Results: We identified 427,576 saxagliptin initiators and 3,535,010 other OAD initiators. There were no increased incidence rates or risk of MACE, infection, AKI, ALF, or severe hypersensitivity reactions between saxagliptin initiators and other OAD initiators within each data source. Meta-analyses resulted in no increased risk of hospitalization/death from MACE (HR, 0.91 [95% CI, 0.85-0.97]), hospitalization for infection (HR, 0.97 [95% CI, 0.93-1.02]), or hospitalization for AKI (HR, 0.99 [95% CI, 0.88-1.11]) among saxagliptin initiators. ALF and hypersensitivity events were too rare to permit meta-analysis.

Conclusions: Saxagliptin initiation was not associated with significantly increased incidence rates of MACE, infection, AKI, ALF, or severe hypersensitivity reactions.

421. Use of Incretin Agents and Risk of Acute and Chronic Pancreatitis: A Population-Based Cohort Study

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Background: Incretins are new therapeutic agents for the treatment of Type 2 Diabetes Mellitus (T2DM), and are a subgroup of the Non-Insulin Antidiabetic Drugs (NIAD). Although incretin agents have demonstrated efficacy for T2DM, they have been associated with pancreatitis. Recent literature shows limited and conflicting evidence for the association between incretin agents and the risk of acute pancreatitis. Furthermore, the risk of chronic pancreatitis with the use of incretin agents has not been investigated.

Objectives: To determine the association between the use of incretin agents and the risk of acute and chronic pancreatitis.

Methods: A retrospective population based cohort study, using data from the Clinical Practice Research Datalink (CPRD) (2007–2012), was conducted. Patients (N=182,428) with at least one NIAD prescription and aged 18+ during data collection, were matched to one control patient without diabetes. Multivariable Cox proportional hazards models and a new user design were used to estimate the hazard ratio of (acute, chronic and any) pancreatitis in incretin users (N=28,370) compared with non-diabetics and other NIAD-treated patients. Time dependent adjustments were made for age, sex, life style, comorbidities and drug use.

Results: Current NIAD use was associated with acute, chronic and any pancreatitis. This risk increased among current incretin users, as compared to non-diabetic controls. However, only any pancreatitis was associated with incretin use when compared to other NIAD-treated patients (HR=1.47, 95% CI 1.06–2.04). Pancreatitis risk was higher among younger patients (age 18-≤59 years), those with a BMI <25 kg/m2, or those using DPP4-Is compared to other NIAD-treated patients. In the new user design cohort, the association between incretin use and acute and any pancreatitis doubled compared to the prevalent cohort.

Conclusions: Incretin use was associated with an increased risk of any pancreatitis. Moreover, risk of pancreatitis was higher among incident incretin users. Further research is necessary regarding the need for clinical consensus between the association of pancreatitis and incretin use in T2DM patients with a history of pancreatitis.

422. Use of Non-Insulin Blood Glucose Lowering Drugs and the Risk of Acute Pancreatitis

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Background: Use of non-insulin blood glucose lowering drugs (NIBGLD) has been associated with acute pancreatitis (AP). For newer NIBGLDs, including GLP-1 based drugs, evidence for such risk is conflicting.

Objectives: To estimate the risk of AP for NIBGLD in databases (DB) participating in the SAFEGUARD project.

Methods: Case-control study was performed nested in a cohort of new NIBGLD users. Incident AP cases were matched with up to 5 controls on DB, sex, cohort entry (±3 months) and date of birth (±1 year) using risk set sampling. Data were retrieved from 7 DBs from Europe (Netherlands: PHARMO; Spain: BIFAP; Germany: GePaRD; Italy: Health Search, Regional DBs of Lombardy and Puglia; United Kingdom: CPRD) and USA (Medicare). Adjusted odds ratios (ORs) and 95% confidence intervals (95%CI) were estimated per DB, comparing current use of metformin +sulfonylureas (reference) with each monotherapy, dual therapy of metformin plus another NIBGLD (not SU) and other combinations. One (ORpool) and two stage (OR meta) pooling was used to combine the database specific data.

Results: In total 3,990 incident AP cases were matched to 19,543 controls. Majority of subjects were male. Drugs known to be associated with AP (class 1), gallstones and alcohol abuse increased risk of AP. Metformin monotherapy was associated with a decreased risk of AP (ORpool 0.88 95%CI:077-1.00; ORmeta 0.84; 0.73-0.96). Regarding GLP-1 based drugs, we observed a statistically non-significant risk for sitagliptin monotherapy (ORpool 1.53; 0.88-2.64; ORmeta 1.29; 0.64-2.58). Monotherapy of glimepiride (ORmeta 1.02;0.84-1.24) and glibenclamide (ORmeta 1.16;0.68-1.97) did not yield an increased risk. Current use of any other NIBGLDs or combinations was not associated with an increased risk of AP in any of the databases (ORpool 1.1; 0.94-1.34; ORmeta 1.01; 0.85-1.20). Recent and past use of any NIBGLD were not associated with an increased or decreased risk of AP (ORmeta 1.10; 0.88-1.36 and 0.93; 0.80-1.09, respectively).

Conclusions: Monotherapy of metformin was associated with a decreased risk of AP, while sitagliptin monotherapy was associated with a statistically non-significant increased risk while a risk≥2.6 could be excluded.

423. Metformin and Cancer Risk in Type 2 Diabetes: An Application of Marginal Structural Models with Inverse Probability of Treatment Weights in the Clinical Practice Research Datalink

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Background: Previous studies provide conflicting evidence on whether metformin is protective against cancer. The effect of time-varying confounders that affect treatment, such as HbA1c, may not have been adequately accounted for. However, such variables may act as both confounders and causal pathway variables, so cannot be handled by standard regression models. Marginal structural models (MSMs) with inverse probability of treatment weights (IPTW) can correctly adjust for such time-varying confounders by creating a pseudo population in which confounders are balanced across treatment groups through time.

Objectives: To estimate the effect of metformin on cancer risk compared to diet alone, using MSMs with IPTW to correctly adjust for time-varying confounding.

Methods: Patients with incident T2DM were identified in the Clinical Practice Research Datalink