# OMALIZUMAB DOSE STEP-UP AND TREATMENT RESPONSE IN PATIENTS WITH CHRONIC IDIOPATHIC/SPONTANEOUS URTICARIA (CIU/CSU): RESULTS FROM THE OPTIMA STUDY


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## INTRODUCTION

- The OPTIMA (efficacy of optimized retreatment and step-up therapy with omalizumab in patients with chronic idiopathic/spontaneous urticaria [CIU/CSU]; NCT02161562) study was designed to address some of the key gaps in the knowledge of optimal CIU/CSU treatment with omalizumab[1]
- Omalizumab is approved for the treatment of adults and adolescents (12 years and above) with CIU/CSU who remain symptomatic despite $H_1$-antihistamine treatment; in Canada the approved dosage is omalizumab 150 mg or 300 mg every 4 weeks[2]
- The treatment algorithm proposed by international guidelines states that the disease should be treated to complete resolution of symptoms[3]
- To date, no data evaluating the efficacy of step-up therapy in patients inadequately controlled with omalizumab 150 mg are available

## OBJECTIVES

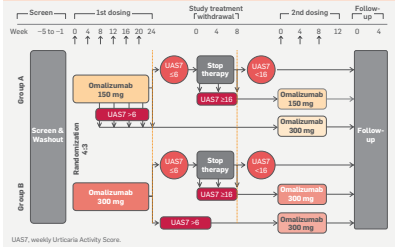
- **Four objectives were to be answered in OPTIMA:**
  - If a patient's signs and symptoms of CIU/CSU are well controlled with omalizumab and the treatment is stopped, will the patient relapse? How long will it take until relapse?
  - If omalizumab treatment is restarted, will the patient respond to retreatment?
  - If the patient does not sufficiently respond to omalizumab 150 mg, will step-up therapy to 300 mg improve the signs and symptoms of CIU/CSU?
  - If the patient does not respond to 300 mg, will treatment extension improve the signs and symptoms of CIU/CSU?
- **This poster will cover the third question**

## METHODS

### Study design

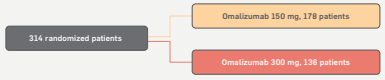
- OPTIMA is a Phase 3b, international, multicenter, randomized, open-label, noncomparator study
- Patients with CIU/CSU who were symptomatic despite $H_1$-antagonists at approved dose were randomized 4:3 to omalizumab 150 mg or 300 mg for 24 weeks (1st dosing period)
- Based on weekly Urticaria Activity Score (UAS7), patients entered one of the following phases: treatment withdrawal (if UAS7 ≤6), step-up to 300 mg (if 150 mg initially and UAS7 >6 at Weeks ≥8 to 24), or continued treatment for 12 more weeks (if 300 mg initially and UAS7 >6 at Week 24)
- Patients who relapsed (UAS7 ≥16) during the treatment withdrawal period were retreated with the same dose (omalizumab 150 mg or 300 mg every 4 weeks) during the 12-week second dosing period

**Figure 1. OPTIMA study design.** The study includes five phases: screening; initial dosing period; withdrawal; a second dosing period for retreatment, dose step-up, or dose extension based on UAS7 response; and follow-up.




UAS7, weekly Urticaria Activity Score.

**Figure 2. Patient randomization ratio**




### Inclusion criteria

- Men or women at least 18 years of age
- Diagnosis of CIU/CSU and the presence of symptoms for ≥6 months prior to the screening visit
- Patient must have been on an approved dose of nonsedating $H_1$-antihistamine for CIU/CSU, and no other concomitant CIU/CSU treatment, for at least the 7 consecutive days immediately prior to the randomization visit and must have documented current use on the day of the randomization visit
- UAS7 score ≥16 (scale 0–42) and itch component of UAS7 ≥8 (scale 0–21) during 7 days prior to randomization

### Exclusion criteria

- Patients having a clearly defined underlying etiology for chronic urticaria other than CIU/CSU
- Patients with urticarial vasculitis, urticaria pigmentosa, erythema multiforme, mastocytosis, hereditary or acquired angioedema, lymphoma or leukemia, active atopic dermatitis, bullous pemphigoid, dermatitis herpetiformis, senile pruritus or other skin disease associated with itch that could interfere with study outcomes
- Patients with a history of malignancy of any organ system
- Patients should stay on same approved dose of nonsedating $H_1$-antihistamine during entire trial duration. No rescue medication was allowed

## RESULTS

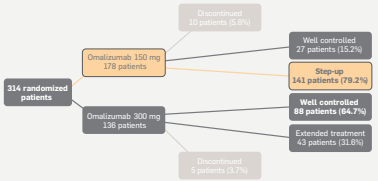
### Baseline characteristics

**Table 1. Demographics and baseline characteristics**

| Characteristic | Omalizumab 150 mg (n=178) | Omalizumab 300 mg (n=136) | Overall (N=314) |
|---|---|---|---|
| Age, mean (range), years | 46.7 (18–79) | 45.8 (20–78) | 46.3 (18–79) |
| Gender, % | | | |
| Male | 27.0 | 27.2 | 27.1 |
| Female | 73.0 | 72.8 | 72.9 |
| Race, % | | | |
| White | 78.4 | 83.1 | 79.3 |
| Asian | 8.4 | 7.4 | 8.0 |
| Black | 5.6 | 4.4 | 5.1 |
| American Indian/Alaska Native | 1.1 | 2.2 | 1.6 |
| Other | 8.4 | 2.9 | 6.1 |
| Time to CIU/CSU symptoms, n (%) | | | |
| ≤1 year | 28 (15.7) | 22 (16.2) | 50 (15.9) |
| >1–≤2 years | 25 (14.0) | 25 (18.4) | 50 (15.9) |
| >2–10 years | 84 (47.2) | 54 (39.7) | 138 (43.9) |
| >10 years | 41 (23.0) | 35 (25.7) | 76 (24.2) |
| Baseline UAS7, mean (range) | 29.7 (16.0–42.0) | 30.0 (16.0–42.0) | 29.8 (16.0–42.0) |
| # Prior medications used for CIU/CSU, mean (range) | 1.8 (0.0–12.0) | 2.1 (0.0–8.0) | 1.9 (0.0–12.0) |

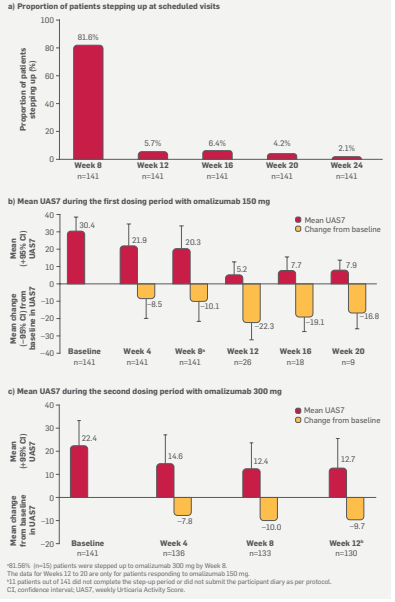
CIU/CSU, chronic idiopathic/spontaneous urticaria; UAS7, weekly Urticaria Activity Score.

**Figure 3. Patient disposition after first dosing period**




- Of those patients with CIU/CSU treated with omalizumab 150 mg, 79.2% (141/178) had to be up-dosed to 300 mg

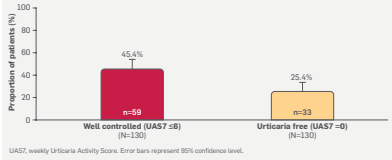
**Figure 4. Proportion of patients stepping up and patient response to omalizumab 150 mg (first dosing) and 300 mg (step-up)**




a1.56% (n=15) patients were stepped up to omalizumab 300 mg by Week 8.
The data for Weeks 12 to 20 are only for patients responding to omalizumab 150 mg.
b11 patients out of 141 did not complete the step-up period or did not submit the participant diary as per protocol.
CI, confidence interval; UAS7, weekly Urticaria Activity Score.

- Step-up treatment to omalizumab 300 mg led to a mean improvement of 9.7 points in UAS7 when compared with the 150 mg dosing period

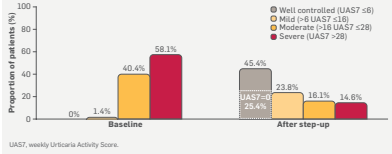
**Figure 5. Proportion of patients who were clinically well controlled (UAS7 ≤6) or urticaria free (UAS7 =0) at the end of step-up phase**




UAS7, weekly Urticaria Activity Score. Error bars represent 95% confidence level.

- Of those patients who had not been well controlled by omalizumab 150 mg, 45.4% were well controlled by omalizumab 300 mg during the step-up phase, and 25.4% of these were even symptom free

**Figure 6. Disease severity distribution at baseline and after step-up**




UAS7, weekly Urticaria Activity Score.

- Step-up treatment improved the disease severity scenario[4]

## CONCLUSIONS

- Of the patients with CIU/CSU treated with omalizumab 150 mg, 79.2% had to be up-dosed to 300 mg owing to insufficient symptom control
- The mean UAS7 improvement after the first dosing period and step-up therapy was 8.0 points and 9.7 points, respectively
- From the step-up patient group, 45.4% of patients achieved symptom control during the 3-month treatment with omalizumab 300 mg
- Disease severity distribution was improved after dose step-up, with the majority of patients having well-controlled (45.4%) or mild (23.8%) disease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### DISCLOSURES

Authors declare the following, real or perceived conflicts of interest: **WG, GS, JH, CWL, KAP,** and **WHY** received honoraria as investigators and consultants. **OC, AV, FdT,** and **LR** are employees of Novartis Pharmaceuticals.


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