lizumab) used in line with the New Drug Application (NDA).
Methods: Data sources were MEDLINE, CENTRAL, ISI Web of Science, ACR and EULAR meeting abstracts, scientific evaluation of the drugs leading to their marketing approval, and clinicaltrials.gov. We selected double-blind randomized controlled trials in adult RA patients, including at least one treatment arm in line with NDA. We performed random effect meta-analysis, with mITT and PP analyses.
Results: Thirty-three trials were included. There was no excess risk of malignancies on anti-TNF-α administered in line with NDA in the PP model (OR, 0.93 95%CI[0.59–1.44]), as well as in the mITT model (OR, 1.27 95%CI[0.82–1.98]). There was a trend for an excess non-melanoma skin cancer risk. mITT analysis overestimated the treatment effect. In contrast, PP analysis underestimated the treatment effect when assessing very sparse events and when many patients dropped out in placebo arms. In univariate metaregression, there was no differential risk among the five drugs.
Discussion: This study did not find any evidence for an excess cancer risk on TNF-α antagonists in adult RA patients the first years of treatment. Both mITT and PP analysis should be presented in such safety analyses.

39-P224
Use of cetuximab in a real-life setting in France with respect to KRAS status – preliminary results of EREBUS 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. In July 2008, this indication was extended to 1st-line therapy and restricted to mCRC patients with wild-type (wt) KRAS gene. We present here the preliminary results of the French EREBUS cohort study and describe cetuximab prescription patterns according to KRAS status in a real-life setting.
Methods: EREBUS is a cohort study conducted in 92 French centres. Patients initiating cetuximab between Jan and Dec 2009 were identified from nominative hospital pharmacy dispensations. The cohort included mCRC patients treated in 1st-line. They were followed for 12 months to evaluate the rate of metastases resection, usage patterns, safety and effectiveness of cetuximab.
Results: To date, 1038 patients treated by cetuximab for colorectal cancer have been identified. Cetuximab was mainly prescribed in mCRC (98.0%): 34.4% as 1st-line treatment, 34.5% 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 these, 94.9% had wt KRAS gene. Investigation of KRAS mutation status and wt status were similar whatever treatment line (investigation: between 93.3% and 100.0%; wt status: between 93.9% and 100.0%). The investigation was performed on primary tumour (82.6%), on metastases (16.3%) or both (1.1%). The main reasons of absence of KRAS status investigation were: previous treatment by cetuximab (42.9%) and absence of available tumour material or technical issue with analysis (33.3%). Investigation of EGFR expression was performed for only 2.4% of the patients.
Conclusions: EREBUS 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.

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Risk assessment of drug-induced DRESS syndrom: 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). This ADR includes: skin rash, fever, eosinophilia and/or atypical lymphocytosis and participation of at least one internal organ. Few drugs are involved but for each drug, the risk of DRESS is currently unclear.
Aim: The aim of this study was first to identify the drugs which are more frequently associated with DRESS and spontaneously reported in the French PharmacoVigilance system (FPVD) and then 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 allows comparison of drug exposure among cases and non cases using the proportional reporting ratio (PRR with its 95% confidence interval).
Results: Three hundred and twelve cases of DRESS were included in the study. Patients have a median age of 57 years and 52.6% were women. Average onset of the 1st symptoms after drug introduction was 30.6 days (median 22 day) and 17 patients (8%) died. The drugs most frequently involved (>20 cases/drug) were: allopurinol, vancomycin, carbamazepine, sulfamethoxazole and sulfasalazine. However using the PRR, the risk of DRESS was higher for sulfasalazine (PRR = 53 [32;87]), allopurinol (PRR = 47 [36;63]), minocycline (PRR = 43 [20;92]) and carbamazepine (PRR = 20 [13;29]); moderate for vancomycin (PRR = 16 [11;23), strontium ralenate (PRR = 9 [4;19]), colchicine (PRR = 7 [3;13]), lamotrigine (PRR = 6 [3;12]) and cotrimoxazole (PRR = 5.3 [3.4;8.4]).
Discussion: The disproportionality analysis can be used to compare the risk of ADR between some drugs. However, this analysis is limited by the difficult exclusion of various biases, particularly those due to unequal ADR reporting among different drugs (ADR notoriety, ...) and to the over-representation of specific ADR for some drugs.
Conclusion: Despite the limits of this study, our results are an interesting approach to compare the risk of DRESS among the drugs which are usually involved in this pathology.

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Emergency admissions for major haemorrhage-related adverse effects of antithrombotic therapy
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Objective: The aim of the study was to describe the frequency and type of major haemorrhage related to antithrombotic therapy, to report the clinical characteristics, management and outcomes of patients admitted to a teaching hospital emergency department (ED).
Methods: Patients older than 16 years admitted in our ED with acute major haemorrhagic while treated by any antithrombotic agent were selected by computer requests from diagnostic codes and specific emergency therapies. Major haemorrhage was defined by at least one the following criteria: unstable hemodynamic, haemorrhagic shock, uncontrollable bleeding, need of transfusions, need of haemostatic procedure, or a life threatened location of bleeding (intracranial, gastrointestinal, pulmonary or peritoneal bleeding, compressive muscular hematoma).
Results: Between January 1 and October 31, 2011, 355 cases were selected which represented more than 1 patient per day. Median age was 82 years ± 10.3 (21–100). One hundred and seventy-four patients were taken vitamin K antagonists (24 in combinations with other antithrombotic agents), 164 patients antiplatelet medications (dual antiplatelet therapy in 14 cases), 17 others antithrombotic agents (heparin, LMWH). Major haemorrhagic accidents were: gastrointestinal tract bleeding in 40.5%, intracranial bleeding in 31.5%, muscular hematomas in 6.8%, epistaxis in 4.9%, haematuria in 3.5%, scalp bleeding injuries in 2.7%, others in 9.9%. Transfusion was needed in 55% of cases. The mean length of hospital stay was 7.7 days. The overall mortality was 12.3%, mostly in the intracranial bleeding group, and was independent to the type of antithrombotic. In the vitamin K antagonist group, only 41% of patients have received K vitamin treatment (dosage >10 mg in 75%), 33% have received prothrombin complex concentrate, 26.5% received both treatments. The mean delay between admission time and reversal time was 4 h 30 ± 3 h 40. Vitamin K antagonist treatment was definitely stopped in 3/4 of cases. In the antiplatelet medication group, no specific treatment was done. Antiplatelet treatment was definitely stopped in 2/3 of cases.
Conclusion: This register shows the magnitude and the severity of haemorrhage-related adverse events in patients treated with antithrombotic agents in a ED, suggesting a great vigilance in risk benefit imbalance in elderly.

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Adverse drug events (ADEs) caused by self-medication (SM) Preliminary results of a prospective multicentric survey in 11 emergency french departments (EDs) (APNET study group)
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Background: The regular use of self-medication to treat minor common illnesses is probably frequent in French population. EDs are an ideal place to observe ADEs and data are available on their frequency among EDs' admission, but little is known about that related to SM (ADEs-SM).
Objective: To measure the frequency of ADEs-SM among EDs' patients, and describe their characteristic.
Method: During 2 months, periods of study were randomized in 11 EDs centres. Every adult patients admitted at theses dates were interviewed, interviewers were medical and pharmaceutical students. The patients unable to answer, or refusing were excluded. The data on medical admission, on pharmaceutical history, on self-medication habits and taken drugs and on clinical outcome were collected. The drug causality assessment was helped by the Naranjo algorithm. All doubtful files, and systematically the ADEs-SM files, were reviewed by an expert committee. The comparison between groups was made by Chi-square for quantitative data, and by t test for qualitative data.
Results: Four thousand six hundred and sixty-one patients were admitted in the EDs during studys' periods. Three thousand and twenty-seven were included.
The reasons of the 1634 (35.06%) exclusions were: self-poisoning (2.17%), patients' refusal (10.62%), patients' inability and refusal of their relatives (1.80%), patients' inability and no relatives (20.47%).
The median age of included patients were 43 years old (18–99), with 46.45% of females, and 16 pregnancies. One thousand eight hundred and fourteen patients have taken at least one prescribed drug, and 1927 declared to have taken at least one self-medication drug during the last 2 weeks. Among the included patients, there was 296 ADEs (9.78%), with 2/3 involvement of drugs in multifactorial pathologic conditions, and 1/3 adverse drug reactions. Fifty-two patients (1.72%) have experienced an ADE related to self-medication, with self-modification of prescribed drug for 19 patients, therapeutic break for 14 and a non prescribed drug for 17 patients.
Conclusion: SM is frequent among EDs' patients and clearly underestimate. The frequency of ADEs-SM is enough to be taken into account. A way to detect self-medication related pathologies should be based on intervention at the bedside of clinical pharmacist and pharmacologist. Therapeutic education in primary care could be a way to prevent ADEs-SM.