Oncological drug-related adverse events reported in the 'FARMAONCO' database in 2014 at the I.R.C.C.S. San Matteo University Hospital in Pavia

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The project FARMAONCO started in 2009 involving 10 oncology units of the Lombardy region. It was developed with the aim of sensitizing Specialists to give more value to the collection of drug-related adverse events (DRAEs), considering the fact that Physicians are often more inclined to accept a toxicity (even clinically relevant), if and when a therapeutic benefit for the patient is clear or, at least expected. Indeed, great attention to the toxicity of oncological drugs is needed to better define the risk/benefit ratio of each oncological drug and this is particularly important in everyday clinical practice, because real world patients have complete different characteristics than those of patients enrolled into clinical trials. According to FARMAONCO rules, both each case of a DRAEs (suspected or certain), as well as its consequences (hospitalization or prolongation of it, severe or permanent disability, life-threatening birth defects in the newborn, death), are collected, graded (from G1 to G5, i.e. toxic death) and coded in a web-based database. Of course, special attention has to be given to those DRAEs which are not reported in the drug's summary of product's characteristics (SmPCs). We checked the database of our hospital for all DRAEs related (certainly or supposedly) to oncological drugs, which occurred (and were notified) during 2014. 24 adverse reactions entered (13 observed in males, 11 in females) were thus evidenced, involving 28 different drugs. In all cases, the reported DRAEs resulted in a permanent or temporary interruption of the treatment (20 cases), in a dose-reduction (7 cases) and/or in the need of administering specific treatment to manage DRAE itself (14 cases). Among the drugs most commonly considered as responsible of the DRAEs collected, there were traditional cytotoxic agents, such as l-OHP (1 DRAEs, drug not discontinued), pemetrexed (2 DRAES, drug discontinued in all 2 cases) and ifosfamide (1 DRAEs, drug discontinued). Among novel targeted agents, there were: cetuximab (2 DRAEs, drug discontinued in all 2 cases), everolimus (6 DRAEs, drug not discontinued in all 6 cases), pazopanib (6 DRAEs, drug discontinued in 2 cases), ipilimumab (3 DRAES, drug discontinued in 2 cases), and bevacizumab (1 DRAE, drug discontinued). All the events that have occurred have been encoded in 40 MedDRA terms. The reactions most frequently reported were diseases of the skin and subcutaneous tissue, including hand foot syndrome (reported within 4 DRAEs) and rash (2 ADR); anemia (4), astenia (4), pneumonia (3), hypertension (2), nephrotic syndrome (2) and sleepiness (2) were also reported. In terms of severity, 6 DRAEs were graded as G1 or G2, 17 were defined as G3 or G4, while 1 unfortunately resulted in patient's death (G5). The patient deceased was in treatment with ipilimumab and died as a result of hypothyroidism and hypogonadotropic hypogonadism. Through this system of pharmacovigilance, the reports of suspected DRAES can be examined cumulatively, as well as one by one, and possibly generate warning signs or confirm/define the risk/benefit ratio of each drug. This is especially important in an quickly evolving area such as oncology, where conventional cytotoxic drugs are continuously joined by novel drugs (mainly targeted agents) that may cause toxicities that are often ill defined; thus, it is of the utmost importance both an adequate and precise post marketing monitoring of the safety of these agents, as well as an informed awareness of medical oncologists and of hospital pharmacists towards this events.