Safety Profile of Anti cancer and Immune-Modulating Biotech Drugs

Used in a Real World Setting in Campania Region (Italy): BIO-Cam Observational Study

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Introduction. Biologic drugs have completely changed the management of several diseases, including cancer and autoimmune diseases. Despite their undeniable advantages, the safety profile of biologic drugs is still not completely known. One of the major safety concern related to biologic drugs is the development of immunogenicity, which consists in anti-drug antibodies production and is associated to both reduced clinical efficacy and increased frequency of adverse events (AEs). Other important risk are infections, neurological, and cardiovascular adverse events. Finally, biologic drugs can also have an important role in cancer immunology surveillance with a consequent increase in the frequency of malignancy. Given the controversial data about the type and incidence rate of AEs associated with the use of biologic agents, real world data deriving from registries and observational studies represent the better instruments able to fill this gap. Taking this into account, we carried out a 5-year observational study in naïve patients receiving biologic drugs in Dermatology (DM), Onco-haematology (OM), Hepato-gastroenterology (HG), Neurology (NE) and Rheumatology (RT) Units in some hospitals of Campania Region. An analysis of all AEs associated to biologic drugs was made.

Methods. This was a prospective observational study on the use of biologic drugs, carried out from April 2012 to December 2016. For each patient the following data were collected: socio-demographic data, clinical diagnosis which required biologic drugs use, type of biologic drug and exposure time, type of AEs. All data related to follow-up were collected as well as reasons of potential patients lost to follow-up.

Results. 775 patients were included in the study. Of these, 55.74% were enrolled in OM Unit, 28.13% in RT, 10.06% in HG, 4.26 in DM, and 1.81% in NE Units. According to patients' distribution by clinical Units, the most common diagnosis were no solid cancers (20%), rheumatoid arthritis (16.51%), colorectal (16.12%), and breast cancer (11.35%). The most commonly prescribed biologic drugs were rituximab, bevacizumab, infliximab, trastuzumab (including emtansine), adalimumab, and cetuximab. A total of 320 patients had at least one AE. Out of a total 1390 AEs, only 11.44% occurred at first injection time and almost 80% were not serious. Biologic drugs more associated to AEs (in descending order) were rituximab, cetuximab, bevacizumab, infliximab, trastuzumab, and adalimumab. These drugs were overall associated to 1157 AEs.

Patients with no solid cancer had the highest number of AEs related to rituximab (N=338), those with colorectal cancer had the highest number of AEs to cetuximab (N=202). Patients affected by breast cancer had more commonly AEs to trastuzumab (N=143). Among RT patients, those with rheumatoid arthritis had the highest number of AEs to abatacept (N=45), while patients with other rheumatic diseases had more commonly AEs to adalimumab (N=16). In both Crohn Disease and

Ulcerative colitis patients infliximab was more commonly associated to AEs (127 and 44), while in psoriasis and psoriatic arthritis patients adalimumab was more commonly associated to AEs (13 and 26). Gastrointestinal, skin and subcutaneous tissue, nervous system, and general disorders were the most common AEs. We observed some differences in the type of AEs by clinical Units. Specifically, adalimumab was more frequently associated to infusion reactions and generalized pain among RT and to generalized oedema and headache among HG patients. Similarly, infliximab was more frequently associated to generalized edema and bone or joint pain among RT and to headache, dizziness, and tachycardia among HG patients.

Conclusions. In conclusion, out of 775 patients included in the study, more than 80% was enrolled in OM and RT Units. Since the beginning of the study 1390 AEs occurred. The majority of AEs, frequently related to the most prescribed drugs, were expected and not serious.