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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/P46/062

Note

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

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Introduction

The MAH has submitted a report for a completed paediatric study for Xolair, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

Novartis has completed the study CIGE025AUS50 (end of data analysis 07 August2017), entitled 'Real-World Effectiveness Study of Moderate-to-Severe Allergic Asthma Patients Exposed to Omalizumab'. The study utilized electronic medical record (EMR) data containing clinical measures of treatment effectiveness such as symptoms, asthma control and lung function to expand the current understanding of omalizumab performance in the US real-world setting in adult and adolescent patients. In addition, this study describes the profile of pediatric allergic asthma patients, including those exposed and unexposed to omalizumab.

A short critical expert overview written by a Novartis employee has also been provided.

1. Scientific discussion

1.1. Information on the development program

CIGE025AUS50 is a stand alone study.

1.2. Information on the pharmaceutical formulation used in the study

Xolair, as approved was used in this study.

1.3. Clinical aspects

1.3.1. Introduction

The MAH submitted a final report for:

- CIGE025AUS50, entitled 'Real-World Effectiveness Study of Moderate-to-Severe Allergic Asthma Patients Exposed to Omalizumab'. End of data analysis was 07 August2017.

1.3.2. Clinical study

CIGE025AUS50

Description

Study [CIGE025AUS50] was a non-interventional, retrospective, US real-world effectiveness study of moderate-to-severe allergic asthma patients treated with omalizumab. The study utilised electronic medical record (EMR) data covering the period 2007 to 2016 containing clinical measures of treatment effectiveness such as symptoms, asthma control and lung function, to expand the current understanding of omalizumab performance in the US real-world setting.

Methods

Objective(s)

The study had the following primary objective:

To evaluate characteristics and long-term outcomes (i.e., asthma exacerbations, asthma control, symptoms, corticosteroid sparing, including patient-reported and healthcare provider [HCP] reported outcomes) of omalizumab-exposed and omalizumab-unexposed moderate-to-severe allergic asthma patients with inadequately controlled symptoms.

In addition there were two secondary objectives:

1. To describe characteristics and outcomes of omalizumab-exposed moderate-to-severe allergic asthma patients with inadequately controlled symptoms and elevated blood eosinophil values (i.e., ≥150/μl and ≥300/μl).
2. To describe characteristics of pediatric (6-11 years old) allergic asthma patients, including omalizumab-exposed and omalizumab-unexposed moderate-to-severe patients with inadequately controlled symptoms.

Study design

This was a retrospective study covering the period from 2007 to 2016. Two different study designs were used to address the primary objective:

- Design 1: a retrospective cohorts design was used to evaluate characteristics and outcomes of omalizumab-exposed and omalizumab-unexposed moderate-to-severe allergic asthma patients with inadequately controlled symptoms
- Design 2: a retrospective pre-post design was used to evaluate outcomes pre- versus post-treatment among omalizumab-exposed moderate-to-severe allergic asthma patients with inadequately controlled symptoms.

The Allergy Partners (AP) Clinic Network electronic medical records (EMR) database was used.

Study population

Adult and pediatric moderate-to-severe allergic asthma patients with inadequately controlled symptoms were classified into one of the two mutually exclusive cohorts based on whether they were exposed to omalizumab therapy following an indicator of inadequately controlled symptoms. Patients with any omalizumab exposure (an omalizumab prescription or injection) following an indicator of inadequately controlled symptoms were classified into the omalizumab-exposed cohort. Patients not exposed to omalizumab were classified into the omalizumab-unexposed (control) cohort.

Results

Recruitment / Number analysed

The data collection included 44 omalizumab-exposed and 917 omalizumab-unexposed patients aged 12-17 years old. A separate cohort of patients 6-11 years were identified where 37 omalizumab-exposed and 2,620 omalizumab-unexposed patients were selected for data collection.

CHMP comment:

The MAH comments that there was an unbalance in demography and disease severity between treated and untreated adolescents making comparisons between these cohorts difficult.

Efficacy results

Sample selection criteria 21 chosen to identify omalizumab-eligible patient but unexposed to it have not permitted to yield a cohort of patients comparable to the omalizumab-exposed one. Omalizumab-exposed patients appeared to be more severe at baseline in terms of lung function, asthma control, symptoms, comorbidities and medications used compared to the omalizumab-unexposed patients. Consequently, the IPTW approach failed to even out the distribution of the patients' characteristics. When outcomes of patients in the two cohorts were compared, the estimated treatment effects likely were not free from the confounding bias.

CHMP comment:

The MAH presents the results for the primary endpoint in tabulated format only, not summarised in this report.

Multiple factors were found to be associated with a significantly higher likelihood of omalizumab exposure. Baseline use of high-dose ICS and LABA was associated with a 159% statistically significant increase in the likelihood of omalizumab exposure, shortness of breath – with a 167% statistically significant increase, and baseline use of OCS – with a 110% statistically significant increase.

Comparison of outcomes in omalizumab-exposed cohort between pre- and post- omalizumab periods showed that exposure to omalizumab was associated with a statistically significant improvement in most symptoms in the post- versus pre-omalizumab period. More specifically, patients were 34% less likely to experience cough (OR [CI]: 0.66 [0.49 – 0.91]), 40% less likely to experience shortness of breath (OR [CI]: 0.60 [0.44 – 0.83]), and 41% less likely to experience wheezing (OR [CI]: 0.59 [0.43 – 0.81]). Although a downward trend was observed in the likelihood of experiencing chest tightness, the change from the pre-omalizumab period was negligible in magnitude and not statistically significant.

Safety results

Due to the non-interventional nature of the study with secondary data collection, there was no safety data collection performed in this study.

1.3.3. Discussion on clinical aspects

The results of this trial raised no new safety concerns and do not change the overall risk/benefit profile of Xolair® (omalizumab). There are no proposed changes to the existing product information. Due to the unbalance in demographics and disease severity between omalizumab treated subjects and controls recorded at baseline only limited information was retrieved from this study. The comparisons pre and post exposure did not reveal any unexpected findings.

2. Rapporteur's overall conclusion and recommendation

The study report for Study CIGE025AUS50 has been provided as requested according to Article 46 of Regulation (EC) No1901/2006, as amended. There were no unexpected findings.

☒ Fulfilled:

No regulatory action required.

☐ **Not fulfilled:**

3. Additional clarification requested

NA