myositis was investigated, IC delta scores of 1.662 and 1.39 were seen for Simvastatin and Cerivastatin but negative scores of -1.907, -0.848, -1.233 and -1.668 were seen for Pravastatin, Fluvastatin, Atorvastatin and Rosuvastatin.

Conclusions: Statins and the term rhabdomyolysis were not highlighted with TPD. Low counts could reflect a rare and/or serious outcome not captured frequently in UK GPD. The more frequently recorded term myalgia-myositis was highlighted for some, but not all, statins, possibly reflecting complex statin switching patterns accentuated by NICE guidelines, but this is to be confirmed. Hypothesis-free signal detection in EMRs is no panacea; more work is needed to determine optimal granularity level for signal detection and whether data sets more reflective of specialist/hospital care are preferred for some DME surveillance.

762. The Impact of Age and Gender on Reporting of Cough and Angioedema with RAS Inhibitors: A Case/Non-Case in VigiBase

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Background: Little is known about the effect of age and gender on reporting of cough/ angioedema with renin angiotensin system (RAS) inhibitors (angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and aliskiren, a direct renin inhibitor (DRI).

Objectives: To assess the impact of age and sex on the occurrence of cough/angioedema with RAS inhibitors using information reported to the World Health Organization (WHO) global individual case safety report database (VigiBase).

Methods: A case/non-case study was performed in VigiBase. Cases were defined as reports of cough/angioedema and non-cases were all reports of other adverse events. Age was divided into 6 categories: infant and childhood (0-11 years), adolescence (12-19 years), young adulthood (20-39 years), middle adulthood (40-59 years), elderly (60-79 years) and late elderly (≥80 years). Logistic regression analysis was used to assess the association between reporting of cough/ angioedema with each class of RAS inhibitors stratified by age/ sex and to control for confounding.

Results: The reporting of cough with ACE inhibitors was significantly higher in women than in men (adjusted reporting odds ratio (ROR): 29.2, 95%CI (28.5-29.9) for men versus 44, 95%CI (43.2-44.8) for women). There was no difference in reporting of cough with ARBs and DRI between men and women. In contrast, the reporting of angioedema with ACE inhibitors and ARBs was significantly higher in men than women but for DRI (aliskiren), women had significantly higher ROR than men. For the effect of age, the reporting of cough with ACE inhibitors was significantly increased with age until reaching a plateau at 60 years and the reporting of angioedema with ACE inhibitors was significantly increased with age until 80 years. Age had only a slight effect on reporting of cough/angioedema with ARBs and DRI.

Conclusions: Age and sex have substantial effects on reporting of cough/angioedema with RAS inhibitors especially with ACE inhibitors. Further studies are needed to study both factors on occurrence of cough/ angioedema with RAS inhibitors and to elucidate the underlying mechanism involved.

763. A Novel Approach to Study the Impact of Ethnicity on Reporting of Cough/Angioedema with RAS Inhibitors in VigiBase

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Background: Cough and angioedema are adverse events associated with especially angiotensin-converting enzyme (ACE) inhibitors but also reported with angiotensin receptor blockers (ARBs) and aliskiren, a direct renin inhibitor (DRI). Susceptibility of developing cough/angioedema with ACE inhibitors depends on ethnicity, which is not documented in spontaneous reporting systems of drug safety.

Objectives: To assess the impact of ethnicity on the occurrence of cough/angioedema with renin angiotensin system (RAS) inhibitors using information

reported to the the World Health Organization database(VigiBase).

Methods: A case/non-case study was performed in VigiBase. Cases were defined as reports of cough/angioedema and non-cases were all reports of other adverse events. The reporting countries were divided into three categories: black African countries, East Asian countries and other countries. Logistic regression analysis was used to assess the association between reporting of cough/angioedema with each class of RAS inhibitors stratified by country group and to control for confounding.

Results: The reporting of cough with ACE inhibitors was significantly higher in East Asian countries than black African countries and other countries (adjusted reporting odds ratios (RORs): 256, 95%CI (236-278), 48.9, 95%CI (42.7-56.1) and 35.4, 95%CI (34.8-35.9), respectively. The reporting of angioedema with ACE inhibitors was significantly higher in black African countries than East Asian countries and other countries (adjusted RORs: 55.3, 95%CI (45.5-67.2), 5.29, 95%CI(3.89-7.21) and 16.5, 95%CI (16.1-16.8), respectively. There was no difference in reporting of cough/angioedema with ARBs and DRI between black African countries, East Asian countries and other countries.

Conclusions: Our results by grouping countries according to ethnicity in VigiBase are consistent with previous results in the literature suggesting that the occurrence of cough with ACE inhibitors is higher in East Asian patients and the occurrence of angioedema with ACE inhibitors is higher in black patients. These findings indicate that ethnicity should be included as scientific parameter in pharmacovigilance.

764. Cardiovascular and Gastrointestinal Safety of Paracetamol in French Population: A Self-Controlled Cohort Study

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Background: Though paracetamol is one of the most commonly used drugs worldwide, very little is known of its cardiovascular (CV) and gastrointestinal (GI) safety.

Objectives: To evaluate the risk of acute coronary syndromes (ACS), stroke and GI bleeding events associated with the use of paracetamol.

Methods: A self-controlled cohort study in EGB, the permanent 1/97 representative sample from the French national healthcare insurance database that covers 84% of paracetamol sales. All exclusive episodes of paracetamol use in patients aged ≥15 years between 2009 and 2012 were identified. Main outcomes were ACS, stroke and GI bleeding. Risk periods were the periods from the first day of exposure (t0) to the next episode of NSAIDs/paracetamol use, or 3 months after t0. Control periods were the non-exposure time right before t0. Risks of outcome occurrence were estimated by comparing hazard rates in risk periods to their control periods by COX proportional hazard models.

Results: 1 026 041 paracetamol exclusive episodes in 342 561 users (mean age 47.2 years; 55.8% female) were included. We identified in total 685 and 843 ACS events (event rate 3.2 and 3.2 per 10,000 episode-months); 340 and 378 stroke events (event rate 1.6 and 1.4); 132 and 227 GI bleeding events (event rate 0.6 and 0.9) during control and risk periods respectively. CV risk did not increase overall (ACS hazard ratio 0.99, 95% CI 0.90 to 1.10; stroke HR 0.90, 0.78 to 1.04). However, if we exclude episodes with co-dispensed low-dose aspirin, ACS risk increased significantly (HR 1.37, 1.21 to 1.55). GI bleeding risk also increased significantly (1.39, 1.12 to 1.73). Episodes with low baseline CV risk were associated with significant increase of stroke risk (1.45, 1.09 to 1.92). Patients aged ≥60 years had significant increases of ACS and GI bleeding risk (1.38, 1.18 to 1.60 and 1.49, 1.11 to 2.00).

Conclusions: Our study contributes data on safety of paracetamol. We found a 37% increase of ACS risk associated with paracetamol without co-dispensed aspirin. Use of paracetamol in the elderly should be reconsidered because of poor CV and GI safety.

765. Cardiovascular and Gastrointestinal Safety of OTC and Prescription-Only Ibuprofen versus Paracetamol in French Population

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