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Determination of the Nail Psoriasis Severity Index improvement rate standards for nail psoriasis treatment in a phase IV clinical trial of ustekinumab: the MARCOPOLO study

Editor

Clinical trials of psoriasis use efficacy assessment tools including the Psoriasis Area Severity Index (PASI), body surface area, physicians' global assessment (PGA) score and Dermatology Life Quality Index (DLQI). A 75% improvement in the PASI score (PASI75) is generally accepted as an indicator of therapeutic effectiveness, and a 90% improvement (PASI90) is thought to depict almost complete clearance. Nail psoriasis is also the target of biologics trials. The Nail Psoriasis Severity Index (NAPSI) is used to evaluate nail improvement.[1] However, NAPSI-specific target improvement rates like PASI75 or PASI90 have not been established. Establishing standard rates would be helpful because they can be used to compare efficacy across trials and evaluate individuals objectively.

This is a *post hoc* analysis of a phase IV, multicenter, open-label, real-world observational clinical trial, the MARCOPOLO study (ClinicalTrials.gov #NCT01677598) to establish standard NAPSI improvement rates. The trial was performed according to current guidelines on good clinical practice and followed institutional regulations. Ustekinumab was administered over a period of 52 weeks. PASI, PGA, DLQI and NAPSI scores were recorded at every visit by the same rater at each site. We selected the assessment data at baseline, 28 and 52 weeks, the time points used in previous clinical trials of ustekinumab.[2,3] The PASI75 and PASI90 achievement rates were calculated to be used as references. NAPSI improvement rates were calculated to estimate the cumulative number of patients that corresponded to the proportion of PASI75 and PASI90 responders.

From 102 patients, we analysed 81 patients who had nail psoriasis. Their mean PASI and NAPSI scores at baseline were 20.8 ± 11.8 and 31.9 ± 35.9, respectively. PASI75 and PASI90 at week 28 were achieved in 70.6% and 32.4% of patients, respectively (Table 1). The corresponding NAPSI improvement rates for the PASI75 and PASI90 were 25% and 63% (Fig. 1a). We selected NAPSI25 and NAPSI65 for convenience. At week 52, PASI75 and PASI90 were achieved in 70.6% and 39.2% (Table 1), and these proportions corresponded to 42% and 71% NAPSI improvement rates, respectively. The nearest NAPSI improvement rates were NAPSI40 and NAPSI70 (Fig. 1b).

Unlike the PASI score, in which PASI75 is accepted as a measure of effectiveness, the NAPSI has been used in different ways. In one trial, NAPSI75 was adopted to compare the effectiveness of etanercept, adalimumab, infliximab and ustekinumab.[4] However, NAPSI75 could not be used to assess nail psoriasis improvement in most phase III clinical trials because NAPSI75 is relatively hard to achieve. A NAPSI50 improvement rate was used in a trial.[5] More commonly, a mean NAPSI improvement rate has been used. A NAPSI improvement rate of approximately 40% to 50% compared with baseline is the usual outcome.[2,6] In addition, because nail psoriasis improves at a slower rate, defining two NAPSI improvement rates at different time points is essential.

It must be noted that our standard was from a trial of ustekinumab only. Other new biologics, such as ixekizumab, may show a NAPSI improvement profile superior to our results.[7] The speed of nail psoriasis improvement varies across biologics. However, we do not have to prepare NAPSI improvement standards for every biologic once we have an acknowledged standard.

In conclusion, NAPSI25 and NAPSI40 could be used as standards corresponding to PASI75 for nail psoriasis in the early phase and late phase, respectively. Because nail psoriasis improves slowly over a year, it would be advisable to wait longer before deciding on the therapeutic success of a modality.

Table 1 Cumulative patient numbers and proportions according to PASI improvement rates from baseline at 28 and 52 weeks

PASI improvement rate	PASI50 n (%)	PASI75 n (%)	PASI90 n (%)	PASI100 n (%)
28 weeks	88 (86.3)	72 (70.6)	33 (32.4)	7 (6.97)
52 weeks	88 (86.3)	72 (70.6)	40 (39.2)	13 (12.7)

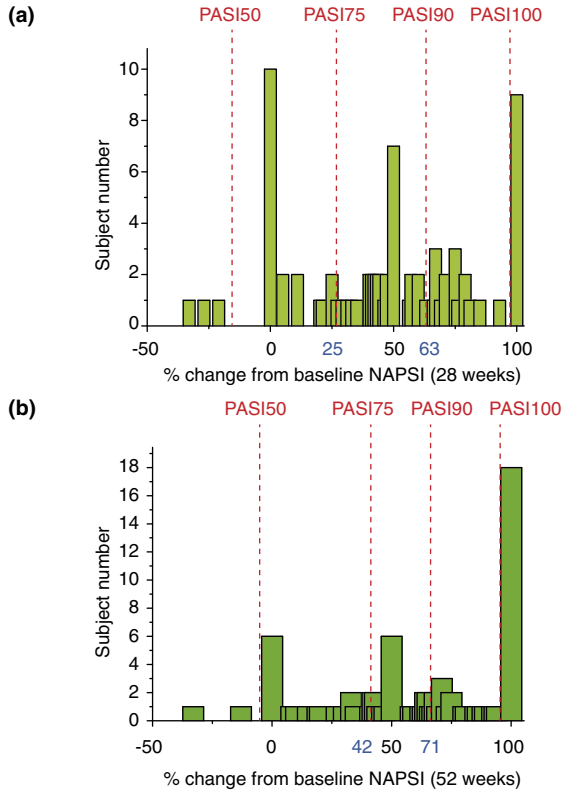

Figure 1 Cumulative number of patients according to NAPSI improvement rates (a) at 28 weeks and (b) at 52 weeks. (a) PASI75 and PASI90 at week 28 were achieved in 70.6% and 32.4% of patients, respectively. The NAPSI improvement rates corresponding to PASI75 and PASI90 achievement rates were 25% and 63% from baseline, respectively. The dotted lines indicate the PASI improvement rates and represent the proportion of patients with a NAPSI improvement rate corresponding to PASI50, PASI75, PASI90 and PASI100. Extreme outliers (over 50% NAPSI aggravation) caused by participant withdrawal were excluded from the graph. (b) PASI75 and PASI90 at week 52 were achieved in 70.6% and 39.2% of patients, respectively. The NAPSI improvement rates corresponding to PASI75 and PASI90 achievement rates were 42% and 71% from baseline, respectively. Extreme outliers (over 50% NAPSI aggravation) caused by withdrawal of participation and early termination of ustekinumab were excluded from the graph.

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Monitoring structural changes in Demodex mites under topical Ivermectin in rosacea by means of reflectance confocal microscopy: a case series

Dear Editor,

Rosacea is a common inflammatory disease, mainly affecting the face and with significant impact on patients' life quality. Just recently, topical Ivermectin (Soolantra® 10 mg/g Crème) has been introduced in the treatment of rosacea thanks to its double anti-parasitic and anti-inflammatory activity, resulting in a reduction in papulo-pustular manifestations, blepharitis and