

# COMPARISON OF TWICE-DAILY AND ONCE-DAILY URTICARIA ACTIVITY SCORE: RESULTS FROM THE FIRST INTERNATIONAL BURDEN OF ILLNESS ASSURE-CSU STUDY IN INADEQUATELY-CONTROLLED CHRONIC SPONTANEOUS (IDIOPATHIC) URTICARIA

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## INTRODUCTION

### Background

- Chronic spontaneous urticaria (CSU), also known as chronic idiopathic urticaria (CIU), is characterised by the occurrence of hives, angioedema or both for 6 weeks or longer due to known or unknown causes<sup>1</sup>
- Several types of patient-reported outcome (PRO) instruments like EQ-5D (generic), Dermatology Life Quality Index or DLQI (dermatological), and total Chronic Urticaria Quality of Life Questionnaire or CU-Q2oL (disease-specific) are used to assess disease burden in CSU
- The Urticaria Activity Score (UAS) assesses patient-reported daily itch and number of hives which summed over 7 days gives the UAS7 score (range: 0-42), with higher scores denoting higher disease activity<sup>2,3</sup>
- The UAS7 is commonly used to assess disease activity in CSU patients, and has been recommended by guidelines to be used in clinical practice to determine disease activity and response to treatment<sup>1</sup>
- Currently, the UAS7 score can be computed using
  - Twice-daily<sup>3,4</sup> patient assessment
    - validated as per FDA guidelines for PROs,<sup>5</sup> could be more burdensome for patients but can capture daily fluctuations of disease activity
  - Once-daily<sup>2</sup> assessment
    - recommended by the EAACI/GA<sub>2</sub>LEN/EDF/WAO international guidelines<sup>1</sup>
    - less burdensome but possibly higher recall bias, compared to the twice-daily version
- It is important to understand whether the two methods capture comparable overall measurement of disease activity over similar periods of time

## OBJECTIVE

- The purpose of the present analysis is to evaluate the comparability of the UAS twice-daily versus once-daily versions

## METHODS

- Data**
  - Data came from ASSURE-CSU,<sup>6</sup> the first non-interventional, international study to quantify the humanistic and economic burden of illness of patients with CSU who are symptomatic despite treatment, and conducted in 7 countries (Canada, France, Germany, Italy, Netherlands, Spain and UK)

### Study design

- The study included a 1-year retrospective medical record abstraction, a cross-sectional patient reported outcomes survey, and a 7-day prospective patient diary which assessed disease activity with UAS

### Patient population

- Adult patients (aged 18 years or older) with a clinician-confirmed, guideline-defined diagnosis of CSU
- Patients had been symptomatic for more than 12 months at least 3 days per week and were currently symptomatic despite treatment

### Urticaria activity score (UAS7) calculation

- The patient diary contained a twice-daily version of the UAS questionnaire, which included morning and evening ratings of hives and itch severity (Table 1)

**Table 1. UAS7 twice-daily version: scoring for itch and hives at each assessment point**

Score	Itch severity at each assessment (AM/PM)	Number of hives at each assessment (AM/PM)
0	None	None
1	Mild, minimal awareness, easily tolerated	1-6 hives
2	Moderate, definite awareness, bothersome but tolerable	7-12 hives
3	Severe, difficult to tolerate	>12 hives

- An additional element of a once-daily version of the UAS questionnaire—the exact 24-hour counts of hives—was collected in the patient diary each evening. Scoring of once-daily version is presented in Table 2

**Table 2. UAS7 once-daily version: daily scoring for itch and hives**

Score	Itch severity (once every 24 hours)	Number of hives per 24 hours
0	None	None
1	Mild (present but not annoying or troublesome)	<20 hives
2	Moderate (troublesome but does not interfere with normal daily activity or sleep)	20–50 hives
3	Intense, interferes with normal daily activity or sleep)	>50 hives

- These data were used to compute the following three UAS7 scores: UAS7 Twice Daily (UAS7<sub>TD</sub>), UAS7 Once Daily, Maximum Itch (UAS7<sub>OD1MAX</sub>), and UAS7 Once Daily, Average Itch (UAS7<sub>OD2AVG</sub>) (Table 3)
- The 2 scores, UAS7<sub>OD1MAX</sub> and UAS7<sub>OD2AVG</sub> were computed as it is unclear whether patients assessed itch severity as overall, maximum or average itch over 24 hours

**Table 3. Summary of UAS7 Scores Computed in ASSURE-CSU**

Score	Daily Hives Scoring Method	Daily Itch Scoring Method	Scoring Methodology
UAS7 <sub>TD</sub>	Daily average of 12-hour morning and evening hives scores	Daily average of 12-hour morning and evening itch severity ratings	The UAS7 <sub>TD</sub> score was obtained by adding the sum of daily average itch and hives scores over 7 days
UAS7 <sub>OD1MAX</sub>	Derived from daily 24-hour exact counts of total hives	Daily maximum of 12-hour morning and evening itch severity ratings	The UAS7 <sub>OD</sub> scores were calculated by adding the daily sum values of hives and daily (maximum/average) itch scores
UAS7 <sub>OD2AVG</sub>		Daily average of 12-hour morning and evening itch severity ratings	

OD1MAX = Once Daily, Maximum Itch; OD2AVG = Once Daily, Average Itch; OD = Once daily; TD = Twice Daily; UAS7 = Urticaria Activity Score Over 7 Days

### Statistical Analysis

- Descriptive statistics were provided and stratified by score bands of disease activity, measured by the weekly UAS7<sub>TD</sub>
- UAS7 disease activity score bands were defined as follows:<sup>7</sup>
  - UAS7=28-42: severe activity CSU
  - UAS7=16-27: moderate activity CSU
  - UAS7=7-15: mild activity CSU
  - UAS7=1-6: well-controlled CSU
  - UAS7=0: urticaria-free (itch- and hive-free) over 7 days
- Pearson correlation coefficients were computed pairwise between the three UAS7 scores (UAS7<sub>TD</sub>, UAS7<sub>OD1MAX</sub>, and UAS7<sub>OD2AVG</sub>) and between the three UAS7 scores with other PRO measures (CU-Q2oL, DLQI and EQ-5D scores)
- Weighted Cohen's kappa coefficients (K) were computed to measure the agreement of disease activity score band assignments based on UAS7<sub>TD</sub> versus UAS7<sub>OD1MAX</sub>, and UAS7<sub>TD</sub> versus UAS7<sub>OD2AVG</sub>

## RESULTS

- Medical records were abstracted for 673 patients; of them, 614 patients returned the UAS7 questionnaire
- A subset of the analyses was restricted to the 501 patients with non-missing UAS7 scores for all three versions (i.e., UAS7<sub>TD</sub>, UAS7<sub>OD1MAX</sub>, UAS7<sub>OD2AVG</sub>)

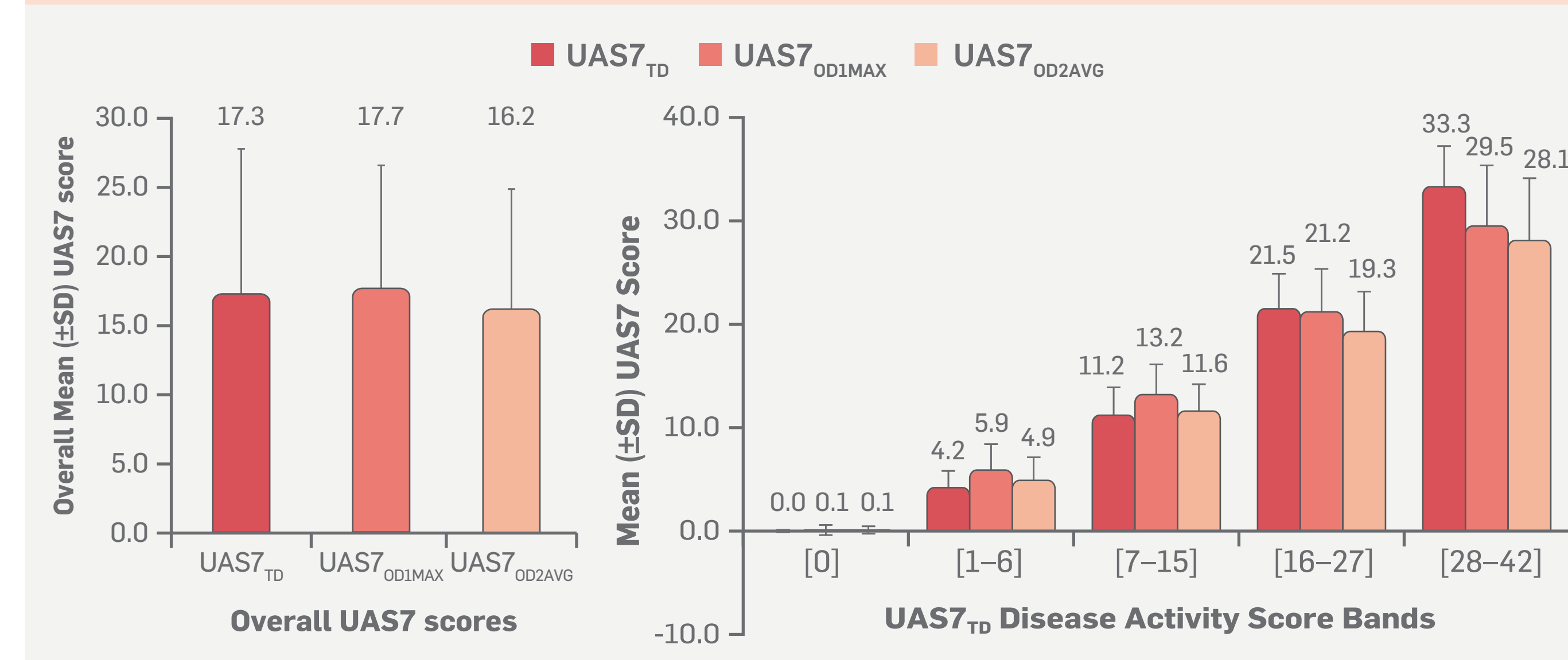
### Patient demographics

- The majority of enrolled patients were female (72.7%) and White/Caucasian (90.4%)
- The mean (SD) age of patients at enrolment was 48.8 (15.47) years

### UAS7 scores (Figure 1a-b)

- Of the 614 patients who completed the diary, 605 had a non-missing UAS7<sub>TD</sub>, and 504 had non-missing UAS7<sub>OD1MAX</sub> and UAS7<sub>OD2AVG</sub>
- UAS7 scores were highest overall for UAS7<sub>OD1MAX</sub> (mean [SD] = 17.7 [8.90]), followed by UAS7<sub>TD</sub> (17.3 [10.49]) and UAS7<sub>OD2AVG</sub> (16.2 [8.68]) (Figure 1a); the trend varied by UAS7<sub>TD</sub> score band (Figure 1b)

**Figure 1. Comparison of Mean UAS7 Scores Analyzed by 3 Versions of UAS7 for the entire cohort (Figure 1a) and Stratified by UAS7<sub>TD</sub> Disease Activity Score Band (Figure 1b)**



- The overall mean (SD) weekly itch score based on the daily maximum of twice-daily ratings (9.9 [5.28]) was higher than that based on the daily average of twice-daily ratings (8.4 [4.97])
- Overall, the mean (SD) weekly hives score based on the daily average of twice-daily ratings was higher (9.0 [6.58]) than that based on exact 24-hour hive counts (7.7 [5.04])

### Correlation of UAS7 scoring methods - between UAS7 scores and other PROs (Table 5)

- The pairwise correlation coefficients between the three UAS7 scores showed very high positive correlation (Table 5)
- Correlation co-efficients between each target score and other PROs were consistent (Table 5)

**Table 5. Correlation co-efficients between patient-reported outcome scores across UAS7 scores and other PROs**

Score	UAS7 <sub>TD</sub>	UAS7 <sub>OD1MAX</sub>	UAS7 <sub>OD2AVG</sub>
UAS7 <sub>TD</sub>	1.00 (n = 605)		
UAS7 <sub>OD1MAX</sub>	<b>0.94 (n = 501)</b>	1.00 (n = 504)	
UAS7 <sub>OD2AVG</sub>	<b>0.95 (n = 501)</b>	<b>0.99 (n = 504)</b>	1.00 (n = 504)
CU-Q2oL Total Score	0.44 (n = 586)	0.45 (n = 490)	0.44 (n = 490)
DLQI Total Score	0.45 (n = 595)	0.47 (n = 496)	0.46 (n = 496)
EQ-5D Utility Index Score	-0.27 (n = 585)	-0.29 (n = 490)	-0.27 (n = 490)

CU-Q2oL = Chronic Urticaria Quality of Life Questionnaire; DLQI = Dermatology Life Quality Index; OD1MAX = Once Daily, Maximum Itch; OD2AVG = Once Daily, Average Itch; TD = Twice Daily; UAS7 = Urticaria Activity Score Over 7 Days

### Concordance across scoring methods

- Of the 501 patients included in the analysis, 388 (77.4%) patients were assigned to the same UAS7<sub>TD</sub> score band for UAS7<sub>TD</sub> vs UAS7<sub>OD1MAX</sub>, whereas 406 (81.0%) patients were grouped in the same band for UAS7<sub>TD</sub> vs UAS7<sub>OD2AVG</sub>

### Agreement across scoring methods

- The Cohen's kappa, κ (95% CI) was 0.78 (0.75-0.82) for UAS7<sub>TD</sub> vs. UAS7<sub>OD1MAX</sub> and 0.82 (0.78-0.85) for UAS7<sub>TD</sub> vs. UAS7<sub>OD2AVG</sub>, showing substantial to almost perfect agreement between the scoring methods (0.61-0.80 = substantial agreement; 0.81-1.00 = almost perfect agreement)<sup>8</sup>

## CONCLUSIONS

- The study found that UAS7 scores based on twice-daily versus once-daily evaluation of itch and number of hives were highly consistent and correlated
- The non-uniform trend in the comparison of weekly hives scores may be driven by questionnaire design
- Overall, the study found good agreement in scores across all the three UAS7 versions, and consistent correlation with other PROs
- These findings provide evidence to support the use of either version of UAS when evaluating CSU activity as long as the chosen version is used consistently over time
- Further research and guidance for use of the instruments and results will be useful

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