

# Correlation between changes in urticaria symptoms and sleep experience in patients with chronic spontaneous/idiopathic urticaria (CSU/CIU): Results from two randomized, double-blind, placebo-controlled, Phase III trials of omalizumab

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## ABSTRACT

**Introduction and objectives:** Patients with chronic spontaneous/idiopathic urticaria (CSU/CIU) report negative effects on sleep (e.g., interference with sleep and sleep disruption), which have consequences such as tiredness, daytime somnolence and lack of energy. As there is no information on the association between improvement in urticaria signs and symptoms and improvements in sleep or reductions in daytime somnolence, the current study explores the correlations between the trajectories of change shown in the Weekly Urticaria Activity Score (UAS7) and Medical Outcomes Study (MOS) Sleep Scale (daytime somnolence and sleep disturbance subscales) across 40 weeks.

**Material and methods:** Data were obtained from two Phase III trials (ASTERIA I and GLACIAL), investigating the efficacy of omalizumab in patients with refractory CSU/CIU. Patient-reported outcome (PRO) data were collected at baseline and Weeks 4, 12, 24 and 40. Urticaria signs (wheals) and symptoms (itching) were measured using the UAS7. Effects on sleep were measured using two domains of the MOS Sleep Scale (a 12-item PRO comprising six theoretical dimensions that measure key aspects of sleep): daytime somnolence and sleep disturbance. Data were analyzed using latent growth modeling (LGM) wherein individual slopes of change and intercepts for UAS7 and MOS daytime somnolence and sleep disturbance were correlated for each patient.

**Results:** In both trials, mean baseline UAS7 score was 30 out of 42, mean MOS daytime somnolence score was 40 out of 100 and mean sleep disturbance score was 47 out of 100. These scores decreased to 10 for UAS7, 25 for MOS daytime somnolence and 29 for sleep disturbance at Week 24. LGM analysis found that changes in UAS7 and MOS daytime somnolence were correlated at 0.67 (ASTERIA I) and 0.72 (GLACIAL), indicating moderate-to-strong correspondence between changes in signs and symptoms and daytime somnolence. This positive correlation indicates that the knowledge of a patient's signs and symptoms of urticaria provides good insight into the extent of daytime somnolence. Changes in the UAS7 and MOS sleep disturbance subscale were correlated at 0.53 (ASTERIA I) and 0.59 (GLACIAL). A patient's UAS7 score yields moderate insight into their sleep disturbance and vice versa.

**Conclusions:** These results indicate strong empirical evidence that sleep is negatively affected by urticaria signs and symptoms. Further, these results appear to be the first to use data from all assessment points simultaneously to demonstrate that improvements in urticaria result in substantial reductions in daytime sleepiness and sleep disruption.

## BACKGROUND

CSU/CIU is defined by the latest European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA<sup>2</sup>LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) guidelines as the occurrence of wheals (hives), angioedema or both for 6 weeks or longer due to known or unknown causes.<sup>1,2</sup>

Omalizumab, a humanized anti-IgE monoclonal antibody is the first and only therapy approved by the European Medicines Agency (EMA) and US Food and Drug Administration (FDA) for the treatment of CSU/CIU in adult and adolescent (≥12 years) patients refractory to H<sub>1</sub>-antihistamines.<sup>3</sup>

Patients with CSU/CIU report negative effects on sleep which have consequences such as tiredness, daytime somnolence and lack of energy.<sup>4</sup>

## OBJECTIVE

To explore the correlations between the trajectories of change shown in the UAS7 and two domains from the MOS Sleep Scale (daytime somnolence and sleep disturbance) across 40 weeks in the ASTERIA I and GLACIAL trials (investigating efficacy of omalizumab in patients with refractory CSU/CIU).

## METHODS

PRO data used for the analysis come from baseline and Weeks 4, 12, 24, and 40 in ASTERIA I and GLACIAL (Figure 1).

UAS7 – daily diary measuring urticaria signs (wheals) and symptoms (itching); weekly scores range from 0 to 42, with higher scores meaning more severe urticaria.

MOS Sleep Scale – a 12-item PRO comprised of six dimensions about key aspects of sleep. The current study focused on two domains of effects on sleep: daytime somnolence and sleep disturbance; scores range from 0 to 100, with higher scores meaning greater somnolence or sleep disturbance.

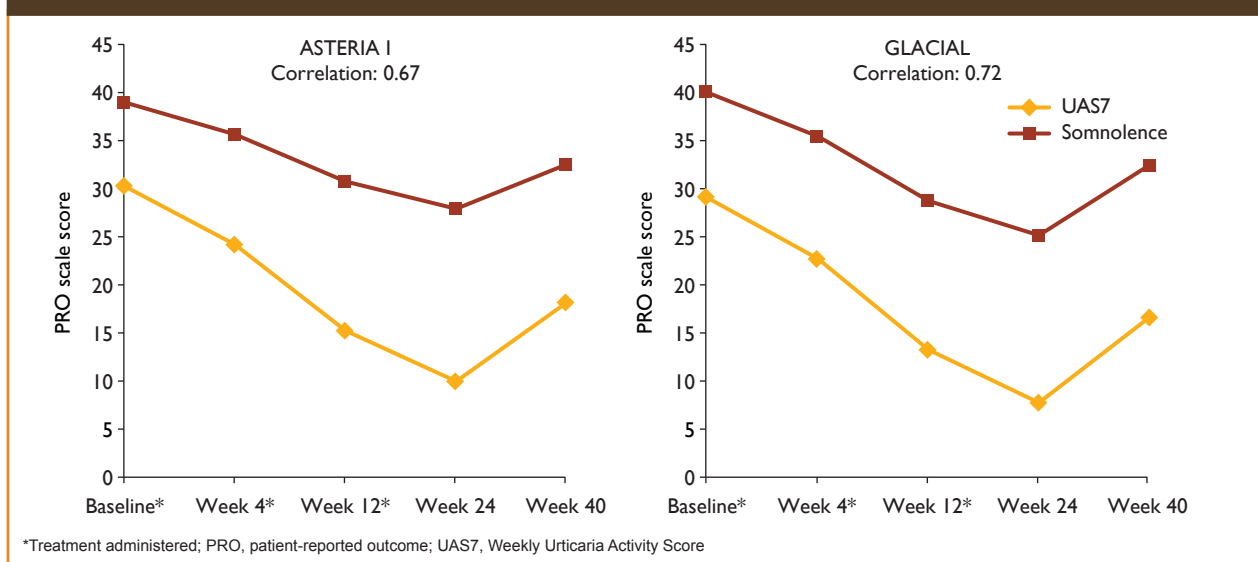
Data were analyzed using LGM<sup>5</sup> wherein individual slopes of change and intercepts for UAS7 and MOS daytime somnolence and sleep disturbance were correlated for each patient (aged 12–75 years).

## RESULTS

### Moderate-to-strong correlation between UAS7 and MOS daytime somnolence

- In both trials, mean baseline UAS7 score was 30 out of 42 and mean MOS daytime somnolence score was 40 out of 100.
  - Mean scores decreased to 10 for UAS7 and 25 for MOS daytime somnolence at Week 24.
- Changes in UAS7 and MOS daytime somnolence were moderately to strongly correlated in ASTERIA I and GLACIAL (Figure 2).

Figure 2. Trajectories of change in UAS7 and MOS daytime somnolence



### Moderate correlation between UAS7 and MOS sleep disturbance subscale

- In both trials, the mean baseline MOS sleep disturbance score was 47 out of 100.
  - Mean scores decreased to 29 for MOS sleep disturbance at Week 24.
- Changes in the UAS7 and MOS sleep disturbance subscale were moderately correlated in ASTERIA I and GLACIAL (Figure 3).

Figure 3. Trajectories of change in UAS7 and MOS sleep disturbance

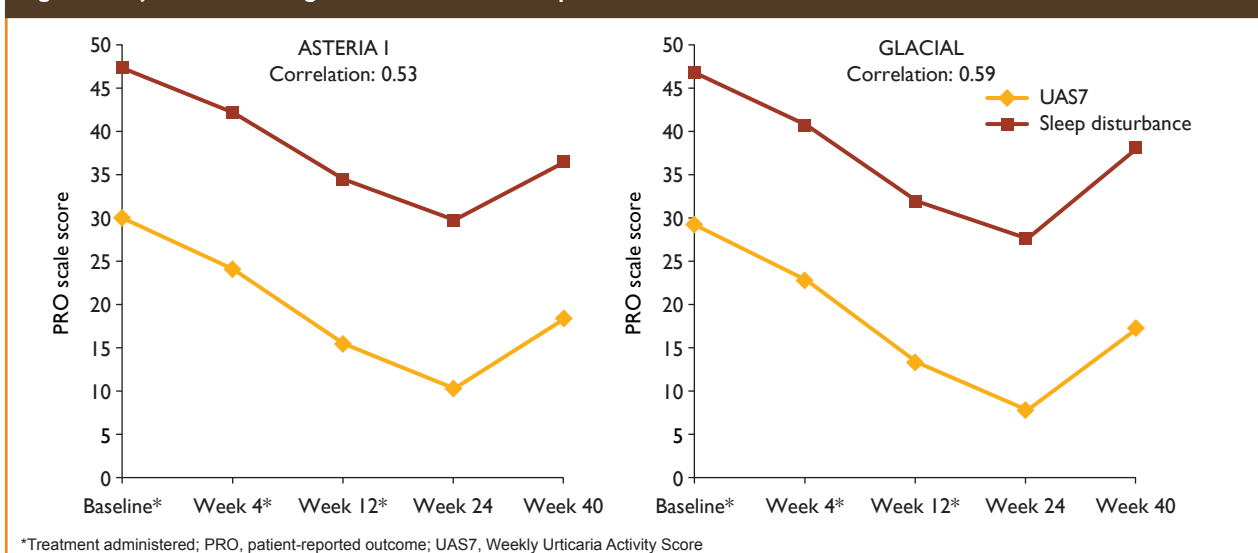
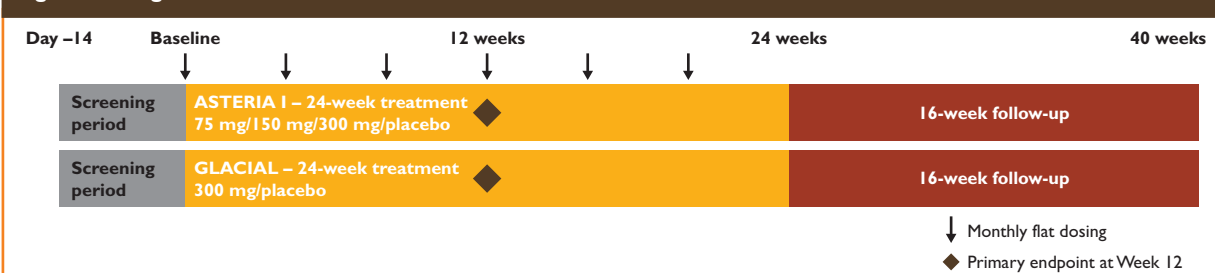


Figure 1. Design of Phase III studies with omalizumab



## CONCLUSIONS

- Improvement in urticaria signs and symptoms is associated with reduced daytime somnolence and sleep disturbance.
- The results indicate strong empirical evidence that sleep is negatively affected by urticaria signs and symptoms and that improving these will reduce daytime somnolence and sleep disturbance.
- Correlations between the changes in the UAS7 and the MOS daytime somnolence ranged between 0.67 and 0.72
  - This indicated a moderate-to-strong correspondence between changes in urticaria signs and changes in daytime somnolence.
- Correlations between the changes in the UAS7 and the MOS sleep disturbance subscale ranged between 0.53 and 0.59
  - This indicated a moderate correspondence between changes in urticaria signs and symptoms and changes in sleep disturbance.
- These positive correlations indicate that knowledge of a patient's signs and symptoms of urticaria provides good insight into the extent of daytime somnolence and sleep disturbance.
- Further, they indicate that changes in signs and symptoms of urticaria are informative about changes in these two sleep domains.
- These results appear to be the first to use data from all assessment points simultaneously to demonstrate that improvements in urticaria result in substantial reductions in daytime somnolence and sleep disturbance.

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