoriatic arthritis (PsA), and ankylosing spondylitis (AS), demonstrating a rapid onset of action and sustained responses with a favorable safety profile[1–7]
- Monoclonal antibody therapies may be associated with immunogenicity and the production of treatment-emergent anti-drug antibodies, which may cause adverse events, and affect drug pharmacokinetics and clinical response
- The incidence of immunogenicity of secukinumab in patients with moderate to severe plaque psoriasis has been assessed previously in the psoriasis phase 3 program as shown by treatment-emergent anti-drug antibodies in <1% patients for up to 52 weeks[1]
- Here, we assess the immunogenicity of secukinumab in patients with PsA and AS, who were treated with secukinumab for up to 52 weeks

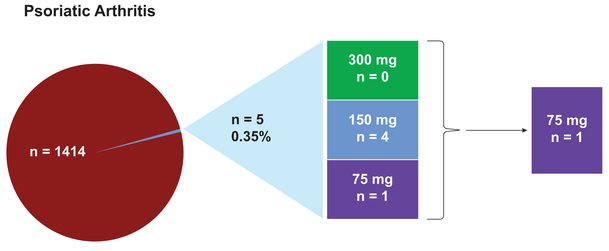
METHODS

- Immunogenicity in patients with PsA (FUTURE 1–3 studies, n = 1414)[2–4] and AS (MEASURE 1–4 studies, n = 1163)[5–8] exposed to secukinumab was evaluated at baseline and at Weeks 16 (AS only), 24, and 52
- Secukinumab immunogenicity was defined as a positive signal for anti-drug antibodies in ≥1 post-treatment sample in patients who were negative at baseline
- Drug tolerance in the meso-scale discovery assay was ≤53.8 µg/mL secukinumab. This was defined as the serum drug concentration above which the assay sensitivity is reduced for a specified level of sensitivity
- Treatment-emergent anti-drug antibody-positive samples were analyzed through Week 52 for the following:
  - drug-neutralizing potential
  - impact of anti-drug antibodies on the pharmacokinetics of secukinumab
  - immunogenicity-related adverse events
  - the impact of anti-drug antibodies on the efficacy of secukinumab

RESULTS

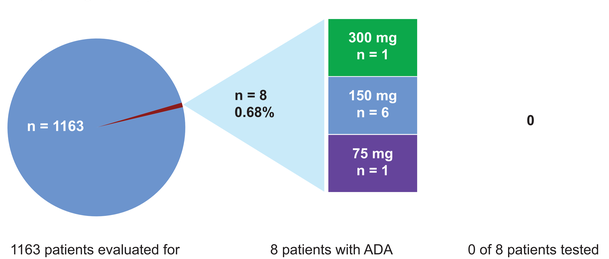
- Of 1414 patients with PsA and 1163 patients with AS who were treated with secukinumab and had samples for immunogenicity evaluation, 5 (0.35%) and 8 (0.68%) developed treatment-emergent anti-drug antibodies respectively, over 52 weeks **(Figures 1 & 2)**
  - 2 of 5 patients with PsA received concomitant methotrexate, 1 of whom received concomitant corticosteroids
  - 1 of 8 patients with AS received concomitant methotrexate, 2 of 8 patients received concomitant sulfasalazine, and 3 of 8 patients received concomitant corticosteroid

Figure 1. Summary of Secukinumab Immunogenicity Across Clinical Studies of Psoriatic Arthritis*



*Immunogenicity in patients with psoriatic arthritis (FUTURE 1–3 studies, n = 1414). Four of five patients were biologic naive. Two of five patients received concomitant methotrexate. ADA, anti-drug antibodies

Figure 2. Summary of Secukinumab Immunogenicity Across Clinical Studies of Ankylosing Spondylitis*



*Immunogenicity in patients with ankylosing spondylitis (MEASURE 1–4 studies, n = 1163). One of eight patients received concomitant methotrexate. Two of eight patients received concomitant sulfasalazine. All ADAs were non-neutralizing. ADA, anti-drug antibodies

- Associations between treatment-emergent anti-drug antibodies and secukinumab dose, dosing frequency, or mode of administration were not observed **(Table 1)**

Table 1. Overview of Patients With Treatment-Emergent Anti-Drug Antibodies

	Study	Secukinumab dose	Prior biologics	ADA (titer) /Neut-Ab[1]	IG-related AE	Impact on efficacy[2]	PK behaviour[3]
PsA	FUTURE 1	PBO-75 mg	0	W24 (Indeterminate)/Y	N	N	Normal
	FUTURE 2	PBO-150 mg	0	W52 (2.99)/N	N	N	Normal
	FUTURE 3	150 mg	Infliximab	W52 (2.14)/N	N	N	Normal
		150 mg	0	W24 (1.00)/N	N	N	Normal
		150 mg	0	W52 (2.59)/N	N	N	Normal
AS	MEASURE 1	10mg/kg (IV)-150 mg	0	W52 (2.39)/N	N	N	Normal
		PBO-150 mg	0	W52 (10.61)/N	N	N	Normal
	MEASURE 2	PBO-75 mg	0	W52 (39.39)/N	N	N	Normal
	MEASURE 3	PBO-300 mg	0	W52 (1.02)/N	N	N	Normal
	MEASURE 4	150 mg	0	W16 (6.35)/N	N	N	Normal
		150 mg No Load	0	W52/(2.96)/N	N	N	Normal
		150 mg	0	W16 (2.70)/N	N	N	Normal
		PBO–150 mg	0	W24/(2.80)/N	N	N	Normal

[1]Only positive anti-drug antibody results at the respective study week are shown. One patient had neutralizing antibodies, though antibody titer could not be determined. [2]Impact on efficacy is defined as: PsA, failure to achieve >20% reduction, compared to baseline, in both tender and swollen joint counts; AS, failure to achieve ASsessment in Ankylosing Spondylitis 20 (ASAS20), after previously achieving such improvement for at least two consecutive visits prior to the first detection of anti-drug antibodies [3]Normal PK: Concentrations in ADA-positive patients within observed range for all patients without anti-drug antibodies.

AE, adverse event; AS, ankylosing spondylitis; ADA, anti-drug antibodies; IG, immunogenicity; PBO, placebo; PK, pharmacokinetics; PsA, psoriatic arthritis; N, none; Neut-Ab, neutralizing antibodies.

- Other than one patient with PsA, all treatment-emergent anti-drug antibodies were non-neutralizing and none were associated with any immunogenicity-related adverse events
- All treatment-emergent anti-drug antibodies were associated with normal pharmacokinetics and none were associated with loss of secukinumab efficacy over 52 weeks
- In the pharmacokinetic (PK) samples from patients with PsA or AS at the time points that immunogenicity was measured, 96% had secukinumab serum concentrations below the drug tolerance level of 53.8 µg/mL, confirming sufficient assay sensitivity for measuring immunogenicity during treatment with secukinumab

CONCLUSIONS

- Secukinumab treatment was associated with treatment-emergent anti-drug antibodies in only 0.35% of PsA patients and 0.68% of AS patients over 52 weeks in a database of >2500 patients from clinical studies
- The formation of anti-drug antibodies was not associated with immunogenicity-related adverse events, potential loss of clinical response and/or deviating pharmacokinetics of secukinumab
- These results are consistent with the low incidence of immunogenicity (0.40%) seen with secukinumab over 52 weeks in clinical studies of patients with moderate to severe plaque psoriasis[1]

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