NCT04823585
Unique Protocol Id HUS/686/2020

Aggravated airway inflammation: research on biological treatment (Mepolizumab)

AirGOs-biologics

Eudra CT 2020-000421-76
21.8.2020

Statistical plan

NCT04823585
Unique Protocol Id HUS/686/2020

Aggravated airway inflammation: research on biological treatment (Mepolizumab)

AirGOs-biologics

Eudra CT 2020-000421-76
21.8.2020

Statistical plan

The statistical analyses will be conducted in the modified intention-to-treat (mITT) population, defined as all randomized participants who received at least one dose of the investigational medicinal product and fulfilled the inclusion criteria. One randomized participant was excluded due to failure to meet inclusion criteria, resulting in 47 participants per treatment group. All analyses were performed blinded to treatment allocation, and the randomization code was opened only after the trial was closed and the primary analyses completed. The sample size was calculated to provide 80% power to detect clinically meaningful differences in the coprimary endpoints using a two-sided significance level of 0.05. Baseline was defined as the recruitment visit, occurring approximately eight weeks prior to initiation of the investigational medicinal product. Participants received four injections over a 16-week treatment period, followed by an additional eight-week observation period without treatment, after which final measurements were obtained. Continuous variables are summarized using means with standard deviations or medians with interquartile ranges, as appropriate, and categorical variables using frequencies and percentages. The coprimary endpoints and all secondary continuous outcomes were analyzed as changes from baseline using linear mixed-effects models. These models included fixed effects for treatment group, time, and their interaction, and a random intercept for participants to account for within-subject correlation over repeated measurements. Group-specific changes from baseline were estimated at each follow-up time point, and treatment effects were assessed by comparing differences in these estimated changes between groups. Results are reported as mean differences with 95% confidence intervals. A two-sided significance level of $p < 0.05$ was applied to all analyses, and no formal adjustment for multiple comparisons was performed. Model assumptions were evaluated by visual inspection of residual plots to assess normality and homoscedasticity, and by examination of fitted values and influence diagnostics to identify outliers or model instability. The linear mixed-effects modeling framework was selected because it accommodates unequally spaced measurements and missing observations and provides unbiased estimates under the missing-atrandom assumption.

No imputation methods were applied for missing data. To assess the robustness of the findings and the plausibility of the missing-at-random assumption, sensitivity analyses were performed. These included a complete-case analysis restricted to participants with available data at all time points and an analysis excluding participants who received systemic oral corticosteroids

for exacerbations at any point during the trial. The corticosteroid exclusion analysis evaluated the coprimary outcomes (Nasal Polyp Score and SNOT-22 total score) as well as lung function outcomes, including relative changes in peak nasal inspiratory flow, peak expiratory flow, forced expiratory volume in one second, and corresponding microspirometry measures. Sensitivity analyses were conducted in the per-protocol population on an available-case basis using the same statistical models, confidence intervals, and significance thresholds as the primary analyses. Consistency of results across analyses was used to support the validity of the primary findings. All statistical analyses were performed using R statistical software, version 4.5.1.