patient's vaccination record and prescribed a chest X-ray,<sup>2,3</sup> a blood smear, infections viral panel, HIV, HBV, HCV, IgG and IgM for VZV.

We dismissed the patient with acyclovir 800 mg every 6 h for 10 days and programmed a control visit.

One month later, all examinations prescribed were negative, and IgG for VZV was positive, but IgM was negative. Moreover, a past vaccination for chickenpox was tracked in the patient's records. Two weeks later, all the cutaneous lesions healed.

Still, patients referred that all his family (wife and the two small children) developed a varicelloid eruption 2 days after first patient admission.

According to Naranjo scale,<sup>4</sup> we considered probable the diagnosis of 'Disseminated herpes zoster' by the SARS-CoV-2 vaccine.

The diagnosis remains probable, despite the solid temporal relationship, due to the inability to perform a rechallenge, although rare cases of skin manifestations such as disseminated varicella have been reported in the literature after SARS-CoV-2 vaccine.<sup>5,6</sup>

We already are aware that infections cause immunodepression, and it is known that Zoster disease may appear in patients affected by several forms of COVID-19,<sup>1</sup> but disseminated varicelloid eruption, a typical sign of VZV reactivation in an immunosuppressed host, is doubtful in healthy subjects.

We believe that the Pfizer vaccine temporarily reduced or altered the responsiveness of cellular immunity to the VZV, causing a disseminated herpes zoster affection.

It is also possible that the initial vaccination for chickenpox was not sufficient and that the virus reinfected the hosts due to the already circulating virus in other family members. However, due to the recorded vaccination, the previous chickenpox infection at a young age and since he was the first family member affected, reinfection appeared quite unlikely.

What we know is that the greater the number of people vaccinated, the greater the cutaneous side effects we have observed, which have always self-resolved until now without any *sequela*.

### **Conflict of interest**

The authors have no conflict of interest to declare.

#### Acknowledgement

The patients in this manuscript have given written informed consent to the publication of their case details.

### **Data availability statement**

Data available on request from the authors.

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# LETTERS TO THE EDITOR

# Perceived stress in four inflammatory skin diseases: an analysis of data taken from 7273 adult subjects with acne, atopic dermatitis, psoriasis or hidradenitis suppurativa

#### Editor

Adult acne (AA), atopic dermatitis (AD), psoriasis (P) and hidradenitis suppurativa (HS) are common and chronic, inflammatory skin diseases with an incidence that has been estimated at almost 15% of the adult population in France.<sup>1</sup> They are often accompanied by increased psychological stress levels.<sup>2</sup>

This observational, cross-sectional, non-comparative study conducted by five patient associations in France between October 2020 and February 2021, assessed perceived stress in adults with AA, AD, P or HS, as well as self-perceived disease severity and quality of life (QoL) in a large population using a digital questionnaire. The questionnaire was distributed directly to patient association members or through social networks. The study complied with local legal requirements for the conduct of this type of study and received ethics committee approval (CPP Ile de France X, 2020-A01621-38).

The questionnaire ensured that the target dermatoses had previously been confirmed by a health care professional. Stress was

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31.62%

45.59%

43

62

31.48%

52.31%

assessed using the validated perceived stress scale (PSS) and QoL using the DLQI.<sup>3,4</sup> The PSS questionnaire measures the degree to which situations in one's life are considered as stressful. Individual scores on the PSS can range from 0 to 40, with higher scores indicating higher perceived stress. Scores ranging from 0 to 13 indicate low perceived stress, scores from 14 to 26 indicate moderate perceived stress and scores from 27 to 40 indicate high perceived stress. A DLQI score above 10 designates an important or very important impact on the patient's QoL. Moreover, patients were asked to assess the severity (mild, moderate or severe) of their dermatosis at the time the study was conducted and to confirm if they had been offered psychological support with regards to their dermatosis.

Overall, 7273 subjects participated in this survey; 1605 subjects had AA, 2538 AD, 2329 P and 801 HS. The average age was 40.6 years; 69.25% were women and 54.37% were employed. The self-assessed disease severity was moderate in 49.73% of subjects.

Stress according to disease is displayed in Table 1. In total, 66.3% of subjects reported stress scores above 27. Results for

Adult acne    N    %    N    %    N    %    N    %      Female    1275    79.4%    768    75.89%    289    88.11%      <25 years    911    56.76%    46.44%    240    73.17%    69      26 -55 years    633    39.44%    48.52%    82    25.00%    60      >56 years    631    39.44%    48.52%    82    25.00%    60      Perceived stress score*	•	Subjects with stress expressed as Severe**	
<25 years	N	%	
26-55 years63339.44%48.52%8225.00%60>56 years613.80%5.04%61.83%4Perceived stress score*<13	95	71.43%	
>56 years    61    3.80%    5.04%    6    1.83%    4      Perceived stress score*    -    -    -    13    101    8.67%    77    9.27%    13    7.03%      14-26    244    20.94%    186    22.38%    31    16.76%      ≥27    820    70.39%    568    68.35%    141    76.22%      Atopic dermatitis    N    %    N    %    N    %      <25 years	51.88%	46.44%	
Perceived stress score*      <13	45.11%	48.52%	
<131018.67%779.27%137.03%14–2624420.94%18622.38%3116.76%≥2782070.39%56868.35%14176.22%Atopic dermatitisN%N%N%<25 years	3.01%	5.04%	
$14-26$ $244$ $20.94\%$ $186$ $22.38\%$ $31$ $16.76\%$ $\geq 27$ $820$ $70.39\%$ $568$ $68.35\%$ $141$ $76.22\%$ Atopic dermatitisN%N%N%Female $1616$ $63.67\%$ $699$ $61.53\%$ $594$ $61.94\%$ $<25$ years $307$ $12.10\%$ $117$ $10.30\%$ $113$ $11.78\%$ $<26-55$ years $307$ $12.10\%$ $117$ $10.30\%$ $113$ $11.78\%$ $<26-55$ years $1761$ $69.39\%$ $774$ $68.13\%$ $684$ $71.32\%$ $>56$ years $470$ $18.52\%$ $245$ $21.57\%$ $162$ $16.89\%$ $< 13$ $338$ $13.60\%$ $239$ $21.09\%$ $76$ $7.97\%$ $<14-26$ $525$ $21.12\%$ $290$ $25.60\%$ $173$ $18.15\%$ $\geq 27162365.29\%60453.31\%70473.87\%PsoriasisN%N%N%<25 years126554.32\%97362.14\%22468.50\%<25 years126554.32\%87354.63\%21365.14\%<56 years33640.19\%62839.30\%9720.66\%<256 years26429.18\%87354.63\%114.04\%<26-55 years26429.18\%43330.86\%6523.90\%<27119062.6\%$			
≥2782070.39%56868.35%14176.22%Atopic dermatitisN%N%N%Female161663.67%69961.53%59461.94%<25 years30712.10%11710.30%11311.78%26~55 years176169.39%77468.13%68471.32%>56 years47018.52%24521.57%1621689%Perceived stress score* $$	8	7.02%	
Atopic dermatitis    N    %    N    %    N    %      Female    1616    63.67%    699    61.53%    594    61.94%      <25 years	18	15.79%	
Female161663.67%69961.53%59461.94%<25 years	88	77.19%	
<25 years	Ν	%	
26-55 years    1761    69.39%    774    68.13%    684    71.32%      >56 years    470    18.52%    245    21.57%    162    16.89%      Perceived stress score*	165	63.22%	
>56 years  470  18.52%  245  21.57%  162  16.89%    Perceived stress score*  -	34	13.03%	
Perceived stress score*    338    13.60%    239    21.09%    76    7.97%      14-26    525    21.12%    290    25.60%    173    18.15%      ≥27    1623    65.29%    604    53.31%    704    73.87%      Psoriasis    N    %    N    %    N    %      Female    1472    63.20%    993    62.14%    224    68.50%      <25 years	188	72.03%	
<13	39	14.94%	
14-26  525  21.12%  290  25.60%  173  18.15%    ≥27  1623  65.29%  604  53.31%  704  73.87%    Psoriasis  N  %  N  %  N  %    Female  1472  63.20%  993  62.14%  224  68.50%    <25 years			
≥27  1623  65.29%  604  53.31%  704  73.87%    Psoriasis  N  %  N  %  N  %    Female  1472  63.20%  993  62.14%  224  68.50%    <25 years	16	6.35%	
Psoriasis    N    %    N    %    N    %    N    %      Female    1472    63.20%    993    62.14%    224    68.50%      <25 years	34	13.49%	
Female    1472    63.20%    993    62.14%    224    68.50%      <25 years	202	80.16%	
<25 years    128    5.50%    97    6.07%    17    5.20%      26-55 years    1265    54.32%    873    54.63%    213    65.14%      >56 years    936    40.19%    628    39.30%    97    29.66%      Perceived stress score*  <	Ν	%	
26-5 years    1265    54.32%    873    54.63%    213    65.14%      >56 years    936    40.19%    628    39.30%    97    29.66%      Perceived stress score*    - </td <td>94</td> <td>64.38%</td>	94	64.38%	
>56 years    936    40.19%    628    39.30%    97    29.66%      Perceived stress score*                                      97    29.66%	6	4.11%	
Perceived stress score*  <	93	63.70%	
<13    82    4.57%    68    4.85%    11    4.04%      14-26    524    29.18%    433    30.86%    65    23.90%      ≥27    1190    66.26%    902    64.29%    196    72.06%	47	32.19%	
14-26  524  29.18%  433  30.86%  65  23.90%    ≥27  1190  66.26%  902  64.29%  196  72.06%			
≥27 1190 66.26% 902 64.29% 196 72.06%	3	2.48%	
—	26	21.49%	
Hidradenitis suppurativa N % N % N %	92	76.03%	
······································	N	%	
Female    674    84.14%    82    85.42%    348    89.00%	201	76.72%	
<25 years 125 15.61% 10 10.42% 61 15.60%	41	15.65%	
26-55 years 635 79.28% 78 81.25% 318 81.33%	203	77.48%	
>56 years 41 5.12% 8 8.33% 12 3.07%	18	6.87%	
Perceived stress score*			
<13 73 17.51% 4 9.76% 35 16.20%	31	22.79%	

Table 1 Perceived stress data for acne, atopic dermatitis, psoriasis and hidradenitis suppurativa

\*According to the PSS scale.

14-26

≥27

\*\*According to the patient (evaluation made on a VAS from 0 to 10).

124

220

29.74%

52.76%

[Correction added on 11 May 2022, after first online publication: In Table 1, there were formatting errors and were corrected in this version.]

8

29

68

113

19.51%

70.73%

	GLOBAL		Perceived stress score <27		Perceived stress score ≥27		P-value	
	N	Mean or %	N	Mean or %	N	Mean or %	Test Student	Pearson's Chi-squared test
Adult acne								
DLQI (mean score)	1003	7.1	276	4.0	726	8.6	<0.0001	
DLQI >10 * (%)	276	27.5%	27	9.8%	249	34.3%		<0.0001
Atopic dermatitis								
DLQI (mean score)	2332	7.2	642	3.6	1623	8.4	<0.0001	
DLQI >10 * (%)	688	29.5%	62	9.7%	626	38.6%		<0.0001
Psoriasis								
DLQI (mean score)	1671	7.0	421	4.2	1189	8.0	<0.0001	
DLQI >10 * (%)	478	28.6%	64	13.3%	414	34.8%		<0.0001
Hidradenitis suppurati	va							
DLQI (mean score)	417	15.9	197	17.9	220	15.8	<0.0001	
DLQI >10 * (%)	309	74.1%	163	82.7%	146	66.4%		0.0001

Table 2 Perceived stress and impact on quality of life

Not all patients have responded to the entire questionnaire.

[Correction added on 11 May 2022, after first online publication: In Table 2, there were formatting errors and were corrected in this version.]

AA, AD and P showed that the more severe the condition, the higher the perceived stress scores. This could not be observed for HS patients.

While the level of stress was very high in all groups and especially in those patients with severe disease forms, less than 15% had been offered psychological support and, when such aid was proposed, only two patients out of three had accepted it. This finding requires special attention for future patient-centred care measures to be put in place.

The DLQI score was significantly higher and impacted the QoL of patients with AA, AD and P more, especially when stress scores were above 27, which should encourage health care professionals to develop a different, patient-centred treatment approach; these results paralleled results observed for perceived stress (Table 2).

The main limitations of our study are that the population may be considered unrepresentative, that there was no control group and that the HS population was potentially too small to detect similar results. Moreover, subjects, as members of patient organizations, may suffer more from their disease and could, therefore, be more stressed. Moreover, the gender distribution is not representative, as a majority of women participated in the survey.

Despite these limits and bias, our study shows that in patients with chronic inflammatory skin diseases, psychological stress is an important issue, requiring specific attention and personalized psychological support. Implementing a patient-centred management in chronic inflammatory skin diseases may reduce psychological stress, and potentially improve treatment adherence and improved treatment outcome.

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# **Conflicts of interest**

None.

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## **Data availability statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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# Long-term drug survival of secukinumab in real life in the era of novel biologics: a 5-year, retrospective study, including difficult-to-treat areas

#### Dear Editor,

Secukinumab has exhibited exceptional performance in randomized clinical trials (RCTs).<sup>1</sup> Nonetheless, efficacy rates may differ over time in everyday practice.<sup>2</sup> This study evaluated the survival rates of secukinumab up to 5 years and determined whether real-life psoriasis patients sustain the long-term beneficial results. The introduction of novel biologics and the involvement of difficult-to-treat areas were also considered.

This is an observational retrospective analysis of clinical data extracted from our university psoriasis outpatient clinic (First Dermatology Department, Thessaloniki, Greece). Adult patients with plaque psoriasis treated with secukinumab between January 2015 and October 2021, with necessarily  $\geq$ 1 follow-up visit, were included. Failure was defined as discontinuing secukinumab definitively or switching to another treatment. All patients received the 300 mg label dose without any dose adjustment or concomitant systemic therapy. Additionally, the involvement at baseline of high-impact areas (nails, scalp, genitals, palms and/or soles) and the introduction of novel agents (brodalumab in July 2018; ixekizumab, guselkumab and risankizumab in January 2021) were analysed. Kaplan–Meier survival estimates and Cox regression (significance level P < 0.05) were used via SPSS 26.0 software (IBM, Armonk, NY, USA).

A total of 172 patients were included. Their median age was 56.2 years [Standard Deviation (SD)  $\pm$ 17.9], 62% were male, 31.3% of patients had psoriatic arthritis and 65.1% were bioexperienced. Regarding difficult-to-treat areas, 18.6% of patients had no involvement, 23.3% had nails psoriasis, 28.5% scalp psoriasis, 19.8% genital and 9.8% palmoplantar psoriasis. Most patients (41.9%) had one difficult-to-treat area affected, 18.6% none, 20.9% two and 18.6% of patients >2 of those sites.

Overall drug survival for secukinumab was 93% (160/172) at 12 months, 86% (129/150) at 18 months, 83.1% (118/

142) after 2 years, 75.4% (95/126) after 3 years, 72.7% (80/ 110) after 4 years and 69.8% (58/83) after 5 years (Fig. 1a). Fifty-two patients (30.2%) discontinued secukinumab treatment prior to 5 years due to loss of efficacy (n = 49; 28.5%) or intolerance (n = 3; 1.7%). The mean overall survival time was 48.9 ± 18.5 months. Psoriasis Area and Severity Index (PASI) 75/90/100 responses at 12 months (83.1%, 71.3% and 63.8%, respectively) were sustained to year 2 (82.2%, 69.8% and 60.4%), and up to year 5 (78.2%, 68.1% and 57.6%).

Five-year drug survival rates were significantly lower for bioexperienced than bionaïve [P = 0.04; hazard ratio (HR): 1.9] and obese patients (P = 0.00; HR: 2.1), while the presence of lesions in any difficult-to-treat area did not influence those rates (Fig. 1b,c).

Unlike the introduction of brodalumab in the management of psoriasis, which did not seem to affect the survival rates of secukinumab (P > 0.05), the probability that secukinumab was discontinued substantially increased after the initiation of ixekizumab and IL-23 agents (P = 0.00; HR: 1.42). The presence of psoriatic arthritis did not impact notably the risk of treatment discontinuation (P > 0.05; Fig. 1d). The other covariates assessed (sex, age and baseline PASI) were not related to drug survival.

The performance of secukinumab in this study is equivalent to that in already published research papers implying that secukinumab yields lower efficacy in everyday practice than in clinical trials.<sup>1–7</sup> This could be partially attributed to the heterogeneity of patients in real-life scenarios. Moreover, the analogous discontinuation rates between patients with and without difficult-to-treat areas involvement corroborate the comparable efficacy of secukinumab even in the long run among all patients, regardless of the presence of psoriasis in those sites.<sup>8</sup> Finally, the introduction of ixekizumab and IL-23 agents were significant determinants of the secukinumab survival rate, as previously reported.<sup>9</sup> However, this result of our study should be interpreted with caution since those novel agents were available in our country not until early 2021, where most secukinumab patients were already in their  $\geq 3$  years of treatment. Our findings indicate the durability of secukinumab therapy up to 5 years in psoriasis patients in the real-world setting irrespective of the lesion localization or the presence of psoriatic arthritis; nonetheless, we report somewhat lower drug survival in bioexperienced and obese patients, and when compared to RCTs results.

# **Conflict of interest** None to declare.

None to declare.

# **Funding source**

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