

# Immunoglobulin prophylaxis prevents admissions for fever in pediatric acute lymphoblastic leukemia: results of a multicenter randomized trial

## *Statistical analysis*

Analyses were performed according to intention-to-treat principle and per-protocol principle (patients that followed IVIG protocol at least one year after diagnosis). Patient characteristics were compared using Pearson Chi Square test for categorical variables and t-test for continuous variables. Due to the presence of overdispersion, a negative binomial regression model was estimated to study the effect of IVIG prophylaxis on the number of admissions for fever. In addition, the impact of IVIG prophylaxis was evaluated in secondary endpoints such as, fever in neutropenia, empirical antibiotic therapy, positive and negative blood cultures, chemotherapy adaptations, ICU admissions and SAEs; age as categorical variable was included in all models. Analysis was performed for the total duration of ALL treatment, and during maintenance treatment, starting 21 weeks after diagnosis, separately. The difference in duration of admission was compared using Mann-Whitney U Tests. Cumulative incidence of relapse, DFS and OS were estimated using Kaplan-Meier's methodology. Logrank test was used to compare differences between estimated survival curves. The total percentage of relapse was computed for each group. For all analyses, a two-sided p-value  $<0.05$  was considered statistically significant. Statistical analyses were performed in SPSS version 26 and in R software environment.<sup>10</sup> The library MASS was used to estimate the negative binomial regression model.