Psychometric Evaluation and Estimation of Meaningful Change Thresholds of Patient-reported Outcome Measures in Chronic Inducible Cold Urticaria

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Introduction

- Chronic inducible cold urticaria (CICU) is characterized by the spontaneous development of itchy wheals (hives), angioedema or both for >6 weeks after skin contact with cold air, cold liquids, cold solid objects, or evaporation-based cooling.[1]
- A 24-week, double-blind, randomized, placebo-controlled study (LIBERTY-CINDU CUrIADS: NCT04681729) evaluated the use of dupilumab in patients with CICU who remained symptomatic despite the use of H1-antihistamine treatment.
- Several patient-reported outcome measures (PROMs) were included in the trial comparing dupilumab with placebo.

Methods

- UCT comprised of 4 items yielding a total score ranging from 0 to 16 where higher score reflects better disease control.
- For the ColdUAS 2-week score, mean score was calculated as the average of the daily ColdUAS sum scores (range 0–6, higher score indicates higher severity) using item 1 (skin reaction) and 2 (skin sensations) scores.
- DLQI comprised of 10 items yielding a total score ranging from 0 to 30 where higher score reflects greater quality of life impairment.
- Data at baseline, Week 12, and Week 24 from LIBERTY-CINDU CUrIADS study were analyzed to investigate:
  - Reliability (internal consistency and test-retest).
  - Construct validity (convergent validity and known-groups validity).
  - Sensitivity to change.
- Anchor-based approach was also used to estimate within-patient and between-group MCTs using Patient Global Impression of Severity (PGIS), Patient Global Impression of Change, and ColdUAS item-5 (overall symptom severity) as anchors.

Objective

- **To assess the psychometric properties, including Meaningful Change Thresholds (MCTs) estimation of three PROMs: Urticaria Control Test (UCT), Cold Urticaria Activity Score (ColdUAS), and Dermatology Life Quality Index (DLQI), in patients with CICU.**

Conclusions

- **The study suggested that the UCT, ColdUAS and DLQI are valid, reliable, and sensitive to change PROMs with a responder definition estimated.**
- **The UCT, ColdUAS, and DLQI are fit-for-purpose to support endpoints in clinical trials in patients with CICU.**

Results

Baseline characteristics

- Analysis was conducted on 82 patients included in the LIBERTY-CINDU CUrIADS trial.
  - The mean (standard deviation [SD]) age at baseline was 35.4 (14.9) years, and most patients were female (76.8%).
- The mean (SD) scores at baseline were 6.24 (3.71) for UCT, 2.68 (1.33) for ColdUAS 2-week score, and 9.51 (6.91) for DLQI.

Test-retest Reliability

- UCT and ColdUAS 2-week score demonstrated adequate test-retest reliability (intraclass correlation coefficient range ≥ 0.70, **Table 1**) and DLQI demonstrated low test-retest reliability.

Table 1. Test-retest Reliability for PROMs Total scores

PROMs	Test-retest reliability, ICC (95% CI)			
	N	*Using PGIS*	*N*	*Using PGIC*
UCT	36	0.90 (0.82, 0.95)	21	0.75 (0.49, 0.89)
ColdUAS 2-week score	28	0.86 (0.72, 0.93)	18	0.71 (0.37, 0.88)
DLQI	17	0.04 (-0.46, 0.51)	15	0.51 (0.06, 0.80)

For UCT and ColdUAS 2-week score, stable patients were defined as those patients with no change on PGIS between screening and baseline and reporting no change on the PGIC at Week 12, while for DLQI it was defined as patients reporting no change on PGIC at Week 24.

CI, confidence interval; ColdUAS, Cold Urticaria Activity Score; DLQI, Dermatology Life Quality Index; ICC, Intraclass correlation coefficient; PGIC, Patient Global Impression of Change; PGIS, Patient Global Impression of Severity; PROMs, patient-reported outcome measures; UCT, Urticaria Control Test.

Convergent Validity

- Moderate-to-strong correlations was demonstrated for scores of similar constructs for UCT and ColdUAS 2-week score (absolute *r* range: 0.68–0.84 and 0.59–0.82, respectively), and low-to-strong correlations for DLQI (absolute *r* range: 0.26–0.91).
- Adequate known-groups validity was demonstrated for UCT distinguishing between severity level groups defined based on PGIS (p <0.001), ColdUAS Item 5 (p <0.01), and DLQI (p <0.001).
- Similarly, adequate known-groups validity was demonstrated for ColdUAS 2-week scores distinguishing between severity level groups defined based on PGIS (p <0.05), ColdUAS Item 5 (p <0.001), UCT (p <0.05), and DLQI (p <0.001).
- DLQI also demonstrated adequate know-groups validity by distinguishing between severity level groups defined based on PGIS (p <0.001) and ColdUAS Item 5 (p <0.01).

Sensitivity to Change

- Significant differences in mean score changes over time were observed for groups defined using target anchors (all p <0.05) supporting the sensitivity to change.

Meaningful Change Thresholds

- Correlations ≥ 0.37 were observed between the change in all PROM scores and anchors.
- MCTs for within-patient improvement was 4 (range: 3–5) for UCT, 1.6 (range: 1.2–2.3) for ColdUAS-2 week score, and 7 (range: 4–10) for DLQI.
- MCTs for between-group improvement was 3.3 (range: 2.5–3.9) for UCT, 1.1 (range: 0.9–1.5) for ColdUAS 2-week score, and 4.7 (range: 3.5–6.8) for DLQI.

REFERENCES: 1. Maurer et.al.*The Journal of Allergy and Clinical Immunology: In Practice*, 2018; 6(4):1119-1130.

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