DESIGN AND RATIONALE OF THE OPTIMA STUDY: RETREATMENT OR STEP-UP THERAPY WITH OMALIZUMAB IN PATIENTS WITH CHRONIC IDIOPATHIC/SPONTANEOUS URTICARIA (CIU/CSU)

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OBJECTIVES

- **PRIMARY:** To assess the effect of optimized retreatment after relapse (defined as weekly urticaria activity score [UAS7] ≥16) in patients with chronic idiopathic/spontaneous urticaria (CIU/CSU) who were clinically well controlled (UAS7 ≤6) following their first course of treatment with omalizumab
- **SECONDARY:** Evaluation of dose step-up therapy in those who do not respond (UAS7 >6) to an initial dose of omalizumab 150 mg; assessment of the time to relapse in patients who initially were well controlled (UAS7 ≤6); and to evaluate the benefit of extending study treatment with omalizumab 300 mg in patients who are not yet clinically well controlled (UAS7 ≤6) after 24 weeks
- **EXPLORATORY:** Evaluation of quality of life and occurrence of angioedema episodes

STUDY DESIGN

- OPTIMA is an international, multicenter, randomized, open-label, noncomparator study of two doses of omalizumab treatment (150 mg and 300 mg) across two dosing periods
- In the initial dosing period, patients receive omalizumab by subcutaneous injection, at the randomized dose, every 4 weeks (**Figure 1**)
- Subsequent dosing is determined based on the patient's UAS7 response (**Figures 2** and **3**)
- Patients are eligible for the OPTIMA study if they are adults diagnosed with CIU/CSU and have been exhibiting symptoms for at least 6 months prior to the study despite concurrent nonsedating H_1-antihistamine therapy
- Refractory to antihistamine therapy is defined as UAS7 ≥16 (scale 0–42) and itch component of UAS7 ≥8 (scale 0–21) despite treatment with an approved dose of nonsedating H_1-antihistamine and no other concomitant CIU/CSU treatment for at least 7 consecutive days

Figure 1. OPTIMA Study design. The study includes 5 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.

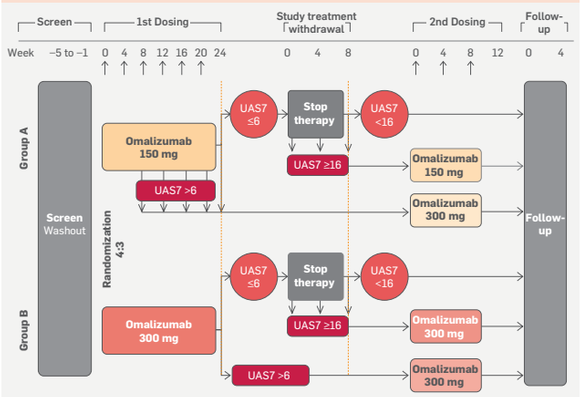


Figure 2. Dosing scenarios for the omalizumab 300 mg treatment group. Patients who are well controlled (UAS7 ≤6) in the 24-week initial dosing period enter the 8-week withdrawal period and then the follow-up phase if they remain well controlled. If relapse (UAS7 ≥16) occurs during withdrawal, patients are retreated in a second dosing period at the same dose (omalizumab 300 mg) for 12 weeks. If symptoms are not well controlled (UAS7 >6) in the initial dosing period, then patients extend treatment for 36 weeks of continuous omalizumab 300 mg treatment.

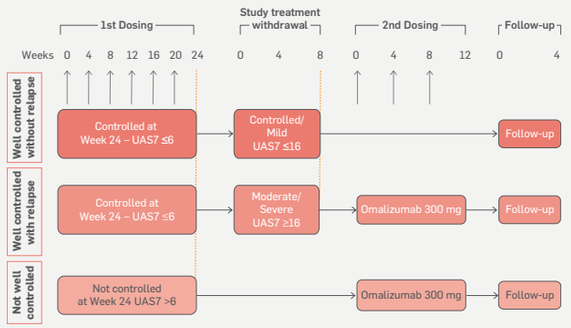
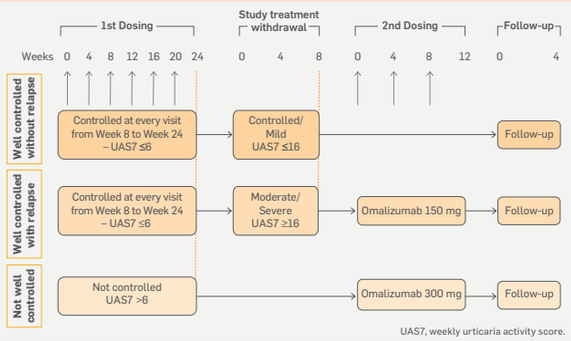


Figure 3. Dosing scenarios for the omalizumab 150 mg treatment group. Patients who are well controlled (UAS7 ≤6) in the 24-week initial dosing period enter the 8-week withdrawal period and then the follow-up phase if they remain well controlled. If relapse (UAS7 ≥16) occurs during the withdrawal period, patients are retreated in a second dosing period at the same omalizumab 150 mg dose for 12 weeks. If symptoms are not well controlled (UAS7 >6) during the initial omalizumab 150 mg dosing period, then patients step up to the omalizumab 300 mg dose at any protocol visit as early as Week 8 to start the second dosing period.



SAMPLE SIZE AND ANALYSIS

Sample size

- The study has been planned to enroll and randomize a total of 320 patients, in a ratio of 4:3, to the doses of omalizumab 150 mg or 300 mg. The sample size is estimated on the basis of assessing the effect of retreatment following relapse (primary endpoint)

Primary endpoint

- Proportion of patients who achieved a UAS7 ≤6 at the end of the second dosing period, after being clinically well controlled (UAS7 ≤6) in the initial dosing period followed by relapse (UAS7 ≥16) when treatment was discontinued

Secondary endpoints

- Difference in the UAS7 between the start and the end of the second dosing period in patients who stepped up treatment from omalizumab 150 mg to 300 mg
- The proportion of patients who were clinically well controlled (UAS7 ≤6) at the end of the second dosing period in patients who stepped up treatment from omalizumab 150 mg to 300 mg
- The time to relapse (UAS7 ≥16) after withdrawal of omalizumab in patients who were clinically well controlled following their first course of omalizumab treatment
- Difference in the UAS7 between the end of the initial dosing period and the end of the second dosing period in patients who extended treatment with omalizumab 300 mg
- The UAS7 change from baseline measured at the end of the initial dosing period in patients who received omalizumab 300 mg
- The UAS7 change from baseline measured at the end of the second dosing period in all patients
- The proportion of patients who remain well controlled (UAS7 ≤6) or who have achieved a UAS7 =0 at Week 8 of the initial dosing period versus Week 8 of the second dosing period
- The proportions of patients who remain clinically well controlled (UAS7 ≤6) at any visit starting at Week 8 of the initial dosing period until the end of the first dosing period

CONCLUSIONS

- **The OPTIMA study will allow better characterization of the appropriate omalizumab treatment regimen in patients with CIU/CSU who relapse or are not well controlled after initial treatment, by answering the following questions:**
  - If a patient is well controlled and therefore treatment is stopped, will the patient relapse? How long will it take to relapse?
  - If treatment is restarted, will the patient respond to retreatment?
  - If the patient does not respond to omalizumab 150 mg, will step-up therapy help?
  - If the patient does not respond to omalizumab 300 mg, will treatment extension help?

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DISCLOSURES

Authors declare the following, real or perceived conflicts of interest: **GS**, **JH**, **WG**, **CL**, and **WHY** received honoraria as investigators and consultants. **GS** received honoraria as speaker of this corresponding study. **OC**, **FdT**, and **LR** are employees of Novartis Pharmaceuticals.

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