REAL WORLD DATA ON THE UTILIZATION PATTERN AND SAFETY PROFILE OF INFLIXIMAB ORIGINATOR VERSUS BIOSIMILARS IN ITALY: A MULTIREGIONAL STUDY

Federica Fraenza[1], Cristina Scavone[1], Maurizio Sessa[1], Emilio Clementi[2], Giovanni Corrao[3], Roberto Leone[4], Alessandro Mugelli[5], Francesco Rossi[1], Edoardo Spina[6], Annalisa Capuano[1]

[1]Campania Pharmacovigilance and Pharmacoepidemiology Regional Centre, Section of Pharmacology "L. Donatelli", Department of Experimental Medicine, University of Campania "L. Vanvitelli", Naples - Italy, [2]Department of Biomedical and Clinical Sciences, L. Sacco University Hospital, Università di Milan, Milan - Italy, [3]Department of Statistics and Quantitative Methods, University of Milan-Bicocca, Milan - Italy, [4]Pharmacology Unit, Department of Diagnostics and Public Health, University of Verona, Verona - Italy, [5]Department of Neurosciences, Drug Research and Child's Health, University of Florence, Florence, Italy, Firenze - Italy, [6]Unit of Clinical Pharmacology, AOU Policlinico "G. Martino", Messina - Italy

Introduction: In recent years, several biosimilar drugs, including those of infliximab, have obtained marketing authorization from the European Medicines Agency (EMA). Given the peculiarity of the safety profile of biological medical products (originator and biosimilars), the evaluation of their tolerability represents an important component of pre-marketing and post-marketing clinical development. For example, infliximab products may cause adverse drug reactions (ADRs) including acute infusion reactions, delayed hypersensitivity reactions, and loss of efficacy, as a direct consequence of immunogenicity. Therefore, specific contraindications, special warnings and precautions have been introduced in the infliximab Summary of Product Characteristics (SPC). The aim was to assess the magnitude of preventable ADRs in individual case safety reports (ICSRs) having infliximab as a suspected drug across Italy (using the spontaneous reporting systems), and the probability of reporting infections, infusion reactions, lack of efficacy, and hypersensitivity for originator and biosimilars of infliximab.

Material and methods: We analyzed ADRs reported across the 2015-2017period in the databases of five Italian regions: Campania, Lombardy, Sicily, Tuscany, and Veneto. Preventability of ADRs was assessed using the P-method. To compare the probability of reporting infections, infusion reactions, lack of efficacy, and hypersensitivity as ADRs as opposed to other types of ADRs between originator and biosimilars of infliximab, we used the reporting odds ratio (ROR). For descriptive purposes, the number of ICSRs involving infliximab, the number of infliximab vials distributed in the aforementioned Italian regions and the relative reporting rate stratified by semester were reported.

Results: From October 2015to October 2017, 459ICSRs reported infliximab as a suspected drug (222ICSRs related to infliximab originator and 237to infliximab biosimilars). In the same period, 81,906vials of infliximab were distributed, resulting in a reporting rate of six ICSRs/1000 vials. Overall, 34cases (7.41%) were categorized as preventable. The most frequently detected critical criteria were "documented hypersensitivity to administered drug or drug class," "inappropriate prescription for patient's underlying medical condition" and "incorrect dose." Biosimilars had, in adjusted analyses, an increased probability of being reported as suspected in ICSRs reporting infusion reactions (ROR 4.09; 95% confidence interval [CI] 1.26-13.32) when compared to Remicade®. On the contrary, they had a decreased probability of being reported as suspected in ICSRs reporting infections or lack of efficacy (ROR 0.33; 95% CI 0.12-0.89; ROR 0.35; 95% CI 0.20-0.61).

Discussion and conclusion: Our study demonstrates that, along with a rapid increase in the utilization of infliximab biosimilars across Italy, there was also an increase in reporting ADRs induced by infliximab biosimilars. Of the reported ADRs, 7.4% were considered preventable. In adjusted analyses, infliximab biosimilars were shown to have an increased probability of being reported as suspected drugs in infusion reactions and a decreased probability of being reported as suspected drugs in cases of lack of efficacy or infection. Considering the potential advantages offered by the utilization of biosimilars in clinical practice, we believe that the use of biosimilars, including those of infliximab, should be supported. In order to achieve this aim, increased knowledge on safety and efficacy of biosimilar drugs should be obtained from real world clinical practice.