STUDY REPORT SYNOPSIS

ORBE II

Observational Retrospective study to characterise and assess clinical outcomes of patients receiving benralizumab after marketing approval in Spain

This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.

Background/rationale: Benralizumab has been marketed in Spain since January of 2019 and more than a thousand of people were treated during the year, however data about eosinophilic asthma in real world populations are lacking in Spain.

There is a current need to gain information on the clinical profile of patients eligible for treatment with benralizumab in a real-world setting in Spain. This retrospective observational study aims to describe the patients receiving benralizumab treatment in the real-world setting, in terms of clinical and demographic characteristics, asthma exacerbations, and previous asthma treatments, as well as clinical outcomes during the follow up period.

Objectives:

Primary:

- Describe the demographic and baseline characteristics in patients with severe eosinophilic asthma in Spain who received at least one dose of Benralizumab, after its marketing authorization.
- To describe background treatment patterns of severe eosinophilic asthma patients at baseline and after benralizumab initiation (treatment duration, discontinuation and reasons, concurrent respiratory medication, background asthma medication).

Secondary:

- To describe clinical outcomes, use of resources and estimate associated cost in severe eosinophilic asthma patients who received at least three doses of benralizumab after its marketing authorization.

Exploratory:

- To describe clinical outcomes among a subset of patients discontinuing or switching from any approved severe asthma biologic to benralizumab.
- To describe the medication dispensation from the hospital and community pharmacies.

Study design: This is a descriptive observational, retrospective, multi-center, longitudinal cohort study in adult patients.

Data source: The only data source will be the electronic medical records available at each hospital.

Study population: All patient who meet the inclusion/exclusion criteria and who provided the informed consent have participated.

The sample size justification was based on feasibility considerations. And, according to the volume of patients managed by the sites involved in this study, inclusion of 200 subjects have been considered.

Inclusion criteria:

- Adult patients (age ≥18 years)
- Diagnosis of severe eosinophilic asthma requiring stable treatment of high doses of inhaled corticosteroids and a long-acting agonist β2 ± additional asthma controller.
- Patients with at least 12-month data available before index date (starting benralizumab treatment) Patients with at least 3-month electronic medical records data available from first benralizumab dose ("index date")
- Informed consent provided

Exclusion criteria:

- Patients who received benralizumab in a clinical trial, during the observation period

Statistical methods:

General descriptive statistics for continuous numerical variables have been includes: the number of observations, the mean, the standard deviation (SD), the median and quartiles Q1 and Q3, the minimum, and the maximum values. For categorical variables, the frequency distribution and percentage of subjects with a certain event/characteristic will be presented. Where relevant, two-sided 95% confidence interval (95% CI) limits of the

mean for numerical variables and 95% CI limits for proportions will be provided. Frequency of missing data have been given for relevant variables.

Missing values have been not considered for calculating percentages or any other descriptive, meaning that only valid values have been presented. No use of any method for the handling of missing data was foreseen.

For patients excluded from the statistical analyses, descriptive of the reasons for non-evaluability have been provided.

Results:

A total of 204 patients treated with benralizumab in 15 centers were analyzed: 62.3% were women, with a mean age (standard deviation, SD) of 56.4 (12.4), a mean body mass index of 28.1 (SD=6.3) and a mean age of onset of asthma of 34.4 years (SD=16.4). One-third of patients had allergic asthma according to their clinical history and 93.6% had at least one comorbidity, the most frequent being chronic rhinosinusitis with nasal polyposis (CRSwNP) (36.8%), obesity (30.4%) and gastroesophageal reflux (20.6%).

Almost a third of patients (30.9%) had received at least one previous biologic and lack of response was the main reason for switching. Additionally, 26.0% were corticosteroid-dependent (≥3 months), with a mean daily dose of 19.7 mg of prednisone (range (5.0-75.0). In the previous year, 84.8% presented severe exacerbations 2 (mean of 3 exacerbations in the previous 12 months). Mean baseline eosinophilia (SD) was 548.5 cells/μL (476.9).

Conclusion: Baseline characteristics of patients in ORBE II study show a population with an eosinophilic phenotype, with features such as high eosinophilia, severe exacerbations, significant use of oral corticosteroids, late onset of asthma and comorbidities (CRSwNP was the most frequent). The significant burden of disease of this population suggests a need for highly effective treatment in patients with severe uncontrolled asthma, even in those with prior use of biologics.