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RAPID COMMUNICATION

Efficacy and Safety of Secukinumab in Elderly Patients with Moderate to Severe Plaque-Type Psoriasis: Post-Hoc Analysis of the SUPREME Study

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Purpose: Secukinumab is a fully human monoclonal antibody that inhibits interleukin (IL)-17A approved for the treatment of moderate to severe plaque psoriasis in adults and children. We compared the efficacy and safety of secukinumab in patients aged < 65 years (adult patients) versus patients aged ≥ 65 years (elderly patients) in a post-hoc analysis of the SUPREME study.

Patients and Methods: Patients with moderate to severe plaque psoriasis received subcutaneous secukinumab 300 mg per week for the first 5 weeks, then 300 mg per month. We compared the following outcomes in patients aged ≥ 65 years vs < 65 years: baseline characteristics; PASI50/75/90/100 response rates (improvements ≥ 50%/75%/90%/100% in Psoriasis Area and Severity Index (PASI) from baseline); changes in Dermatology Life Quality Index (DLQI); Hospital Anxiety and Depression Scale (HAD-A, HAD-D) score changes; treatment-emergent adverse events (TEAEs).

Results: Secukinumab was slightly less effective in elderly patients than in adult patients (response rates at week 16: PASI90, 69.4% vs 80.9%, p = 0.4528; PASI100, 44.4% vs 56.7%, p = 0.8973). Elderly and adult patients showed a similar time course of changes in absolute PASI scores. Patients aged ≥ 65 years had a statistically significantly lower improvement in quality of life (mean DLQI reduction) than patients aged < 65 years at week 16 [−5.4 (±4.3) vs −8.8 (±6.9), p = 0.0065] and at week 24 [−5.3 (±4.4) vs −9.2 (±7.1), p = 0.0038]. Secukinumab treatment resulted in comparable mean reductions in anxiety and depression scores in both cohorts at 24 weeks [HAD-A, −1.3 (±3.3) vs −2.1 (±3.8), p = 0.9004; HAD-D, −1.0 (±3.3) vs −1.5 (±3.1), p = 0.4598]. The frequency of TEAEs in the two cohorts was similar (16.7% vs 14.6%, p = 0.7391).

Conclusion: Secukinumab is a valid option for the management of moderate to severe psoriasis in elderly patients.

Keywords: psoriasis, biologics, interleukin-17A, secukinumab, elderly

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Introduction

Psoriasis is a common inflammatory, immune-mediated skin disease; its prevalence tends to increase with age.[1–3] Due to the steadily increasing number of people aged ≥ 65 years worldwide, the population of geriatric patients with psoriasis is expanding.[4–6] The management of psoriasis in the elderly can be difficult as the presence of comorbidities and the resulting use of concomitant medications, organ dysfunction, impaired immune system, and altered pharmacokinetics complicate the balancing of benefits and adverse effects of anti-psoriasis treatment.[5,7,8] The use of topical medications is complex in this age group and the compliance to topical therapies is generally low. Also, patients aged ≥ 65 years are usually excluded from clinical studies and, therefore, evidence-based guidance for dermatologists is lacking.

The introduction of targeted systemic therapies with biologics has considerably improved the management of moderate to severe psoriasis.[9] Secukinumab, a fully human monoclonal antibody that inhibits interleukin (IL)-17A is approved by the European Medicines Agency (EMA) for the treatment of moderate to severe plaque psoriasis in adults and children, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis), and juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis). Evidence of its effectiveness in elderly patients with psoriasis is limited.[5]

The recent SUPREME study (NCT02394561) was performed to determine whether the presence of the allele HLA-Cw6 within the chromosomal psoriasis susceptibility gene 1 (PSORS1) influences the response to treatment with secukinumab.[10,11] The study showed that secukinumab ensures high rates of skin clearance regardless of HLA-Cw6 status.[10,11] Here we present the results of a post-hoc analysis of the SUPREME study comparing the efficacy and safety of secukinumab in patients aged < 65 years (adult patients) versus patients aged ≥ 65 years (elderly patients).

Materials and Methods

The design of the SUPREME study has been described in detail in a previous report.[10] Briefly, SUPREME was a 24-week, phase IIIb, multicentre, prospective study conducted across 50 centers in Italy, with an extension period of up to 72 weeks, and involving patients aged ≥ 18 years with moderate to severe plaque psoriasis. Eligible patients were treated with subcutaneous secukinumab 300 mg per week for the first 5 weeks, followed by a maintenance period of 300 mg per month.

The post-hoc analysis of SUPREME presented here compared the following outcomes in patients aged ≥ 65 years vs patients aged < 65 years: baseline characteristics; PASI50/75/90/100 response rates (improvements ≥ 50%/75%/90%/100% in Psoriasis Area and Severity Index (PASI) from baseline); changes in Dermatology Life Quality Index (DLQI); Hospital Anxiety and Depression Scale (HAD-A, HAD-D) score changes; treatment-emergent adverse events (TEAEs). Results are reported as absolute numbers and percentages or mean ± standard deviation (SD) as appropriate. Significance tests for differences between patient groups included *t*-test, Wilcoxon test, chi-square test, or Fisher exact test as appropriate. A nominal p-value of < 0.05 was considered statistically significant. A logistic regression model was used to evaluate difference in PASI response (taking into account the following covariates: height, weight, waist, age at psoriasis diagnosis and presence of metabolic syndrome), while Kaplan-Meier survival curve and Log rank test was used for time to reach PASI responses. All statistical analyses were performed using SAS software 9.2 (SAS Institute, Cary, NC, US).

Results

Of the 433 patients treated in the SUPREME study, 36 (8.3%) were aged ≥ 65 years. Mean age was 69.2 (±4.2) years and 43.1 (±11.5) years in the elderly and adult cohorts, respectively. In both cohorts, males were predominant [26/36 (72.2%) and 284/397 (71.5%), respectively]. Elderly patients had a higher mean waist circumference [101.9 (±14.1) vs 96.1 (±15.1) cm; p = 0.0336], were older at diagnosis [45.5 (±14.6) vs 25.8 (±12.8) years old; p < 0.0001] and suffered more frequently of comorbidities (83.3% vs 60.2%; p = 0.0061), in particular metabolic syndrome (41.7% vs 14.4%; p < 0.0001).

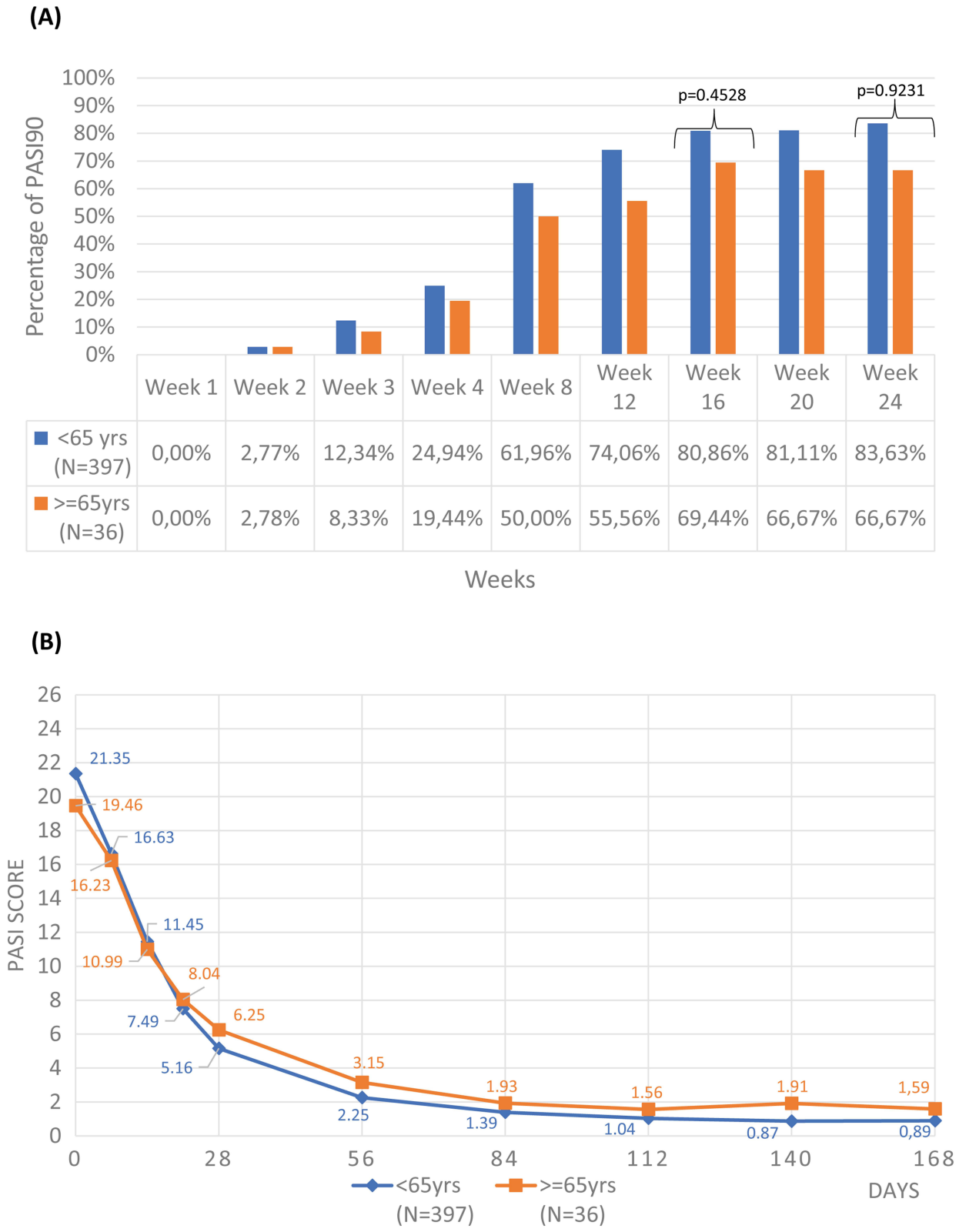

Figure 1 Efficacy of treatment with secukinumab in patients with moderate to severe psoriasis stratified by age < 65 years and ≥ 65 years. (**A**) PASI90 response rates during treatment. (**B**) Absolute PASI scores during treatment.

Table 1 Summary of TEAEs

Overall Analysis	Age < 65 Years (N=397)		Age ≥ 65 Years (N=36)		Total (N=433)	
	n	%	n	%	n	%
Number of TEAEs	579	–	83	–	662	–
Number of patients with TEAEs	215	54.6	17	47.22	232	53.58
Number of patients with serious TEAEs	28	7.05	3	8.33	31	7.16
Number of patients with TEAEs related to study drug	69	17.38	7	19.44	76	17.55
Number of patients with TEAEs leading to discontinuation of study drug	27	6.80	3	8.33	30	6.93
Deaths	1	0.25	1	2.78	2	0.46

Abbreviation: TEAEs, treatment-emergent adverse events.

Significantly fewer older patients were current smokers (27.8% vs 48.6%, p = 0.0012). Mean PASI score at baseline was numerically lower for elderly patients [19.5 (±7.7) vs 21.3 (±9.7); p = 0.2587)] who showed, however, a significantly greater rate of prior therapies with anti-TNFα biologics (44.4% vs 28.2%; p = 0.0410). In both cohorts, biologics were discontinued mostly due to lack or loss of efficacy. Of note, most elderly patients (75%) interrupted biologic therapy for loss of efficacy.

Especially in terms of PASI90 and PASI100 responses, secukinumab was slightly less efficacious in elderly patients than in adult patients (response rates at week 16: PASI90, 69.4% vs 80.9%, p = 0.4528 (Figure 1A); PASI100, 44.4% vs 56.7%, p = 0.8973). The time to first PASI90 response was similarly short in both cohorts (median time to PASI90 response, 61 vs 58 days, respectively; log-rank, 0.1761). Elderly and adult patients showed a similar time course of changes in absolute PASI scores (Figure 1B).

Elderly patients had a statistically significantly lower improvement in quality of life (mean DLQI reduction) than adult patients at week 16 [−5.4 (±4.3) vs −8.8 (±6.9), p = 0.0065] and at week 24 [−5.3 (±4.4) vs −9.2 (±7.1), p = 0.0038]. At week 16, significantly fewer older patients achieved DLQI 0/1 than adult patients (51.5% vs 71.7%, p = 0.0157). Secukinumab treatment resulted in comparable mean reductions in anxiety and depression scores in both cohorts at 24 weeks [HAD-A, −1.3 (±3.3) vs −2.1 (±3.8), p = 0.9004; HAD-D, −1.0 (±3.3) vs −1.5 (±3.1), p = 0.4598].

The frequency of TEAEs in the two cohorts was similar (respectively, 16.7% vs 14.6%, p = 0.7391) (Table 1).

Discussion

This post-hoc analysis of the SUPREME study provides a glimpse of the characteristics of elderly patients with moderate to severe plaque psoriasis and the outcomes of systemic treatment with secukinumab. Elderly patients accounted for less than 10% of the SUPREME population confirming the limited presence of patients aged ≥ 65 years in clinical studies. The baseline characteristics of this subgroup were in line with those reported in other studies evaluating older patients, including the higher frequency of comorbidities, lower frequency of current smoking, and later disease onset.[4,8,12,13] Secukinumab was efficacious and well tolerated through week 24 regardless of age. PASI90 and PASI100 response rates tended to be lower in patients aged ≥ 65 years than in younger patients, but the differences between the two cohorts were not statistically significant. Improvements in quality of life during treatment were also less pronounced in elderly patients.

Few studies have addressed the efficacy and safety of secukinumab in psoriasis patients aged ≥ 65 years. A pooled analysis of three Phase III trials evaluated secukinumab after patient stratification by age and found equivalent efficacy of this anti-IL17 in patients aged ≥ 65 years and in younger patients.[12] The rapidity and duration of response were also similar between older and younger patients, in agreement with our observations.[12] A retrospective analysis investigating

the effectiveness of anti-IL17 therapies for psoriasis in elderly patients confirmed the efficacy results reported in clinical trials.[13] Notably, elderly and younger patients had a similar profile of adverse events, despite the higher frequency of comorbidities of the elderly subgroup.[13] The safety findings of our analysis confirm this observation.

The fact that the improvement of the quality of life of the elderly patients treated with secukinumab in the SUPREME study was significantly inferior to that experienced by patients aged < 65 years may reflect the greater disease and treatment burden on elderly patients. At the same time, it highlights the need for tools able to describe more adequately outcomes relevant to the older population. As pointed out by a recent survey among psoriasis patients from different age groups, greater efforts should be devoted to the individualized management of elderly with psoriasis, because their needs differ substantially from those of younger patients with psoriasis.[4,14] A personalized approach to elderly patients with psoriasis may reduce the disease burden and improve treatment outcomes.

Our analysis is limited by its post-hoc nature and the small number of elderly patients in the SUPREME study.

Conclusion

We believe that this analysis provides useful information on the use of secukinumab in patients aged ≥65 years and confirms that this anti-IL17 agent is a valid option for the management of moderate to severe psoriasis in elderly patients.

Data Sharing Statement

The statistically analyzed data is available in the text, and the detailed data will be available on request from the corresponding author.

Ethics Statement

All patients provided written informed consent before enrolment into the study. The study was approved by all competent Ethics Committees and regulatory authorities (Supplementary Table 1). The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice, and in compliance with all federal, local and regional requirements.

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Disclosure

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