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Procedure Management and Committees Support 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/P46/051

## Note

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

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# Introduction

On Dec 15 2015, the MAH submitted the study, CIGE025ABR01 for Xolair, including paediatric subjects, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

Xolair is approved as add-on therapy to children 6-12 years of age to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist. A similar indication is approved for adolescents and adults. It is also indicated for adults and adolescents (12 years of age and above) with chronic spontaneous urticaria (CSU) refractory to standard of care.

Study CIGE025ABR01 was a randomized, open-label, parallel group study conducted in Brazil.

A short critical expert overview has also been provided.

# 1. Scientific discussion

## *1.1. Information on the development program*

The MAH stated that study CIGE025ABR01 is a stand alone study.

## *1.2. Information on the pharmaceutical formulation used in the study*

Xolair, as approved in Brazil was used in this study.

## *1.3. Clinical aspects*

### 1.3.1. Introduction

The MAH has completed study CIGE025ABR01 (last patient last visit on 28-Apr-2010), which was a randomized, open-label, multicenter study to evaluate the effect of Xolair® as add on therapy to inhaled corticosteroid and long acting beta agonist compared to patients receiving inhaled corticosteroid and long acting beta agonist, on asthma related quality of life in subjects with severe persistent allergic asthma. This study was conducted at 18 centers in Brazil, and enrolled male and female patients >12 to < 75 years of age, with severe persistent allergic asthma who continued to demonstrate inadequate control despite regular treatment with ICS (≥500 mcg/day of fluticasone or equivalent) and LABA. Patients were randomized 2:1 to the Xolair group (Xolair added to ICS and LABA treatment) or the control group (ICS and LABA treatment). They received treatment for 20 weeks.

## 1.3.2. Clinical study CIGE025ABR01

## Description

## Methods

### *Objectives*

The purpose of this study was to evaluate the impact of omalizumab on the quality of life in Brazilian patients with severe allergic asthma.

**Primary objective**

Assess the effect of Xolair compared to the control group on the mean change from baseline in the overall asthma related quality of life questionnaire (AQLQ)

**Secondary objectives**

1. Assess the effect of Xolair compared to control group in subjects with severe persistent allergic asthma and verify the increase > 1.5 in AQLQ in both groups
2. Assess the effect of Xolair to increase > 0.5 and 1.0 in AQLQ compared to control group
3. Assess the difference between Xolair and control group in mean change from baseline in AQLQ score
4. Assess the difference between Xolair and control group in use of rescue medication
5. Assess the difference between Xolair and control group in asthma exacerbation episodes
6. Assess the difference between Xolair and control group in perception of treatment efficacy among physicians
7. Assess the difference between Xolair and control group in perception of treatment efficacy among subjects
8. Safety, including evaluation of parasitic (geohelminths) infection.

### *Study design*

### *Study population /Sample size*

A total of 116 patients were randomized and made up the ITT population: 78 in the Xolair group and 38 in the control group. Twelve patients discontinued and 104 patients completed the trial. Reasons for discontinuation included protocol violations (5 patients total, 4 in the Xolair group and 1 in the control group), adverse events (2 patients in Xolair group), “other” (2 patients in the control group), pregnancy (1 patient in the Xolair group), lost to follow up (1 patient in the control group) and administrative reasons (1 patient in the Xolair group).

Most of the patients were female (approximately 76% in both the Xolair and control group). The mean age was 43.8 years in the Xolair group and 45.2 years in the control group. Two paediatric patients both ages 13 were enrolled in the Xolair group and completed the trial. There were no paediatric patients in the control group.

***Treatments***

Subjects in experimental arm received Xolair at the dose of 150 to 375 mg (every 2 or 4 weeks), with mean dose equal to 249.0 ± 72.0 mg. Dose variation was not permitted.

**Results**

***Efficacy results***

**Primary endpoint**

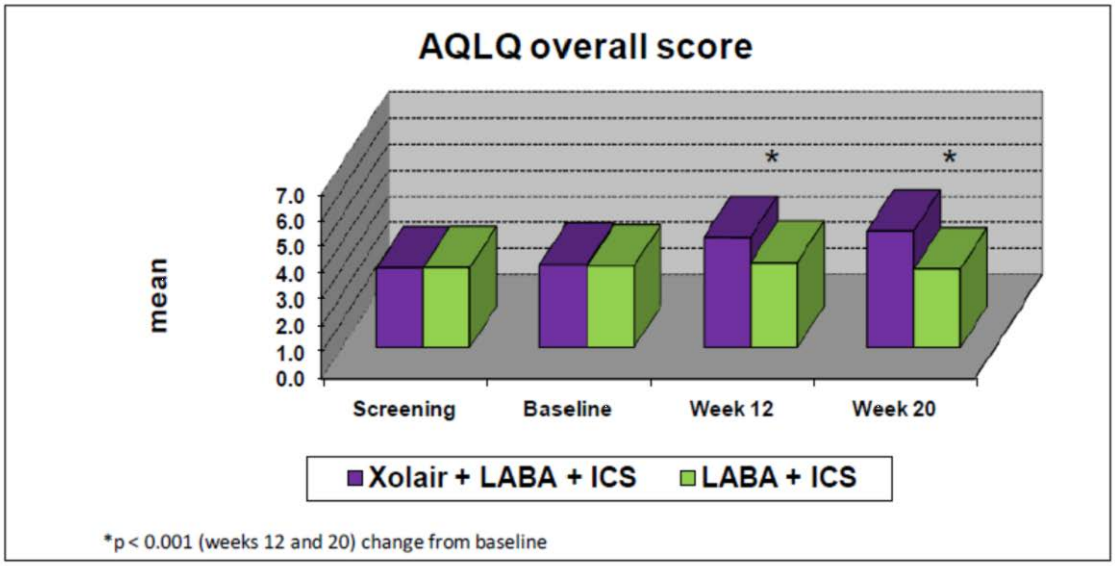


**Figure 1 AQLQ overall score.**

The mean ± SE change from baseline in AQLQ overall score was 1.0 ± 0.2 for the Xolair group and 0.2 ± 0.1 for the control group at Week 12. Differences between change from baseline AQLQ scores for the Xolair and control groups were significant ($p<0.001$). The mean ± SE change from baseline in AQLQ overall score was 1.3 ± 0.1 for the Xolair group and -0.1 ± 0.1 for the control group at Week 20. Differences between change from baseline AQLQ scores for Xolair and control groups were significant ($p<0.001$).

In the Xolair group, the percentage of subjects who had an increase of >1.5 points from baseline on AQLQ overall score was 29.6% at week 12 and 41.9% at week 20. In the control group, this percentage was 11.4% at week 12 and 2.8% at week 20. The difference between the Xolair and control groups at week 20 was significant ($p<0.001$).

In the Xolair group the percentage of subjects who had an increase of >0.5 points from baseline in AQLQ overall score was 67.6% at week 12 and 71.6% at week 20. In the control group this percentage was 28.6% at week 12 and 22% at week 20. There were significant differences between the Xolair and control groups at weeks 12 ($p<0.001$) and 20 ($p<0.001$).

There was no significant difference between the Xolair and control groups regarding the use of rescue medications or exacerbation episodes.

***CHMP's comment:***

The efficacy results are difficult to interpret as this is an open-label study. The effect of omalizumab (Xolair®) in patients with allergic asthma was as expected. Of notice, the study was performed between 2007 and 2010.

***Safety results***

In the Xolair group 56 (71.8%) patients were reported as having some adverse event. In the control group 22 (57.9%) patients were reported as having some adverse event. Sixteen events (7.7%) were suspected related to study drug. Study drug was permanently discontinued in 4 patients in the Xolair group. These discontinuations were due to headache, insomnia, pneumothorax and pregnancy (1 patient each). In the Xolair group there were 3 serious adverse events (SAEs) - pneumonia, pneumothorax and pregnancy and no SAEs in the control group. The pneumonia resolved and was reported as relationship suspected to study drug. The pneumothorax resulted in the patient being hospitalized and the patient discontinued participation in the study. The pregnancy was followed until delivery and no congenital anomaly or birth defect was reported. Respiratory, thoracic and mediastinal disorders (27.4% of the AEs in the Xolair group and 22.9% in the control group), nervous system disorders (20.7% and 15.7%) and gastrointestinal disorders (10.1% and 14.3 %) were the most often reported SOC classes of adverse events. Headache (18.8% of AEs in the Xolair group and 14.3% in the control group), rhinitis (4.8% and 8.6%) and sinusitis (5.3% and 2.9%) were the most commonly reported AEs. At week 20, the percentage of positive parasitic infection tests was 2.9% in Xolair group and 7.1% in control group ($p > 0.05$). There were no deaths in this study.

***CHMP's comment:***

No new or unexpected safety events were identified. Three SAEs were reported where one (pneumonia) was reported as probably related to the study drug.

***Paediatric summary***

There were 2 paediatric patients both 13 years of age randomized to the Xolair group. There were no paediatric patients in the control group. Both of these patients completed the study. Efficacy data was reported for the overall study population; efficacy was not reported separately for the paediatric patients. Available efficacy data from their individual case report forms reported the investigator and patients global evaluation responses as excellent and good at week 20. Three AEs- upper respiratory tract infection, stomatitis, and fever were reported in one patient and 3 AEs- 2 reports of headache and foot sprain were reported in the other paediatric patients. All of these AEs were assessed as not being related to study drug. There were no SAEs reported in these two patients.

***CHMP's comment:***

The MAH has presented paediatric data as requested in legislation. Only two paediatric patients were included in this study, why no conclusion can be drawn on efficacy in the paediatric population. No SAEs were reported in these two pediatric patients. However, no listing of the paediatric patients could be found by the CHMP in the clinical study report.

## 2. Discussion on clinical aspects and CHMP's overall conclusion and recommendation

Study CIGE025ABR01 was an open-label, noncomparative, post marketing study performed in Brazil. No unexpected findings were noted. The effect of omalizumab (Xolair®) in patients with allergic asthma was as expected and no unexpected safety issues occurred. Only two paediatric patients were included in this trial and no SAEs were reported for these patients. The presented data does not change the benefit risk for omalizumab in the paediatric approved indications. No changes are warranted in the SmPC.

### Overall conclusion

The study report for Study CIGE025ABR01 has been provided as requested according to Article 46 of Regulation (EC) No1901/2006, as amended. There were no unexpected findings.

### Recommendation

☒ **Fulfilled:** No regulatory action required.