Use of cetuximab in a real-life setting in France with respect to KRAS status - preliminary results of ERBUSB cohort study

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Background: Cetuximab demonstrated survival outcome improvement in metastatic colorectal cancer (mCRC). Cetuximab was first launched as a 2nd-line therapy in mCRC. The current study extends to 1st-line therapy and to KRAS wild-type (wt) CRC patients. We present here the preliminary results of the first French ERUSB cohort study and describe cetuximab prescriptions over a period of 1 year (2009-2010) in a real-life setting.

Methods: ERUSB is a cohort study conducted in 92 French centres. Patients initiating cetuximab between Jan and Dec 2009 were identified from non-surgical hospital pharmacy dispensations. The cohort included mCRC patients treated in 1st-line. They were followed for 12 months to evaluate the rate of metastases recurrence, progression and survival according to KRAS status.

Results: To date, 1038 patients treated by cetuximab for colorectal cancer have been identified. Cetuximab was primarily prescribed in mCRC (95.0%). 34.4% as 1st-line treatment, 18.9% as 2nd-line, 21.4% as 3rd-line and 9.7% as 4th or more. The investigation of KRAS status was performed in 94.4% of the patients and, of those, 9.5% had wt KRAS genes. Investigation of KRAS mutation status and wt status were similar whatever treatment line (investigation: between 93.3% and 100.0%: wt status: between 91.3% and 100.0%). The investigation was performed on primary tumour in 51.7% (36.3% for 1st-line and 71.1%). The main reasons of absence of KRAS status investigation were: previous treatment by cetuximab (42.8%) and absence of available tumour material or technical issue with analysis (33.3%). Investigation of IGER expression was performed for only 2.6% of the patients.

Conclusions: ERUSB is the first post-marketing cohort study conducted in France to describe the usage patterns of cetuximab. Extensive investigation of KRAS status and the high proportion of patients with wt status indicates adherence to market authorisation, although EGFR expression remains rarely investigated.

Risk assessment of drug-induced DRESS syndrome: a disproportionality analysis using French pharmacovigilance database

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Drug reaction with eosinophilia and systemic symptoms (DRESS) is an uncommon severe adverse drug reaction (ADR) in France. Aims: skin rash, fever, eosinophilia and/or atypical lymphoproliferative and/or internal organ involvement. Few drugs are involved, but for each drug, the risk of DRESS is currently unclear.

Aim: The aim of this study was to identify the drugs which are more frequently associated with DRESS and spontaneously reported in the French Pharmacovigilance database (AFSAPS) and to compare the risk between these drugs.

Method: All cases of DRESS reported from September 1st 2007 to August 31st 2010 were included. For the drugs most frequently involved in DRESS, a disproportionality analysis was performed considering that cases were all reports of DRESS and non-cases all the remaining ADR reports for the same drug. This method makes it possible to compare the reporting ratio (PRI) with its 95% confidence interval.

Results: Three hundred and twelve cases of DRESS were included in the study. Patients have a medium age of 57 years and 52.6% were women. Average onset of the 1st symptoms after drug introduction was 30.6 days (median 22 days) and 17% (9/53) of cases involved >20 cases-drug: allopurinol, vancomycin, carbapenem, sulfamethoxazole and sulfasalazine. However, using the PRI, the risk of DRESS was higher for sulfamethoxazole (PRI = 53 [3.87-837]), followed by allopurinol (PRI = 30 [4.00-293]) and carbapenem (PRI = 20 [1.25-325]); moderate for vancomycin (PRI = 17 [1.07-280]), carboplatin and cyclophosphamide (PRI = 7 [1.57-135]), lamotrigine (PRI = 6 [3.12]) and cinoxacin (PRI = 5.3 [3.4-8.4]).

Discussion: The disproportionality analysis can be used to compare the risk of ADR between one drug and another and it is limited by the difficulty of the various biases, particularly those due to unequal ADR reporting among different drugs (ADR notoriety, ...). and to the overlap of specific ADR for some drugs.