CONTENT VALIDITY and ASSESSMENT OF THE PSYCHOMETRIC PROPERTIES and SCORE INTERPRETATION OF A PRURITUS NUMERIC RATING SCALE in ATOPIC DERMATITIS

Gil Yosipovitch[1], Alissa Rams[2], Jessica Baldasaro[2], Laurine Bunod[2], Laure Delbecque[3], Sara Strzok[2], Juliette Meunier[2], Hany Elmaraghy[3], Luna Sun[3], Evangeline Pierce[3]

[1]Dr Phillip Frost Department of Dermatology and Itch Center, Miller School of Medicine, OR, USA, [2]Modus Outcomes, Cambridge MA, USA & Lyon, France, [3]Eli Lilly and Company, Indianapolis, IN, USA.

BACKGROUND

- Pruritus is a key symptom of atopic dermatitis (AD)[1]; mitigating itch is an important outcome of treatment[2, 3, 4].
- The Pruritus Numeric Rating Scale (PNRS) is a single item that assesses worst itch severity over the past 24 hours using an 11-point NRS ranging from 0 (no itch) to 10 (worst itch imaginable) (Figure 1).

OBJECTIVE

- This mixed-methods study aimed to gather evidence regarding the content validity and psychometric properties of the PNRS to determine whether it is fit-for-purpose[5] for use in AD clinical trials.

KEY RESULTS

Qualitative Results

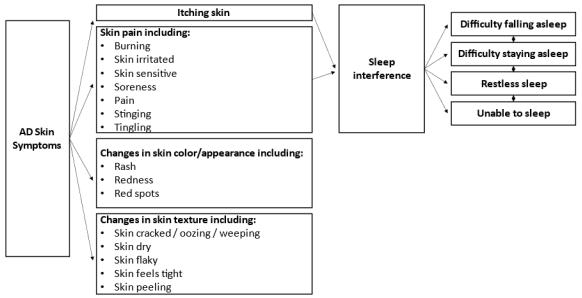
- Most patients stated that a 2-point (n=6) or 3-point (n=10) decrease in PNRS score indicated meaningful improvement.
- Cognitive interview results indicated that the PNRS is relevant, appropriate, and interpreted as intended by adults and adolescents and its recall period and response scale are acceptable and well-understood.

Quantitative Results

- Meaningful within-patient change (MWPC) was defined as a 3-point improvement using the clinical trial data.
- Large ES (> 0.80) were observed for improvement according to the change in IGA (Figure 3) and according to the GAC-AD at Week 16 (Figure 4);

RESULTS

Figure 2. Conceptual model of itch experience in AD



Abbreviation: AD: atopic dermatitis;

Table 2. Correlations between the Pruritus NRS and IGA, EASI, BSA, DLQI, and POEM at baseline and Week 16

	Polychoric Correlation coefficients	
	Pruritus NRS score at baseline N=261	Pruritus NRS score at Week 16 N=180
IGA Score	0.24	0.52
EASI Score	0.31	0.48
BSA	0.22	0.43
DLQI Total Score	0.41	0.65
DLQI1-How Itchy, Sore, Painful, Stinging?	0.73	0.77
POEM Total Score	0.58	0.76
POEM-How Many Days of Itchy Skin?	0.71	0.83

Abbreviations: BSA: Body Surface Area; DLQI: Dermatology Life Quality Index; EASI: Eczema Area and Severity Index; IGA: Investigator Global Assessment; POEM: Patient Oriented Eczema Measure

CONCLUSION

- The PNRS provides a valid and reliable patient-reported measure of itching severity in patients with AD and can detect change.
- A 3-point improvement on the PNRS reflects MWPC according to qualitative and quantitative data.
- These findings provide evidence supporting the scale is fit-for-purpose for inclusion as an endpoint to evaluate the efficacy of AD treatments in moderate-to-severe AD patients.

LIMITATIONS

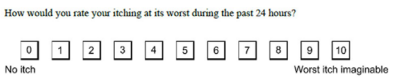
- The quantitative analysis for phase 2b study was carried out only in adult population.
- There is not an even distribution of races and ethnicity for the adolescent population in the qualitative analysis.

METHODS

Qualitative Methods

- Concept elicitation and cognitive interviews with 21 patients (≥12 years) with moderate-to-severe AD were conducted to understand patients' experiences with AD and debrief the PNRS.
- Interview transcripts were analyzed thematically[6], and saturation was assessed[7] to ensure data adequacy.
- Concepts extracted from interviews were categorized into a conceptual model of patient experience of itch in AD.
- Debriefing analysis assessed patients' understanding of the item and response choices. Patients' interpretations of meaningful change for the PNRS were compiled.

Figure 1. Pruritis Numeric Rating Scale



Quantitative Methods

- Data collected daily from adults with moderate-to-severe AD enrolled in a phase 2b, randomized, double-blind, placebo-controlled study (NCT03443024) were used to assess the psychometric performance.
- PNRS was summarized by a prorated weekly average for each visit. Test-retest reliability, construct validity, and ability to detect change (responsiveness) were used to assess the psychometric performance of the PNRS.
  - Reliability was assessed by computing intraclass correlation coefficients (ICCs) between Week 12 and Week 16 in a subsample of patients who had no change in the Investigator Global Assessment (IGA) between the two timepoints of interest.
  - Construct validity was assessed by computing polychoric correlation coefficients with clinician-reported outcomes (ClinROs) and patient-reported outcomes (PROs).
  - Responsiveness was assessed by calculating effect-sizes (ES) in subgroups of patients defined by the Global Assessment of Change – AD (GAC-AD) and change from baseline in IGA at Week 16.
- Anchor-based methods (using IGA and GAC-AD as anchors) were used to determine MWPC in the PNRS.

RESULTS

Qualitative Results

- 15 adult and 6 adolescent patients aged 12-64 years were interviewed (Table 1). All reported some itching within the last 24 hours; 12/21 rated their worst itching at 6 or 7 points on the 11-point PNRS.
- All patients confirmed that itch is a core concept in AD (n=20 reporting spontaneously, n=1 probed). Saturation was met for symptoms related to AD. 21 unique AD symptom concepts were organized into a conceptual model (Figure 2).
- Patients cited the persistent nature of itching and frequency of itch along with distraction and interference with daily activities, including sleep interference, caused by itching as the main reasons they found itching the most bothersome symptom of AD.

Quantitative Results

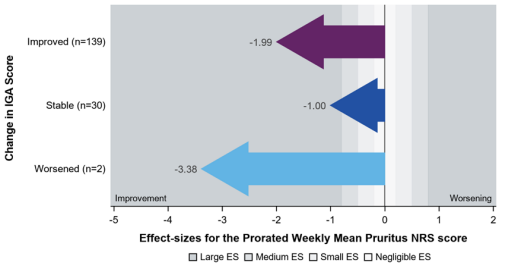
- Mean age of the clinical trial population was 39 years (range: 18-87) with 59% of females. Mean time with atopic dermatitis was 23 years (range: 1-73).
- In stable patients defined by IGA, ICC was 0.89 between Week 12 and Week 16. Lower correlations were observed with ClinROs than with PROs, as expected, and correlations were higher at Week 16 than at baseline (Table 2).

Table 1. Qualitative study demographic and health data (N=21)

	Adult (n=15)	Adolescent (n=6)
Age (in years)		
Mean (SD)	30.4 (12.9)	13.0 (1.0)
Gender, n (%)		
Female	11 (73%)	3 (50%)
Race, n (%)		
Asian	8 (53%)	5 (83%)
Black	0 (0%)	1 (17%)
Native Hawaiian/Pacific Islander	1 (7%)	0 (0%)
White	4 (27%)	0 (0%)
Biracial	1 (7%)	0 (0%)
Missing	1 (7%)	0 (0%)
Ethnicity, n (%)		
Non-Hispanic/Non-Latino	13 (87%)	6 (100%)
Education level, n (%)		
Elementary/primary school	0 (0%)	3 (50%)
Some high school	0 (0%)	3 (50%)
Some college	5 (33%)	0 (0%)
Associate degree	1 (7%)	0 (0%)
Bachelor's degree	7 (47%)	0 (0%)
Post-graduate	1 (7%)	0 (0%)
Trade	1 (7%)	0 (0%)
BSA (in %)		
Mean (SD)	17.1 (1.0)	16.8 (7.1)
Min-Max (%)	10-40	10-30

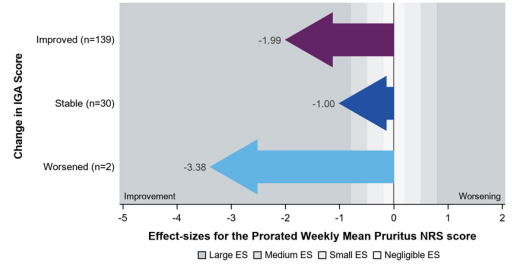
Abbreviation: BSA=body surface area; Max = maximum, Min = minimum, n = number of patients, SD = standard deviation

Figure 3. Effect-sizes of the change in Pruritus NRS according to the change in IGA between baseline and Week



Abbreviation: IGA: Investigator Global Assessment; NRS: Numeric rating scale

Figure 4. Effect-sizes of the change in Pruritus NRS according to the GAC-AD at Week 16



Abbreviation: AD: atopic dermatitis; ES: Effect sizes; NRS: Numeric Rating Scale; GAC: Global Assessment of Change;

DISCLOSURES

- This research was funded by Eli Lilly & Company. Gil Yosipovitch conducted clinical trials or received honoraria for serving as a member of the Scientific Advisory Board of Eli Lilly, TREVI, Novartis, Regeneron, Sanofi, Galderma, Pfizer, Bellus, Kiniksa, and LEO and received research funds from Pfizer, LEO, Novartis, and Eli Lilly. Alissa Rams, Jessica Baldasaro, Laurine Bunod, Sara Strzok, and Juliette Meunier are employees of Modus Outcomes, which was hired to conduct this research. Laure Delbecque, Hany Elmaraghy, Luna Sun, and Evangeline Pierce are employees of Eli Lilly & Company.
- "Almirall has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications including atopic dermatitis in Europe. Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside of Europe".

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