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Human Medicines Evaluation Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Xolair

omalizumab

Procedure no: EMEA/H/C/000606/P46/066

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Table of contents

1. Introduction 3

2. Scientific discussion 3

2.1. Information on the development program 3
2.2. Information on the pharmaceutical formulation used in the study.....3
2.3. Clinical.....3
2.4. aspects 3
2.4.1. Introduction.....3
2.4.2. Clinical study 3
Description.....3
Methods 3
Results 5
2.4.3. Discussion on clinical aspects 5

3. Rapporteur's overall conclusion and recommendation 6

Fulfilled: 6

1. Introduction

On 26 November 2018, the MAH submitted a completed paediatric study for Xolair, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

Study CIGE025EIN01 is a stand-alone study

2.2. Information on the pharmaceutical formulation used in the study

Xolair, marketed in India.

2.3. Clinical

2.4. aspects

2.4.1. Introduction

The MAH submitted a final report for:

• Study CIGE025EIN01, entitled 'A prospective, Post Marketing Surveillance study to study the safety and effectiveness of omalizumab in Indian patients with Chronic Spontaneous Urticaria refractory to standard of care'.

2.4.2. Clinical study

Description

Study [CIGE025ENI01] was a 2 year prospective PMS study mandated by the Indian Health authority as part of conditional approval for market authorization and to fulfil a commitment to observe Indian patients on omalizumab with CSU refractory to standard of care under current real-life medical practice in a real-world setting. This study evaluated safety parameters (adverse events), changes in effectiveness parameters such as time to response, itch free days, patients who needed retreatment and health-related quality of life and pharmacoeconomic assessments for cost-effectiveness of omalizumab.

Methods

Objective(s)

The primary objective of the study was to obtain safety data from Indian patients with CSU refractory to standard of care treated with omalizumab. The primary objective was evaluated by summarization of all TEAEs.

Secondary study objectives included:

- Collect effectiveness data during real-world use of omalizumab from patients with CSU

- Provide real-world quality of life (QOL) data in patients with CSU treated with omalizumab
- Assess Indian patients' with CSU journey while treated with omalizumab in real-world scenario.

The secondary efficacy objectives were evaluated by:

- The change from baseline in the urticaria activity score over 7 days (UAS7) at week 12, 24 and end of treatment
- The change from baseline in the weekly itch severity score at week 12, 24 and end of treatment
- The time taken by patients treated with omalizumab to attain UAS7 ≤ 6
- The time taken by patients treated with omalizumab who maintain their response UAS7≤ 6
- Number of omalizumab injections over treatment period
- The number of itch free days during treatment period
- Number of Pruritus free days (nPFD) during baseline and treatment standardized to 30- day period (PFD30) as - PFD30 = (nPFD / total evaluated days) x 30
- The number of patients who needed retreatment with omalizumab
- The impact on the quality-of-life measured by means of the Dermatology Life Quality Index (DLQI) questionnaire.

Exploratory study objectives included:

- To assess the cost-effectiveness of omalizumab.

Study design

Study [CIGE025EIN01] was an open-label, multicenter, prospective, PMS to study the safety and effectiveness of omalizumab in Indian patients with CSU refractory to standard of care in clinical practice. This study was conducted at 8 sites in India, which were supervised by individual Principal Investigators (PI).

Omalizumab was prescribed to patients with CSU who met the inclusion criteria for study entry. Eligibility for study entry was determined by the study investigator, in accordance with the selection criteria and who signed the Informed Consent. Patients were treated according to local routine clinical practice and the selection of the treatment for CSU was separated from the decision to include the patient in the study and was made at the discretion of the treating physician in accordance with standard medical practice and approved by the PI. No diagnostic or monitoring procedures additional to standard care and routine practice were performed for the purpose of the study. Patient diary and pharmacoeconomic questionnaires were used to collect data on efficacy and exploratory endpoints.

Safety data was retrieved during the study to parallel and meet the regulatory requirement of reporting to the Periodic Safety Update Report (PSUR). Safety data was collected at 6 month intervals for 2 years. Every patient included was planned to be followed in the study for 30 months (up to 129 weeks). To have at least 24 weeks of patient data, recruitment was stopped at 18 months or attainment of the target number of patients, whichever occurred first. Study visit intervals were not fixed per protocol but were adhered to as regular practice for this indication at each site. As the study is non-interventional in nature, the protocol did not mandate patient visits. However, it was requested to have patients' data at least at the intervals of 12 and 24 weeks and end of treatment.

Omalizumab was administered in accordance with the approved local label and from available commercial sources using the standard local clinical practice and with clinical judgment to make the decision to prescribe.

Study population /Sample size

The study population consisted of male and female patients with CSU refractory to standard of care who were not treated with omalizumab 6 months prior to entering the study. Patients had to be able to comply with completing a diary and questionnaires during the study to assess the effectiveness and pharmacoeconomic effects of omalizumab.

Treatments

Outcomes/endpoints

Statistical Methods

Results

Among the 143 patients enrolled in Study CIGE025EIN01, 1 patient was <18 years of age who enrolled in the study 03 August 2017. The patient summary is described below.

The patient was female, 17 years of age with a body weight and height at baseline of 45 kg and 145 cm respectively. The patient had no family history of urticaria. Her medical history included acne (Grade 1) since 2015 but no other comorbid disorders. She was taking concomitant medications (hydroxyzine tablets and montelukast/levocetirizine both as needed and ongoing during the study).

She was first diagnosed with CSU in May 2017 and suffered from a recurrent form of urticaria without angioedema. She was also taking concomitant medications of cetirizine and fexofenadine as related to the CSU. She was prescribed one dose of 300 mg omalizumab on 03 August 2017 (at baseline) and there were no further records of exposure to omalizumab during the study. She completed Visit 2 on 09 November 2017, Visit 3 on 01 February 2018 and Visit 4 on 10 April 2018. She had intense hives and severe pruritus at baseline which continued to be of same severity until the last available assessment on 01 February 2018 (Visit 3). Her UAS7 score was 42 at baseline which continued to be the same until the last available assessment on 01 February 2018 (Visit 3). The number of itch free days between the study visits was reported as zero. There was no change in her quality of life as reported from the DLQI scores (DLQI scores were 11 at baseline, Visit 2 and Visit 3 respectively). She was reported to have Grade 1 acne during the physical examination at Visit 2. There was no acne reported during Visit 3. She did not experience any SAEs during the study. The patient completed the study on 10 April 2018. On follow-up a few months later, the investigator reported the patient was doing better with fexofenadine treatment.

2.4.3. Discussion on clinical aspects

As only one patient <18 years was included this is to be regarded as a case report of Xolair use once with no effect on CSU symptoms.

3. Rapporteur’s overall conclusion and recommendation

The inclusion of the single paediatric patient in study CIGE025EIN01 is noted. No regulatory action is warranted.

☒ **Fulfilled:**

No regulatory action required.