Difference in health-related quality of life between anxiety and depressive symptoms in Japanese patients with plaque psoriasis: the ProLOGUE study

Dear Editor

Anxiety symptoms and depressive symptoms are observed in approximately 20%–50% and 30% of patients with psoriasis, respectively.\(^1,2\) To date, however, evidence for the association of these symptoms with patients’ direct perception of their disease (called patient-reported outcomes [PROs]) remains limited. We assessed the association of anxiety symptoms and depressive symptoms with the severity of psoriasis, psoriatic symptoms, health-related quality of life (HRQoL) and satisfaction levels in Japanese patients with psoriasis using baseline data of participants from a single-arm, open-label, multicentre, prospective cohort study – ProLOGUE (Japan Registry of Clinical Trials identifier: JRCTs031180037).\(^3\) Patients (aged ≥18 years) who had plaque psoriasis without peripheral arthritis symptoms and were eligible for self-administration of brodalumab were enrolled at 15 facilities across Japan (study period, October 2017–March 2020).\(^3\)

The outcomes of interest were the Psoriasis Area and Severity Index (PASI) score and PRO scores captured using an electronic system at baseline, such as the Generalized Anxiety Disorder-7 (GAD-7),\(^4\) Patient Health Questionnaire-8 (PHQ-8),\(^5\) Dermatology Life Quality Index (DLQI), European Quality of Life 5-Dimension 5-Level Utility Index (EQ-5D-5L UI) calculated using the Japanese tariff,\(^6\) Activity Impairment domain of the Work Productivity and Activity Impairment-Psoriasis questionnaire (WPAI-PSO AI)\(^7\) and Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9).\(^8\) Anxiety symptoms and depressive symptoms were defined as a baseline GAD-7 score of ≥5\(^7\) and baseline PHQ-8 score of ≥5,\(^5,9\) respectively.

Seventy-three patients were included in the analysis (male, 82%; median age, 54 years),\(^3\) and anxiety symptoms and depressive symptoms occurred in 20 (27%) and 16 (22%) patients, respectively (Table 1). Notably, 10 (14%) patients had both anxiety symptoms and depressive symptoms. None of the patients reported clinically diagnosed anxiety disorder or depression.

The GAD-7 score was significantly higher in patients with vs without depressive symptoms, and the PHQ-8 score was

| Clinical parameters | GAD-7 score ≥5 (n = 20) | GAD-7 score ≤4 (n = 53) | P value | PHQ-8 score ≥5 (n = 16) | PHQ-8 score ≤4 (n = 57) | P value |
|---------------------|-------------------------|------------------------|--------|-------------------------|------------------------|--------|
| PASI score          | 12.95 (9.80–16.80)       | 11.70 (8.20–15.30)     | 0.26   | 11.80 (8.40–14.50)       | 12.60 (9.00–16.10)     | 0.70   |
| Itch NRS score      | 4.50 (2.0–7.0)           | 4.0 (2.0–6.0)          | 0.42   | 6.0 (4.0–7.5)            | 3.0 (1.0–6.0)          | 0.009  |
| Skin pain NRS score | 2.0 (1.0–6.0)            | 1.0 (0.0–3.0)          | 0.06   | 2.5 (1.5–7.0)            | 1.0 (0.0–3.0)          | 0.01   |
| SPI-II score        | 51.88 (49.78–53.29)      | 54.69 (46.27–60.30)    | 0.15   | 47.68 (42.06–51.88)      | 54.69 (49.08–60.30)    | 0.002  |
| GAD-7 score         | 6.5 (6.0–8.0)            | 0.0 (0.0–2.0)          | <0.001 | 7.0 (2.5–8.0)            | 0.0 (0.0–4.0)          | <0.001 |
| PHQ-8 score         | 5.0 (2.0–8.0)            | 2.0 (0.0–3.0)          | <0.001 | 7.5 (6.5–11.5)           | 2.0 (0.0–3.0)          | <0.001 |
| DLQI score          | 12.0 (7.0–16.0)          | 6.0 (3.0–8.0)          | <0.001 | 14.5 (10.0–21.0)         | 6.0 (3.0–8.0)          | <0.001 |
| EQ-5D-5L UI score   | 0.8230 (0.6615–0.8950)   | 0.8950 (0.8230–1.0000) | 0.014  | 0.7530 (0.5415–0.8810)   | 0.8950 (0.8230–1.0000) | <0.001 |
| WPAI-PSO AI score   | 45.00 (15.00–70.00)      | 10.00 (0.00–30.00)     | 0.008  | 55.00 (15.00–80.00)      | 10.00 (0.00–30.00)     | 0.003  |
| TSQM-9 domain scores, % |                      |                        |        |                         |                        |        |
| Effectiveness       | 50.00 (33.33–58.33)      | 50.00 (33.33–61.11)    | 0.76   | 44.44 (33.33–58.33)      | 50.00 (33.33–61.11)    | 0.54   |
| Convenienci        | 47.22 (38.89–61.11)      | 50.00 (50.00–66.67)    | 0.05   | 50.00 (30.56–58.33)      | 61.11 (44.44–66.67)    | 0.01   |
| Global satisfaction | 50.00 (28.57–67.86)      | 50.00 (35.71–64.29)    | 0.99   | 46.43 (32.14–57.14)      | 50.00 (42.86–64.29)    | 0.19   |

Data are presented as median (Q1–Q3), tested using the Wilcoxon rank sum test. Itch NRS and Skin Pain NRS scores may range from 0 (no itch/pain) to 10 (worst imaginable itch/pain). The SPI-II score may range from 0 to 21, and a score of ≤5 indicates anxiety symptoms. The PHQ-8 score may range from 0 to 24, and a score of ≥5 indicates depressive symptoms. The EQ-5D-5L UI score may range from –0.25 to 1.00, and higher scores indicate higher health utility. The WPAI-PSO AI score may range from 0% to 100%, and higher scores indicate more impaired regular activity. The TSQM-9 domain scores may range from 0% to 100% each, and higher scores indicate higher levels of satisfaction with medication. DLQI, Dermatology Life Quality Index; EQ-5D-5L UI, European Quality of Life 5-Dimension 5-Level Utility Index; GAD-7, Generalized Anxiety Disorder-7; NRS, Numeric Rating Scale; PASI, Psoriasis Area and Severity Index; PHQ-8, Patient Health Questionnaire-8; Q; quartile; SPI-II, Sleep Problems Index II; TSQM-9, Treatment Satisfaction Questionnaire for Medication-9; WPAI-PSO AI, Activity Impairment domain of Work Productivity and Activity Impairment-Psoriasis.
significantly higher in patients with vs without anxiety symptoms. No statistically significant difference was observed in the PASI score between patients with vs without anxiety symptoms or patients with vs without depressive symptoms. All the HRQoL-related PRO scores (DLQI, EQ-5D-5L UI and WPAI-PSO AI) were significantly more impaired in patients with vs without anxiety symptoms and patients with vs without depressive symptoms (Table 1).

To estimate the optimal cut-off values of the DLQI score for anxiety symptoms and depressive symptoms, a receiver operating characteristic curve was generated using a logistic regression model. The DLQI score cut-off value was 9 for anxiety symptoms (Fig. 1a) and 10 for depressive symptoms (Fig. 1b).

In the current analysis, anxiety symptoms and depressive symptoms were associated with HRQoL but not with satisfaction (TSQM-9 effectiveness and global satisfaction domains).
Moreover, depressive symptoms were associated with psoriasis-related symptoms, such as itching, skin pain and sleep problems, whereas no association was observed between anxiety symptoms and these psoriasis-related symptoms. Taken together, depressive symptoms may have a greater impact on psoriasis or patients’ HRQoL than anxiety symptoms.

Evidence suggests that DLQI measurements are suboptimal indicators for the screening of anxiety symptoms and depressive symptoms in patients with psoriasis. However, a DLQI cut-off score of 11 may help identify patients with anxiety symptoms and depressive symptoms in daily dermatology practice, despite a lack of questionnaire items directly related to anxiety or depression.

In summary, this analysis indicated that a substantial number of Japanese patients with psoriasis suffer from anxiety symptoms, depressive symptoms or their co-occurrence, and a DLQI score ≥11 can be an indicator of anxiety or depressive symptoms in patients with psoriasis. Our results also suggested that patients with depressive symptoms may need more attention in clinical practice than patients with anxiety symptoms.

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References
1 Fleming P, Bai JW, Pratt M, Sibbald C, Lynde C, Gulliver WP. The prevalence of anxiety in patients with psoriasis: a systematic review of observational studies and clinical trials. J Eur Acad Dermatol Venereol 2017; 31: 798–807.
2 Dowlatshahi EA, Wakkee M, Arends LR, Nijsen T. The prevalence and odds of depressive symptoms and clinical depression in psoriasis patients: a systematic review and meta-analysis. J Invest Dermatol 2014; 134: 1542–1551.
3 Imafuku S, Kanai Y, Murotani K et al. Utility of the Dermatology Life Quality Index at initiation or switching of biologics in real-life Japanese patients with plaque psoriasis: results from the ProLOGUE study. J Dermatol Sci 2021; 101: 185–193.
4 Spitzer RL, Kroenke K, Williams JBW, Loeve B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006; 166: 1092–1097.
5 Kroenke K, Strine TW, Spitzer RL, Williams JBW, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord 2009; 114: 163–173.
6 Ikeda S, Shiroya T, Igashiri A et al. Developing a Japanese version of the EQ-5D-5L value set. J Natl Inst Public Health 2015; 64: 47–55.
7 Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoconomics 1993; 4: 353–365.
8 Bharma M, Payne K, Atkinson MJ, Desrosiers MP, Morisky DE, Gemen E. Validation of an abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9) among patients on antihypertensive medications. Health Qual Life Outcomes 2009; 7: 36.
9 Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. Psychiatr Annals 2002; 32: 509–515.
10 Lamb RC, Matcham F, Turner MA et al. Screening for anxiety and depression in people with psoriasis: a cross-sectional study in a tertiary referral setting. Br J Dermatol 2017; 176: 1028–1034.

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