OBJECTIVES: Romiplostim and eltrombopag are thrombopoietin receptor (TPOr) agonists that promote megakaryocyte differentiation, proliferation and platelet production in patients with chronic idiopathic thrombocytopenic purpura and adult chronic idiopathic thrombocytopenic purpura patients who are refractory to other treatments. Due to increasing platelet counts above the normal range may represent a risk for thromboembolism, we assessed whether TPOr agonists affect thromboembolic risk through a systematic review and meta-analysis of ran- domised controlled trials (RCTs). METHODS: We searched PubMed, SCOPUS, Co- chrane Central Register, regulatory agencies websites and publicly available registries of manufacturers (before January 2011). RCTs using romiplostim or eltrombopag in at least one group were included. Absolute risk ratio (ARR) and number needed to harm (NNH) were calculated to provide the population health impact of the exposure. Relative risks (RR) were also provided. Data were pooled using fixed-effects models. Heterogeneity was assessed using Cochran’s Q test and 12 tests. RESULTS: Forty-two RCTs met the inclusion criteria (n = 1,180 patients). In the TPOr agonist group, as compared with the control group (e.g. placebo and/or standard of care), the meta-ARR for thromboembolism was 1.8% (95% CI, 0.0% to 3.6%), and the meta-RR was 1.5 (95% CI, 0.7 to 3.3). Fifty-five patients would have to be treated using TPOr agonists to produce thromboembolisms in a patient (meta-NNH = 55). Non heterogeneity was found (Cochran’s Q test, P = 0.9; I² = 0.0%). CONCLUSIONS: Although the small numbers reported, thromboembolism should be considered as identified risks for these drugs. Healthcare providers should be aware when administering these agents to patients with known risk factors for thromboembolism.

PCVE

COMPARISON OF BLEEDING RATES BETWEEN STATIN AND STATIN-FREE PATIENTS ON WARFARIN: A CLAIMS DATABASE APPROACH

Guerin A1, Hylek EM2, Frosi C3, Ponce de Leon Barido D1, Marrocco CE2, Bae JP1, Zhao Y1
1Analytic Group, Inc., Boston, MA, USA, 2Boston University, School of Medicine, Boston, MA, USA, 3Eli Lilly and Company, Indianapolis, IN, USA

OBJECTIVES: In a recent study in patients receiving warfarin, the initiation of st- atins and the cytoprotective P2Y12 inhibitors was associated with an increased risk of hospitalization for gastrointestinal bleeding in a Medicare-insured population, while the initiation of pravastatin was not. The present research attempted to address some of the study limitations and assess whether similar findings are applicable in a more recent, commercially-insured U.S. population. METHODS: A retrospective matched-cohort design was used to compare baseline characteristics and bleeding rates (e.g. gastrointestinal and non-gastrointestinal) between statin and statin-free patients receiving warfarin concomitantly. Patients were matched on a 1:1 ratio to balance patient characteristics, and a cox proportional hazard model was used to test for confounding variables. The analyses were performed for a matched “stabilized” population, i.e., patients who had been on warfarin for ≥6 months, did not have prior bleeding events, and did not use another statin before the index date. For the matched “stabilized” populations, sub-group analyses were performed on patients with atrial fibrillation, patients with venous throm- bosis, patients age ≥65 years, patients age ≥75 years, prevalent/persistent warfarin users, and by statin therapy. RESULTS: The method produced a small matched sample of 6306 (8.2%) out of 123,328 statin users and 41,734 statin-free patients. There were no statistically significant differences in bleeding rates between statin users and statin-free patients. RESULTS were similar for the sub-group analyses. CONCLUSIONS: Using a claims database approach, high degree of heterogeneity between statin users and non-users was found, resulting in a low matching rate. This higher degree of heterogeneity suggests that claims databases may be insuf- ficient to detect/conclude as to differences in bleeding rates between statin versus statin-free patients on warfarin. Alternative methods and additional clinical information are needed to more accurately characterize bleeding rates in patients tak- ing warfarin and a statin therapy concomitantly.

PCV9

TOBACCO ADDICTION INFLUENCE IN LATER DEVELOPMENT OF CARDIOVASCULAR EVENTS: 3 YEARS FOLLOW-UP

Sicras-Mainar A1, Diaz-Cerezo S2, Sanz de Burgos V3, Navarro-Artieda R4
1Directorate of Planning, Badalona Serveis Assistencials, Badalona, Barcelona, Spain, 2Pfizer Spain, Madrid, Spain, 3Pfizer Spain, Alcobendas (Madrid), Spain, 4Hospital Universitari Germans Trias i Pujol, Barcelona, Spain

OBJECTIVES: To determine tobacco consumption effects on metabolic control (biochemical/anthropometrics parameters), mortality and on CVE relapses inci- dence during a 3 year follow-up. METHODS: Multicentric observational study un- dertaken through the retrospective review of the medical records of patients at six primary health-care centres and two hospitals. Inclusion criteria: subjects ≥ 30 years of age with at least one cardiovascular risk factor; CVE between 2001-2007; Follow-up: 36 months. Groups: smokers, ex-smokers and non-smokers. Main mea- sures: sociodemographics, morbidity, biochemical/anthropometrics parameters (systolic and diastolic arterial pressure (mmHg), baseline glycaemia (mg/dL), body mass-index (BMI) [kg/m²], waist circumference (WC) [cm], HDL cholesterol and LDL-cholesterol (mg/dL)), mortality and later CVE (ischaemia, infarct- ion, strokes, ischemic accident, peripheric arteriopathy). Statistical analysis: lo- gistic regression model and Kaplan-Meier curves. RESULTS: 2,540 participants fulfilled the inclusion criteria (62.8% with CVE). In the smokers group, smokers: 8.4%, ex-smokers: 38.7%, non-smokers: 53.9%. Mean age: 68.1 years old, men: 60.7%. By groups: patients showed a similar distri- butions of comorbidities. 19.1% of smokers still smoked after the first CVE. Smoking addiction was related with COPD (odds ratio OR = 2.4, 95%CI: 1.7-3.5) and depres- sive syndrome (OR = 1.5, 95% CI: 1.1-2.9). The smoking condition mean time was 24.4 (14.5) years for smokers and 4.2 (1.2) years for ex-smokers. Comparing baseline (during hospitalization) and final (3 years follow-up), in the non-smokers group, all parameters showed a significant reduction (p < 0.05); in exsmokers (6/8) and in smokers group only 4/8. All mortality causes (intra-hospital and follow-up included) was 4.2% (N=106; 95%CI: 3.4-5.0%), in smokers: 4.2%, ex-smokers: 5.9% and non- smokers: 1.8%; p=0.001. Incidence rate of new CVE’s was 15.2% (95%CI: 13.8-16.6%) in smokers: 16.5%; ex-smokers: 16.5%; non-smokers: 9.6%; p<0.001. CVE’s were present in 8.2%, 6.0% and 3.3% respectively, p<0.05. CONCLUSIONS: In routine clinical practice, smokers compared with ex-smokers and with non-smokers still support a high future risk of suffering a CVE and higher mortality rates.