PCR152

Assessment of content validity and psychometric properties of the Wheal Intensity Likert Scale in chronic inducible cold urticaria

ColdU

Stephanie Rhoten[1], Ashna Alladin[2], Isabelle Guillemin[3], Renata Martincova[4], Chien-chia Chuang[5], Jérôme Msihid[6], Jingdong Chao[7], Efstathios Zikos[6], Lydia Braham-Chaouche[6], Marieke Krol[8], Ella Brookes[9]

[1]IQVIA, San Francisco, CA, USA; [2]IQVIA, Munich, Germany; [3]IQVIA, Lyon, France; [4]Sanofi, Prague, Czech Republic; [5]Sanofi, Cambridge, MA, USA; [6]Sanofi, Gentilly, France; [7]Regeneron Pharmaceuticals Inc, Tarrytown, NY, USA [8]IQVIA, Amsterdam, Netherlands; [9]Sanofi, Reading, UK

Background

- Chronic inducible cold urticaria (ColdU) impacts the health-related quality of life of affected patients[1,2].
- The Wheal Intensity Likert Scale (WILS), a clinician-reported outcome (ClinRO) instrument, assesses the severity of cutaneous reactions, ranging from 0 (no wheals) to 5 (a large, very edematous wheal with pseudopodia).
- WILS was used in the phase 3 LIBERTY-CINDU CUrIADS trial (NCT04681729) among patients with ColdU treated with dupilumab or placebo.
- Qualitative research to gather clinician perspectives and generate evidence of the content validity of WILS is essential.
- Additionally, evaluating its psychometric properties is crucial to ensure meaningful and interpretable measures using this instrument.

Objective

- **To understand the most relevant signs and symptoms of ColdU from clinicians' perspectives.**
- **To generate evidence of content validity and appropriateness of WILS in ColdU.**
- **To generate evidence of psychometric properties and interpretability (clinical meaningfulness) of WILS.**

Conclusions

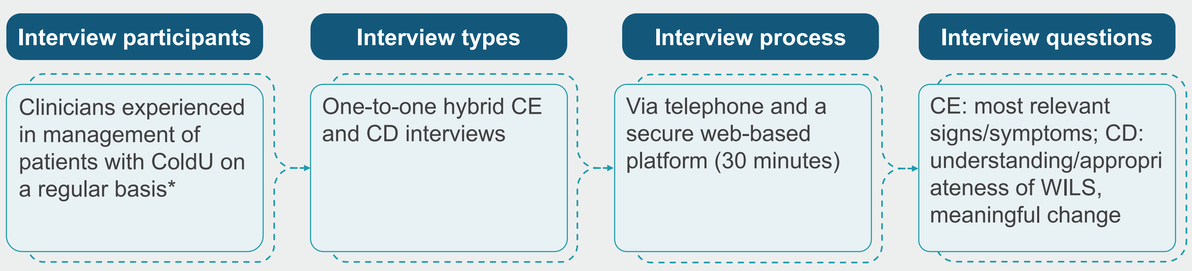
- **Qualitative interviews depicted key clinical characteristics of ColdU and demonstrated the content validity of WILS for use in patient with ColdU.**
- **However, due to clinician reservations, appropriate modifications need to be considered for WILS to ensure consensual understandability.**
- **WILS showed good construct validity and sensitivity to change, providing thresholds to aid interpretation of data.**
- **These findings support the use of WILS to assess ColdU severity. However, further research is needed to refine the instrument and enhance its acceptability among clinicians.**

Methods

Content validity analysis

- A qualitative interview study involving clinicians from the United States (US) with over 5 years of experience in ColdU (**Figure 1**).

Figure 1. Qualitative interview process



*Defined as seeing at least five patients per month
CD, cognitive debriefing; CE, Concept elicitation; ColdU, Chronic inducible cold urticaria

Psychometric analysis

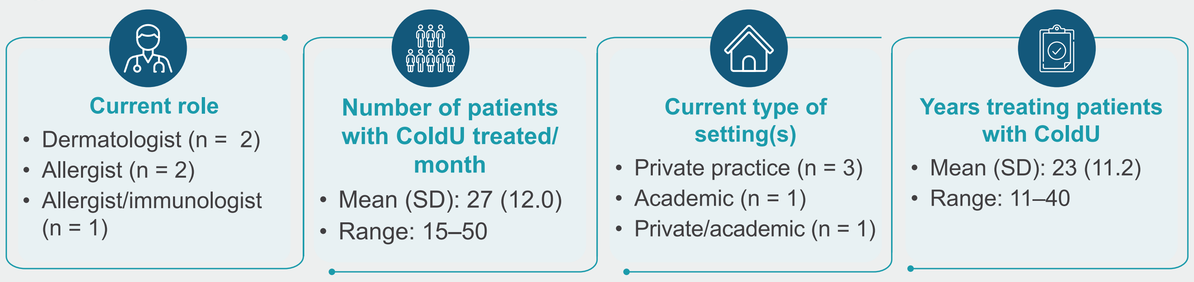
- Data from LIBERTY-CINDU CUrIADS trial were used to assess convergent validity, known-groups validity, and sensitivity to change of WILS.
- Within-patient and between-group meaningful change thresholds (MCTs) using Patient Global Impression of Severity (PGIS) and Patient Global Impression of Change (PGIC) as anchors were estimated for WILS in the Phase 3 context of use.

Results

Clinician Characteristics

- Interviews were conducted with five male ColdU clinicians (**Figure 2**).

Figure 2. Characteristics of interviewed clinicians (N = 5)



ColdU, Chronic inducible cold urticaria; N, total number of clinicians; n, number of observations; SD, standard deviation

Clinician interviews: Concept Elicitation

- Nine key ColdU-related signs/symptoms were reported by the clinicians.
- The most frequently reported signs/symptoms were hives, itch, and burning (**Figure 3**).
- Hives (n = 3/4), itch (n = 3/4), and pain (n = 1/4) were reported as the most clinically important signs/symptoms.

Figure 3. Signs/symptoms of ColdU reported by clinicians

Hives, n = 5/5

"*They can just be walking through a grocery store, through the frozen food section, and break out in urticarial lesions on their hands and their arms*."

Itch and burning, n = 5/5 each

"*The affected site becomes itchy and/or associated with a burning sensation in most cases*."

Pain, n = 3/5

"*Pain is kind of like itch and tingling and stuff like that*."

Fatigue, n = 1/5

"*But all urticaria patients do have a component of fatigue. We don't necessarily log that in our EHR because it is a more subjective complaint. But fatigue can be added in manually if necessary*."

Angioedema, n = 3/5

"*I mean, it is relevant, but all these things generally correlate. If you have lots of wheals, they tend to be a little bigger and thicker… it doesn't, for us, represent enough of… that we call it out specifically*."

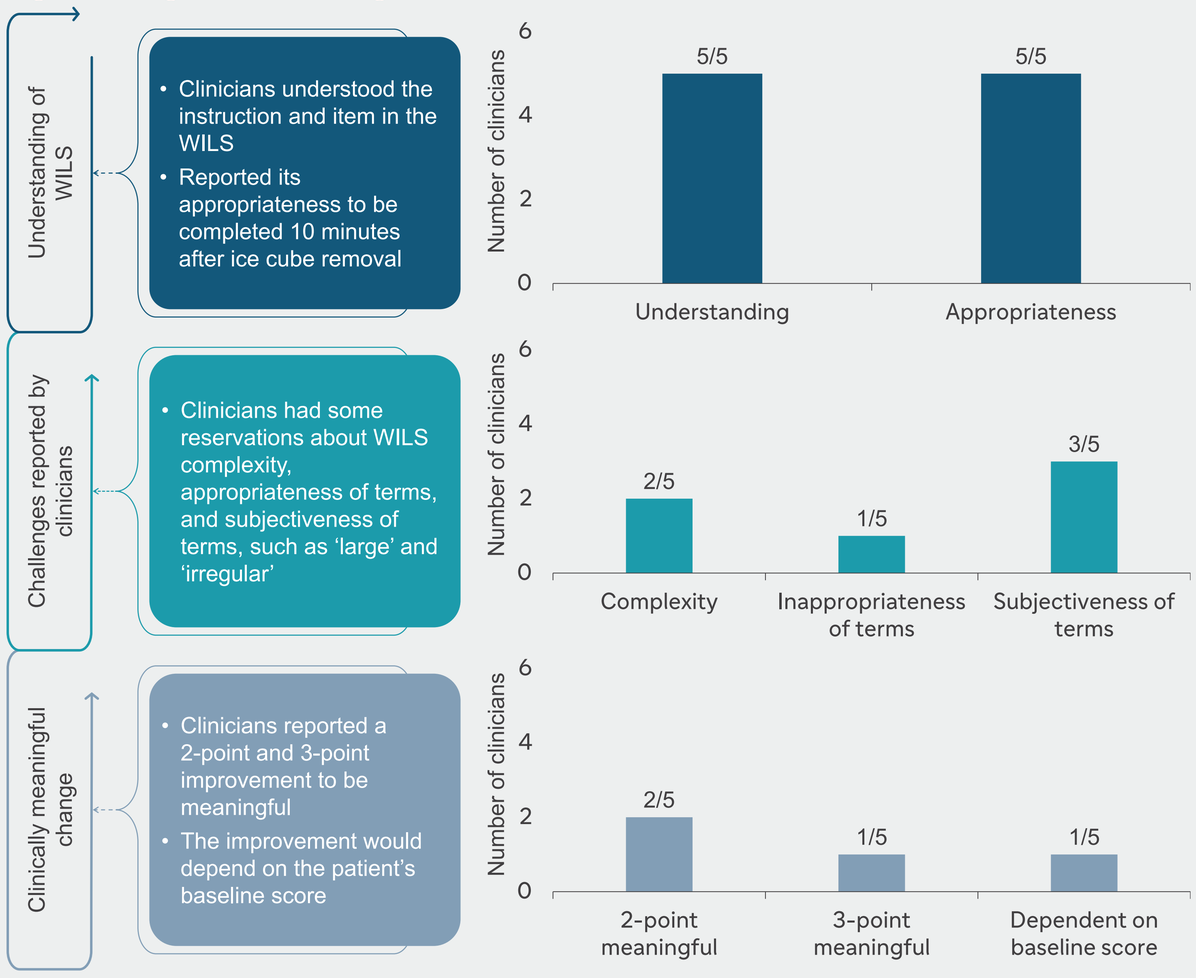
Respiratory, gastrointestinal, and cardiovascular, n = 1/5 each

"*Like, extensive cold contact, such as swimming in cold water may result in generalized urticaria and even anaphylaxis, with symptoms involving respiratory, gastrointestinal, and/or cardiovascular system. That would be severe*."

Clinician interviews: Cognitive Debriefing of WILS

- All clinicians understood the WILS instructions and items and found it appropriate to complete 10 minutes after ice cube removal (**Figure 4**).

Figure 4. Cognitive debriefing results



Clinician interviews: Limitations

- Due to the small sample size, results may not fully represent all clinicians' opinions on ColdU.
- As the research involved only US clinicians, further studies are needed to apply these findings globally.

Psychometric Analysis

- Psychometric analyses involved 82 patients, with a mean age of 35.4 years.
- At baseline, the mean (SD) WILS score was 3.18 (1.01), which decreased to 1.56 (1.65) by Week 24.
- Moderate-to-strong correlations were observed between most scores of similar constructs for convergent correlations and change in WILS score.
  - Low correlations noted for Peak Pain- Numeric Rating Scale (**Table 1**).
- WILS demonstrated adequate known-groups validity, defined based on PGIS groups (p <0.001).
- Correlations of ≥ 0.37 were reported between change from baseline to Week 24 in WILS score and PGIS (absolute r: 0.61) and PGIC (absolute r: 0.49).
- MCTs for within-patient improvement was 2.0 (range: not provided due to equal PGIS and PGIC anchor-based estimates) and for between-group improvement was 1.0 (range: 0.6 to 1.2).

Table 1. Convergent validity and sensitivity to change of WILS

Score	Convergent validity at Week 24		Sensitivity to change from baseline to Week 24	
	N	r	N	r
Ice cube provocation test	62	0.88	62	0.74
PP-NRS	56	0.50	55	0.46
Peak Pain-NRS	56	0.41	55	0.44
PBS-NRS	56	0.52	55	0.45
PGIS	56	0.75	56	0.61
PGIC	-	-	56	0.49

N, Number of observations; NRS, Numerical rating scale; PBS-NRS, peak burning sensation NRS; PGIC: Patient Global Impression of Change; PGIS: Patient Global Impression of Severity; PP-NRS, peak pruritus NRS; r, correlation coefficient; WILS, Wheal Intensity Likert Scale.

REFERENCES

1. Dressler et al. *J Allergy Clin Immunol*. 2018;141 (5): 1726-1734.
2. Muñoz et al. *Curr Allergy Asthma Rep*. 2024; 24 (8): 457–469.

CONFLICTS OF INTEREST

SR, AA, IG, and MK are employees of IQVIA who were contracted to conduct the psychometric analysis. RM, CC, JM, EZ, LC, and EB are employees of Sanofi and may hold stock or stock options in the company. JC is an employee of Regeneron and may hold stock or stock options in the company.

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