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patients with heart failure, and it is also unclear whether risk differs by kidney function.

Objectives: To measure the absolute and relative risks of hyperkalemia associated with adding spironolactone to loop diuretics among patients with heart failure.

Methods: Patients with heart failure and loop diuretic use were identified in MarketScan commercial claims data (MS) from 2010–15 (*N* = 5448), and the Geisinger Health System (GHS) from 2004–16 (*N* = 7448). Medication use was determined through dispensing data (MS) and prescription orders (GHS). We quantified the incidence of hyperkalemia, defined as inpatient encounters with hyperkalemia diagnosis codes, comparing rates on treatment (from spironolactone initiation among initiators) with those on control (from a randomly selected loop diuretic prescription among those not using spironolactone). We evaluated whether spironolactone use was associated with higher risk of hyperkalemia in patients with estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m^2 compared to ≥60 ml/min/1.73m^2 using negative binomial regression. All models were adjusted for baseline serum potassium, demographics, comorbidities, and medication use and, in sensitivity analyses, we repeated the analysis matching treatment 1:1 to controls using propensity scores.

Results: Among individuals with incident heart failure (MS: treatment *n* = 759 and control *n* = 4689; GHS treatment *n* = 1242 and control *n* = 6206), the treatment groups were younger, and more likely to be male, have liver disease, and take cardiovascular medications (all $p < 0.05$). Baseline mean potassium was lower (−0.06 mEq/L) and eGFR was higher (+2.6 ml/min/1.73m^2) in the treatment group in GHS. Overall, there were 68 hyperkalemia events [4.6 vs 2.5 per 1000 person-months in treatment and controls, respectively] in MS, and 208 (3.4 vs 1.4) in GHS. In adjusted analyses, treatment was associated with an incidence rate ratio of 1.95 [95% confidence interval (CI): 1.05–3.64] and 2.90 (CI: 1.95–4.33) for hyperkalemia events in MS and GHS, respectively. There were no differences in hyperkalemia risk by level of kidney function in either cohort (p for interaction between treatment status and kidney function - MS: 0.89; GHS: 0.64). Results were similar in propensity score matched analyses.

Conclusions: The initiation of spironolactone among loop diuretic users with heart failure was associated with a greater risk of hyperkalemia, but the risk did not differ by baseline level of kidney function.

1184 | Monitoring the safety of Exenatide once-weekly (Bydureon®) in primary Care in England: Results from a PASS

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Background: Clinical trials have reported specific safety concerns such as acute pancreatitis (AP) in patients (pts) taking Bydureon® (exenatide once-weekly) for type 2 diabetes mellitus (T2DM). A Post-Authorisation Safety Study (PASS) was conducted to monitor the real-world safety of Bydureon® in primary (1°) care in England.

Objectives: To estimate the incidence of targeted safety outcomes in pts prescribed Bydureon® in 1° care.

Methods: Pts identified from dispensed Bydureon® prescriptions in England (2012–2016). Questionnaires sent to prescribing general practitioners (GPs) at ≥12-months observation collected event information. Events of interest included AP, pancreatic cancer (PC), thyroid neoplasm (TN), gallstones, biliary colic or cholecystitis (GBC), acute renal failure (ARF), type 1 hypersensitivity (T1H), and cardiac events (CE). 12-month incidence estimates (on Bydureon® or ≤ 10 weeks after stopping) were calculated; results were stratified according to prior exenatide use (i.e. Byetta®).

Results: Questionnaire response rate = 37.2% (7752/20860). Total cohort = 6294 pts prescribed Bydureon® for T2DM (median age 57 years [IQR 50, 65]; 55.2% male). Exenatide naïve *n* = 4556 (72.4%), previous Byetta® users *n* = 1629 (25.9%), previous Byetta® use unknown *n* = 109 (1.7%). Risk of AP in total cohort 0.2% (95% CI [0.1, 0.4]; *n* = 14). 2 pts had a prior history. Risk of AP was similar for exenatide naïve (0.2% (95% CI [0.1, 0.4]; n = 10) and previous Byetta® users (0.2% (95% CI [0.0, 0.5]; *n* = 3). Rate of AP in total cohort was 2.5/1000 person-years (95% CI [1.5, 4.3]) and no statistically significant difference was observed between the 2 user groups. Time-to-event analyses suggested no clear pattern in the hazard function of AP over time. For 12 of the 14 pts, Bydureon® was stopped due to AP. AP complications; necrosis/pseudocyst n = 1, fatal outcome *n* = 1. PC 0.1% (n = 4); a fatal outcome was reported in 3 of these pts. TN 0.0% (*n* = 0). GBC 0.6% (95% CI [0.4, 0.8]; *n* = 38); 15 of which had a prior history of GBC. ARF 0.5% (95% CI [0.3, 0.7]; *n* = 29). T1H 0.7% (95% CI [0.5, 0.9]; *n* = 44). CE 3.6% (95% CI [3.2, 4.1]; *n* = 227). No statistically significant differences in risk between the 2 user groups were observed.

Conclusions: Incidence of AP was low in Bydureon® users and consistent with prior clinical trial/observational data. No unexpected findings were identified. This study has unique strengths, including collection of timely, granular real-world data from GPs, facilitating accurate estimates. The study is part of a broader literature on the safety of Bydureon® and conclusions should be made in context with other post-marketing findings.

1185 | Incidence and risk factors for hypoglycemia in patients with diabetes hospitalized in a quaternary Care Centre in South India

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Background: Hypoglycemia occurs in 8% of hospital admissions and is an important complication of type 2 diabetes that can have a major

impact on health outcomes. The 2017 Standards of Medical Care highlight renal insufficiency and cognitive dysfunction as important risk factors for hypoglycemia but other risk factors remain less documented.

Objectives: To identify potential risk factors in the development of hypoglycemia in hospitalized diabetic patients and to evaluate their influence in patients admitted to critical care and non-critical care units.

Methods: In this prospective, non-randomized study a number of potential risk factors for the development of hypoglycemia in hospitalized patients such as clinical condition of the patient, duration of diabetes, blood sugar level at the time of admission, type of feed and surgical status were predefined based on the literature. The influence of these factors were then evaluated in patients admitted to critical and non-critical care units. Blood glucose measurement was done by point-of-care testing. All Type II diabetic patients admitted to the hospital (>18 years) were included and Type 1 diabetic patients and hyperglycemia without a history of diabetes were excluded. The influence of risk factors in the development of hypoglycemia were analyzed and compared the data of critical and non critical care units using chi square method with $p < 0.05$ to be significant.

Results: The study revealed that 14.3% of the diabetic patients developed hypoglycemia and the incidence of events was found to be 31.25%. There was no significant difference in age (65 ± 9.5 vs 64.5 ± 9.6 $p = 0.764$) and time of hypoglycemic attack (46% vs 54.5% $p = 0.344$) in patients admitted to critical and non critical care units whereas duration of diabetes (44% vs 6% $p = 0.000$), blood sugar at the time of admission (30.5% vs 47% p = 0.000), surgical status (5% vs 30% p = 0.000) significantly differed. There was also significant difference in the incidence of hypoglycemia based on the type of feed in both groups; normal intake (15% vs 50.5% $p = 0.05$), decreased intake (6.8% vs 30% p = 0.05), RT feed (40.7% vs 6% p = 0.05). Terminal illness was considered a major risk factor for hypoglycemia and the relationship between hypoglycemia and mortality(10% vs 1.5% $p = 0.001$) was stronger among patients who had multiple events of moderate hypoglycemia(40–60 mg/dl) during their hospital stay.

Conclusions: Hypoglycemia is a common problem in hospitalized diabetic patients and the influence of these risk factors should be considered in hypoglycemic risk assessment when individualizing diabetes care for older patients.

1186 | Incretin mimetic drugs (GLP-1 receptor agonists and DPP-4 inhibitors) and associated adverse events and renal outcomes: A Pharmacoepidemiologic analysis using the FAERS database

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Background: Clinical studies demonstrated the efficacy and safety of incretin memetic drugs among patients with diabetes, however, the impact of these drugs on renal function is still not settled.

Objectives: 1) To identify potential signals of adverse events that are frequently reported but not currently stated on drug labels. 2) To explore the potential impact of incretin mimetic drugs on renal outcomes using a real world data.

Methods: Retrospective descriptive analysis of adverse events reported to the US Food and Drug Administration Adverse Events Reporting System (FAERS) database from quarter 1, 2012 to quarter 2, 2018. Our Analysis focused on three drugs of the incretin mimetic class resulted in a postmarket safety communications by the FDA, namely Exenatide, Sitagliptin and Saxagliptin. The most common adverse events (AEs) were compared with the current warnings on each drug label. Renal adverse event reports AE reports were identified using text string search queries of preferred terms related to the renal system.

Results: A total of 72,035 AEs were identified for the study drugs (Exenatide, 41,089, Sitagliptin, 25,091, Saxagliptin, 5,855). The most common AEs that are not posted on label N(%) were: For Exenatide, Hypertension 317(1.26%), Bladder Cancer 234 (0.93%), Anxiety 230(0.92%), Depression 181 (0.72%), Myocardial Infarction 159 (0.63%), and Pneumonia 142 (0.57%); For Sitagliptin, Pneumonia 1127(2.74%), Asthenia 1015 (2.47%), Hypertension 889(2.16%), Anemia 857(2.09%), Bladder Cancer 847(2.06%); For Saxagliptin, Hyperglycemia 424 (7.24%), Diarrhea 279 (4.77%), Nausea 233 (3.98%), fatigue 231(3.95%), weight reduction 233 (3.81%). The most common renal AEs for Exenatide were: Acute Kidney Injury 217 (0.86%), Renal failure 213 (0.85%), Urinary Tract Infections 112 (0.45%); for Sitagliptin were: Renal failure 907 (2.21%), Acute Kidney Injury 768 (1.87%), and Urinary Tract Infection 705 (1.72%); and for Saxagliptin: Urinary Tract Infections 123 (2.1%), Renal Failure 115 (1.96%), Acute Kidney Injury 80 (1.37%).

Conclusions: Renal adverse events seem more commonly reported for Sitagliptin and Saxagliptin compared with Exenatide. Hypertension, myocardial infarction and pneumonia were identified for all drugs and not currently addressed on drug labels and need further assessment.

1187 | Diabetes management protocol: Impact in the incidence of hypoglycemia

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Background: Hypoglycemia occurs in 7.7% of hospital admissions and is associated with increased length of stay and increased mortality. It is suboptimally treated and has severe consequences. There remains a need for the development, implementation and adherence to a diabetes management protocol that reduces the incidence of hypoglycemia.

Objectives: To develop a protocol in the management of hospitalized diabetic patients and to evaluate its impact during post interventional phase.

Methods: In this prospective, interventional, non randomized study, abetes management protocol was developed according to ADA

guidelines. All Type II diabetic patients admitted in a Quaternary Care Centre in South India in the age group ≥18 years of either sex irrespective of comorbidities and medications were included in the study and those with gestational diabetes or hyperglycemia without a history of diabetes were excluded. Blood glucose measurement was done by point-of-care testing. The impact of protocol in reducing hypoglycemic events were analyzed and compared the data of pre intervention with post intervention using chi square method with $p < 0.05$ to be significant.

Results: Pre intervention data showed 85 hypoglycemic events (15.8%) in 535 diabetic patients and in post intervention phase,57 (14.3%) events were observed in 400 patients. There was statistically significant reduction in the severity of hypoglycemia (23.5% vs 6.4%, $P = 0.035$), incidence in patients with normal diet (73.3% vs 43.2%, $p = 0.00$) and an increase in referral to specialist(30.6% vs 43.2%, $P = 0.000$) and regular monitoring (47.1% vs 94.4%, $P = 0.001$) after implementing the protocol.

Conclusions: Development and implementation of a diabetes management protocol, significantly reduces the incidence and severity of hypoglycemia. Adherence to protocol, regular monitoring, proper feed and early referral to specialists may help to reduce the hypoglycemic episodes.

1188 | Risk and signals of ketoacidosis among sodium-glucose Cotransporter-2 (SGLT2) inhibitors: Analysis of post marketing FDA adverse event reporting system (FAERS) database, 2013–2018

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Background: Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors are considered a novel treatment option for patients with diabetes, due in part to their cardiovascular protective effects and their availability as oral medications. However, the risk of ketoacidosis has substantially increased in par with reports concerning the health effects of this group of medication, as regarded by health institutions and regulatory authorities.

Objectives: To analyze and compare the risks of ketoacidosis among Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors in the FDA Adverse Event Reporting System (FAERS) database over 5 years.

Methods: Reports of ketoacidosis and related terms events (e.g. diabetic ketoacidosis) submitted to FAERS in the period between March 2013 and March 2018 were retrieved and analyzed by the reporting odds ratio (ROR). Using FAERS database, the ROR of case/non-case reports of ketoacidosis and its related terms associated with SGLT2 inhibitors was compared. All data were analyzed by using the Statistical Analysis Software (SAS), version 9.4.

Results: 6,809 reports of ketoacidosis were reported during the study period in FAERS database among the total of 6,583,341 unique reports. Majority of reports of ketoacidosis during the study periods were linked to SGLT2 inhibitors (73%). Around 2,692 reports linked canagliflozin to ketoacidosis and the proportion of ketoacidosis reports with canagliflozin—among all canagliflozin reports—was 11.5%. There were 1,217 reports linked dapagliflozin to ketoacidosis, and the proportion of this was 12.2%, while it was 13.2% for empagliflozin with 1,064 reports connected to ketoacidosis. The annual number of reports increased yearly (2013 to 2018) with a high spike in 2015. The association between ketoacidosis and its related terms was statistically significant with the use of all three medications with different with the degree of association. ROR was 162 [95% CI 152–173]) with dapagliflozin, ROR 173 [95% CI 161–186] with empagliflozin, and ROR 205 [95% CI 195–216] with canagliflozin.

Conclusions: There is a significant risk of ketoacidosis with the use of the SGLT2 inhibitors. However, the risk varies within SGLT2 inhibitors, with an increase among canagliflozin and a decrease with dapagliflozin.

1189 | Pancreatic safety of sodium-glucose co-transporter 2 inhibitors in patients with type 2 diabetes: A systematic review and meta-analysis

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Background: Sodium-glucose cotransporter 2 (SGLT2) inhibitors, a novel class of oral antidiabetic drugs, have been suggested a potential risk of acute pancreatitis in patients with type 2 diabetes (T2D). However, the pancreatic safety of SGLT2 inhibitors in patients with T2D is not well known.

Objectives: This study aimed to systematically evaluate the association between SGLT2 inhibitors and pancreatic safety in patients with T2D.

Methods: We systematically searched PubMed, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov through May 2018 to identify randomized controlled trials that reported adverse events on acute pancreatitis, pancreatitis, or pancreatic cancer among the adults with T2D treated with SGLT2 inhibitors compared with placebo or other active antidiabetic drugs. Peto odds ratio (OR) with 95% confidence interval (CI) was used to pool the data. The GRADE framework was introduced to assess the quality of evidence.

Results: Thirty-one trials involving 39,002 patients with T2D, with a median duration of 52 weeks were included. Meta-analysis of 16 trials