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The Value of Achieving Complete or Near-Complete Resolution of Psoriasis

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BACKGROUND

- Psoriasis adversely affects important aspects of patients' lives, including physical functioning and mental functioning, to a degree comparable to that of other major diseases such as cancer, arthritis, hypertension, heart disease, diabetes, and depression.[1]
- Among the most widely utilized tools for evaluating psoriasis treatment benefit are the Psoriasis Area and Severity Index (PASI) for clinical efficacy and the Dermatology Life Quality Index (DLQI) for health-related quality of life (HRQOL).
  - The PASI assesses four body regions (head, trunk, upper extremities, and lower extremities) for erythema, infiltration, desquamation and body surface area. The instrument yields a single score that ranges from 0 (no disease) to 72 (maximal disease).[2]
  - The DLQI is a patient-administered, 10-question, validated general dermatology quality of life questionnaire that assesses the following six domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The questionnaire yields a score ranging from 0 to 30, with a lower score indicating that the disease and/or treatment has less impact on a patient's daily life.[3,4] Absolute scoring for the DLQI has been further categorized into bands as follows: 0 to 1 indicates that the disease or treatment has no effect, 2 to 5 indicates a small effect, 6 to 10 indicates a moderate effect, 11 to 20 indicates a very large effect, and 21 to 30 indicates an extremely large effect.[5]
- A 75% improvement in the PASI (PASI 75) is generally considered the clinical gold standard of treatment efficacy in patients with psoriasis.[6] Outcomes for patients who achieve higher levels of response such as 90% or 100% PASI improvement (PASI 90 or PASI 100) are not fully characterized.

OBJECTIVE

- To summarize the incremental benefits in outcomes, such as HRQOL, associated with achieving complete or near-complete resolution of psoriasis, indicated by PASI ≥ 90 and/or Physician Global Assessment (PGA) score of 0, compared with lesser response.

METHODS

- A targeted literature search was conducted in the PubMed and Embase databases using a date limit of 10 years (January 1, 2005–March 10, 2015) to identify clinical or observational studies or literature reviews written in English on the benefits of achieving complete or near-complete resolution of psoriasis in patients with moderate to severe disease.
- Complete or near-complete resolution of psoriasis was defined as follows:
  - 90%-99% or 100% improvement in PASI score (ie, PASI 90 or PASI 100)
  - PGA score of 0
- One reviewer performed level 1 screening on 328 titles and abstracts and level 2 screening on 92 full-text articles.
- 14 articles were selected for inclusion using the following criteria:
  - Patients with moderate to severe psoriasis
  - Included both clinical (PASI and/or PGA) and HRQOL data
  - Included treatments of interest: adalimumab, infliximab, ustekinumab, ixekizumab, brodalumab, and secukinumab
- The following were extracted from each selected article, where available:
  - Study design elements
    - Study type (eg, randomized controlled trial, observational study)
    - Treatment and treatment duration
- Definition of resolution of psoriasis (PASI, PGA)
- Patient-reported outcome (PRO) measure used (eg, DLQI, Short-Form [SF]-36 Health Survey [SF-36])
- Relationship of complete or near-complete resolution and PROs, such as:
  - Proportion of PRO responders by PASI level (PASI 75, PASI 90, PASI 100)
  - Mean change in PRO by PASI level (PASI 75, PASI 90, PASI 100)
  - Proportion of PRO responders by PGA response level
  - Mean change in PRO by PGA response level
  - Correlation between PASI and PRO (eg, DLQI)

RESULTS

- A total of 14 articles were included in the literature review focusing on the added value of complete or near-complete resolution of psoriasis.
  - The majority of studies were randomized controlled trials (n = 5) or pooled analyses or subanalyses of clinical studies (n = 5). The remainder of the studies were a mix of literature reviews (n = 2) and observational studies (n = 2).
  - Most studies defined resolution of psoriasis based on the PASI (n = 10), whereas a smaller proportion used the PGA (n = 2) or both PASI and PGA (n = 2).
  - No articles or conference abstracts were found for ustekinumab or secukinumab that measured the added value of complete or near-complete resolution of psoriasis.
- The most commonly reported PRO instrument was the DLQI (n = 11). A few studies (n = 3) reported results of other instruments, including the psoriasis-specific Psoriasis Symptom Inventory (PSI) (n = 1), the Zung Self-rating Depression Scale (ZDS) (n = 1), and an itch visual analog scale (VAS) (n = 1).
- The presented clinical studies and literature reviews (n = 10) focused on the association of scores (either observed/absolute or change) between the PASI or PGA and PROs.

Objective Psoriasis Severity and Patient-Reported Outcomes

Correlation Between Psoriasis Activity and Severity Index and Patient-Reported Outcomes

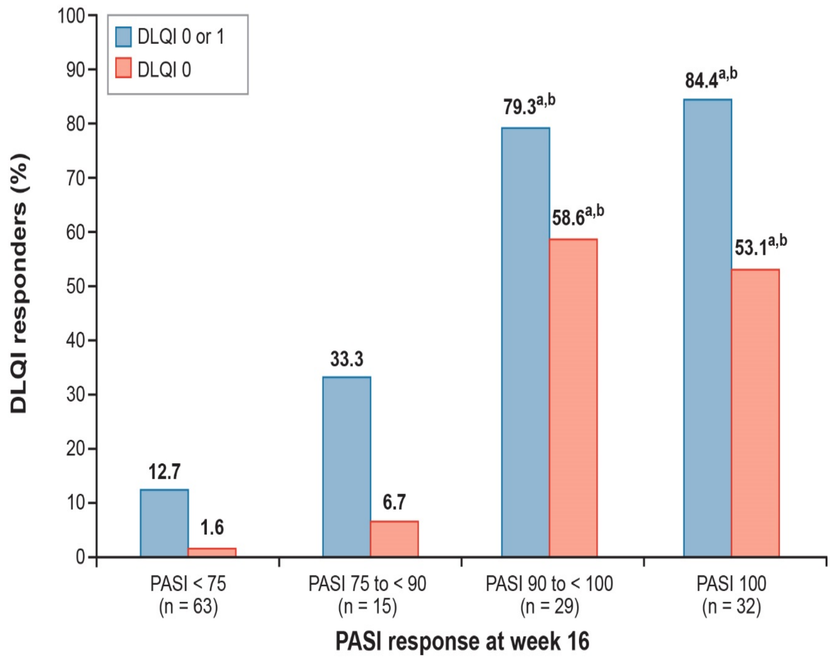
- The correlation between PASI improvement and HRQOL improvement (ie, DLQI and depressive symptoms) has been reported in several studies.[7-9] This relationship is similar for absolute scores in addition to change scores.
  - In a systematic review of randomized controlled trials of biological agents for the treatment of moderate to severe psoriasis, Mattei et al.[7] reported a coefficient of determination (R^2) value of 0.80 when mean percentage reduction in PASI score was plotted against mean reduction in DLQI score across 22 treatment arms ($P < 0.01$). The results indicated that an improvement from baseline in PASI predicts a reduction in DLQI and thus an improvement in HRQOL.[7]
  - Menter et al.[8] sought to determine the effect of adalimumab on depression symptoms in patients with psoriasis. Attainment of a PASI 75 response was associated with a significant improvement in depression symptoms measured by the ZDS.
  - A phase 3 multicenter European and Canadian study (EXPRESS) evaluated the impact of long-term infliximab maintenance therapy for moderate to severe psoriasis and demonstrated a correlation between the absence of skin symptoms and maximal improvement in HRQOL. At week 24, approximately 70% of patients with a PASI absolute score of 0 also had a DLQI score of 0, whereas only a small percentage of patients with a PASI score greater than 5 achieved a DLQI score of 0.[9]

RESULTS (continued)

Achieving Complete or Near-Complete Resolution is Associated With Significantly Greater Improvements in Patient-Reported Outcomes Compared With Lesser Response

- Edson-Heredia et al.[10] examined whether greater improvements in PASI score were associated with larger improvements in DLQI score and pruritus severity (itch VAS) in patients with moderate to severe plaque psoriasis. In a randomized, double-blind, placebo-controlled phase 2 clinical trial in patients with psoriasis treated with ixekizumab or placebo, significantly greater improvements in DLQI score and itch VAS mean score were observed with increasing PASI response ($P < 0.05$, all comparisons).
  - In both the PASI 100 and PASI 90 to < 100 groups, greater than 50% of patients reached a DLQI of 0 (no effect of psoriasis on HRQOL) at week 16, compared with 6.7% for the PASI 75 to < 90 group and 1.6% for the PASI < 75 group (Figure 1).[10]
  - At week 16, achieving a PASI 100 response was associated with a 50.8-point decrease (improvement) in itch VAS score, which was significantly better than the 20.1-point improvement observed in the PASI 75 but less than PASI 90 response group ($P = 0.05$).[10]

Figure 1. Change From Baseline to Week 16 on DLQI Total Scores for PASI Response Groups



[a] P < 0.05 for pairwise comparison vs. < PASI 75; [b] P < 0.05 for pairwise comparison vs. PASI 75 to < 90. Edson-Heredia et al.[10]

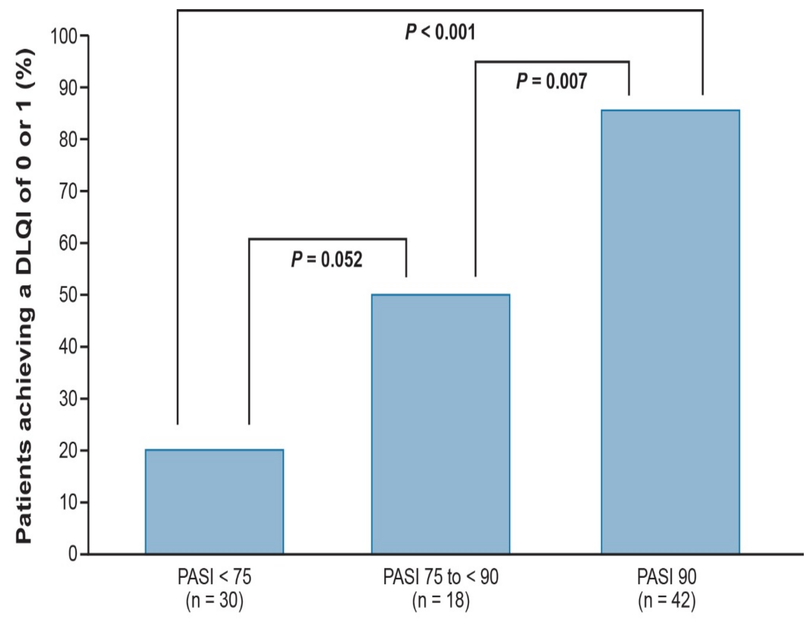
- Viswanathan et al.[11] examined the effects of total skin clearance on HRQOL and psoriasis symptom severity in subjects with moderate to severe psoriasis using pooled data from a phase 2 dose-ranging trial in psoriasis using brodalumab. HRQOL was measured by the DLQI and psoriasis symptom severity by the PSI in patients with moderate to severe psoriasis following 12 weeks of treatment. Dermatology HRQOL and psoriasis symptom severity was compared between patients with total skin clearance (static Physician Global Assessment [sPGA] score of 0 or PASI 100) and those whose skin was almost clear (sPGA score of 1 or PASI 75 to < 100).
  - 60.7% of patients with a PASI 100 response at week 12 had a DLQI score of 0, compared with 53.2% of patients with a PASI 75 to < 100 response ($P = 0.5$).
  - 64.8% of patients who achieved total skin clearance (PASI 100) had a PSI total score of 0, compared with 45.7% of patients with a PASI 75 to < 100 response ($P = 0.04$).[11]
- Zhu et al.[12] conducted an analysis using data from a randomized, double-blind, placebo-controlled phase 2 clinical trial in patients with moderate to severe plaque psoriasis treated with ixekizumab or placebo to determine whether high levels of clinical response are associated with greater improvements in PROs. Changes in DLQI and itch VAS scores from baseline to week 16 were compared among sPGA groups (0, 1, 2, and > 2). Patients who had complete resolution (sPGA score of 0) or minimal disease (sPGA score of 1) had significantly greater reductions in mean DLQI total score (–9.9 and –7.6, respectively) and mean itch VAS scores (–55 and –41, respectively) than those with an sPGA score of 2 or greater. In addition, significantly greater proportions of patients who had sPGA of 0 or sPGA of 1 achieved a DLQI response of 0 or 1 (82% and 65%, respectively) than those with sPGA of 2 (30%, $P < 0.05$) or sPGA > 2 (9%, $P < 0.001$). Similarly, significantly greater proportions of patients with sPGA of 0 (51%) or sPGA of 1 (44%) achieved DLQI response of 0, compared with those with sPGA of 2 (0%, $P < 0.001$) or sPGA > 2 (2%, $P < 0.001$).[12]
- Data from patients with moderate to severe plaque psoriasis were pooled from a phase 2 clinical trial of brodalumab to examine the relationship between achieving higher levels of improvement in PASI score and PROs as measured by the PSI and the DLQI.[13] The PSI contains eight items that measure psoriasis symptoms at either a 24-hour or 7-day recall; the best possible score of 0 indicates no symptoms.
  - In the PASI 100 group:
    - A PSI score of 0 (24-hour recall) was achieved by 66% of patients, compared with 14% of the PASI 75 to < 90 group.
    - A DLQI score of 0 was achieved by 61% of patients, compared with 31% in the PASI 75 to < 90 group.[13]

RESULTS (continued)

- Strober et al.[14] compared changes in PROs between patients with moderate to severe psoriasis who achieved sustained robust response (SRR) with adalimumab therapy for psoriasis and those who did not. Patients were categorized as achieving SRR to adalimumab therapy if they had at least PASI 90 response at all visits from week 16 to week 52. Patients with SRR were 4.5 times more likely to achieve clinically important improvements in DLQI (≥ 5-point improvement) at week 52 compared with those patients without SRR ($P < 0.0001$).
- In a pooled analysis from two Japanese phase 3 clinical trials in patients with moderate to severe psoriasis treated with infliximab, the percentages of patients achieving a DLQI score of 0 or 1 at the complete assessment (week 66 in the double-blind trial or week 50 in the open-label trial) increased with the increasing percentage improvement in PASI[15]:
  - 20.0% (6/30) of PASI 75 nonresponders
  - 50.0% (9/18) of PASI 75-90 responders
  - 85.7% (36/42) of PASI 90 responders

  The percentage of patients achieving a DLQI of 0 or 1 among PASI 90 responders was significantly higher than patients achieving a DLQI of 0 or 1 among PASI 75 to < 90 responders ($P = 0.007$) (Figure 2).[15]

Figure 2. Percentage of Patients Achieving a DLQI Score of 0 or 1 According to Percentage Improvement in PASI at the Complete Assessment (Week 50 or Week 66)



Torii et al.[15]

- Revicki et al.[16] conducted a secondary analysis of two phase 3 clinical trials of adalimumab (CHAMPION and REVEAL) in patients with moderate to severe plaque psoriasis. They reported statistically significant differences between PASI response groups in DLQI total scores and in SF-36 summary and domain scores ($P < 0.0001$).
  - The PASI 100 and PASI 90 to < 100 groups demonstrated improvements of greater than 10 points in DLQI total scores, statistically significantly greater than the improvements observed for the PASI 75 to < 90 and other response groups ($P < 0.001$).

DISCUSSION

- Several analyses of clinical studies of adalimumab, infliximab, ixekizumab, brodalumab, and combined treatments have indicated that achieving PASI 90, PASI 100, and/or a PGA score of 0 yields benefits as demonstrated by significant improvements in PROs (eg, DLQI score, measures of symptom severity) compared with a lower PASI or PGA response.
- Most studies assessing the relationship between improvements in psoriasis severity and PROs utilized the DLQI, which appears to capture significant incremental improvements in patients with psoriasis achieving complete or near-complete skin clearance. The relationship between degree of skin clearance and other PROs such as depression, work productivity, and health care resource utilization should be further assessed.

CONCLUSIONS

- This literature summary provides further evidence that achieving complete or near-complete resolution in psoriasis is associated with greater improvement in PROs.
- Accordingly, establishing complete or near-complete resolution as the therapeutic goal would have a significant impact on HRQOL and other outcomes in patients with moderate to severe psoriasis.

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ISPOR 18th Annual European Congress; Milan, Italy; 7-11 November 2015

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