Real world data about biosimilar and originator somatropin use in clinical practice: an Italian population-based multiple databases study during the years 2009-2014

1)Ingrasciotta Y. 2)Marcianò I. 3)Giorgianni F. 4)Ientile V. 5)Chinellato A. 6)Tari DU. 7)Gini R. 8)Cannavò S. 9)Pastorello M. 10)Scondotto S. 11)Cananzi P. 12)Traversa G. 13)Trotta F. 14)Belleudi V. 15)Genazzani AA. 16)Trifirò G.

Dept. of Biomedical and Dental Sciences and Morpho-functiona

Background: Somatropin (rGH) is a biological product containing recombinant growth hormone approved for a wide range of conditions involving growth disturbances and short stature due to growth hormone deficiency, Turner syndrome, chronic renal insufficiency or in short children/adolescents born small for gestational age. From 2006, biosimilar rGH is available on the Italian market. To date, no population-based data about prescribing pattern of originator and biosimilar rGH in Italian routine care are available.

Aims: To explore and to compare the pattern of use of biosimilar and originator somatotropin in six large Italian centres, where various health policy interventions promoting biosimilar use were taken.

Methods: A population-based, retrospective drug utilization study was conducted in the years 2009-2014, through administrative databases of Tuscany, Lazio and Umbria Regions and Caserta, Treviso and Palermo Local Health Units (LHUs), covering a total population of more than 14 million persons. Characterization of naïve rGH users (users without any rGH dispensing within one year prior to the Index Date, i.e. date of the first dispensed somatropin during the study years), the prevalence of biosimilar and originator rGH users and the time to discontinuation of rGH therapy were assessed over time and across centers. Data were anonymised in all the analysis. This study was conducted in the context of the "Assessment of Short and Long Term Risk–Benefit Profile of Biologics Through Healthcare Database Network in Italy" project, funded by the Italian Ministry of Health.

Results: Overall, 6,785 patients were treated with rGH in the years 2009-2014. Of these, naïve users were 4,493 (66.2%), with a median age of 12 years. Naïve rGH users were more likely to be males (N= 2,549; 56.7%) and almost half of them received at least one concomitant drug, other than rGH (N= 2,110; 47.0%). The overall prevalence of rGH use slightly increased from 2009 to 2010 (from 0.2 to 0.3 per 1,000 inhabitants), remaining stable thereafter, but it was however heterogeneous across centers (centre n. 2 reported two fold higher prevalence of use than centre n. 4 and 1 in 2014). Overall, the proportion of biosimilar rGH users was constantly low (from 6.6% in 2009 to 7.8% in 2014), although heterogeneity across different centres and calendar years was reported, with increasing trend over time in centre n. 3 (5.2-16.9%), n. 4 (4.7-11.6%) and n. 5 (5.0-7.5%), and decresing trend in centre n. 6 (7.7-1.9%) and n. 1 (11.6-2.1%).

More than half of rGH naïve users (N= 2,428; 54.0%) discontinued the therapy during the study observation, more frequently in females than males (58.1% vs. 50.9%). The overall median time to treatment discontinuation among those who stopped somatotropin therapy was 5 months. Within

one year after the Index Date, discontinuation was frequent (N= 1,656; 36.9%), especially in naïve users > 25 years (N= 914, 55.2%) and between 6-11 years (N= 433, 26.1%). No statically significant differences (p-value>0.05) in the treatment persistence were observed focusing between biosimilar and originator somatropin.

Conclusions: A relevant geographical variability in the prevalence of rGH use was observed, confirming previous concerns about potential inappropriate use of the drug. The proportion of biosimilar rGH users slightly increased over time but was rather low, as compared to other biosimilars (e.g., epoetin alpha and filgrastim). A marked variability of biosimilar somatotropin uptake among centres was probably due to different loco-regional healthcare policies. Since rGH ranks first for the pharmaceutical expenditure of hormonal preparations in Italy, more effective post-marketing monitoring is required to ensure appropriate treatments, and new strategies promoting the use of biosimilars are needed to guarantee the sustainability of NHS.