Final report abstract

Title

Dulaglutide Modified-Prescription-Event Monitoring Study and network database study: a multi-database collaborative research program of observational studies to monitor the utilisation and safety of dulaglutide in the EU.

Keywords

Trulicity, dulaglutide, safety, utilisation, pancreatitis

Rationale and background

This multi-data source post authorisation safety study (PASS) programme was aimed to assess safety outcomes of interest for dulaglutide in the European Union (EU) as part of the Risk Management Plan to further characterise the safety profile of dulaglutide in real-world use, and to understand utilisation patterns. Information was collected with respect to important identified risks, important potential risks, and in subpopulations of patients in whom safety data was considered missing at the time of initial marketing authorisation.

Research question and objectives

To assess and understand the safety profile of dulaglutide in patients with type two diabetes mellitus (T2DM) with regard to medical conditions of interest. The primary objective was to estimate the cumulative incidence in the first 12 months of treatment of the following:
(a) Acute pancreatitis
(b) Hypersensitivity [including anaphylaxis, and injection-site reactions]
(c) Cardiovascular (CV) events [heart rate / rhythm (supraventricular arrhythmias/ tachycardia) and conduction abnormalities (atrioventricular block)]
(d) Gastrointestinal (GI) effects [gastrointestinal stenosis, gastrointestinal obstruction, and delayed gastric emptying]
(e) Medication errors [frequency of administration > once weekly]
Secondary objectives included a description of baseline characteristics, health profile and antidiabetic treatment regimen of patients for whom dulaglutide was prescribed for the first time. Further secondary objectives included an exploration of time to onset of events of interest and predictors of risk, a description of the safety profile in sub- populations, and an estimation of the period prevalence of pancreatic and/or thyroid cancer.

Study design

The common study design was a retrospective observational cohort design.

Setting

The PASS programme included four data sources; three databases (consisting of healthcare and administrative databases) based in Germany, the Netherlands and Italy, and one non database data source in England (Modified Prescription Event Monitoring Study [M-PEM]).

Subjects and study size

In the three databases, the study population consisted of patients who were prescribed

dulaglutide for the first time and met study-specific eligibility criteria. Data sources for the three databases included the Leibniz-Institute for Prevention Research and Epidemiology – BIPS (BIPS) in Germany, the PHARMO Database Network in the Netherlands (PHARMO), and Caserta Local Health Unit (LHU) in Italy (University of Messina). In the M-PEM study, all patients who received a prescription from a general practitioner (GP) for dulaglutide (initiators) and for whom it was dispensed, were eligible for inclusion. The number of patients with type 2 diabetes mellitus (T2DM) were 13651, 296, 671 and 7289 in the BIPS, PHARMO, Messina and M-PEM cohorts, respectively.

Variables

Variables included demographic data, indication for treatment, selected treatment details, selected medical history and medication use prior to or present at index date and clinical events of medical interest. Outcomes of interest and potentially relevant co-variates were defined in the three databases using appropriate diagnostic codes. For the M-PEM study, these were captured from Data Collection Forms (DCFs) sent to prescribers 12 months after the first dulaglutide prescription. In the three other databases, the average frequency of dulaglutide prescriptions per week over the given time period was calculated. This calculation was used as a rough surrogate to estimate potential medication errors of > 1 injection per week across these databases.

Results

The main analysis was conducted on patients with reported diagnosis of T2DM from these data sources.

Across these four data sources, the incident risk of acute pancreatitis (amongst patients with no prior history of acute pancreatitis) ranged from 0.1% (95% CI 0.0-0.2, M-PEM) to 0.3% (95% CI 0.0-1.1, Messina).

The number of reported events of hypersensitivity in the first two weeks after starting dulaglutide were small, and the incident risk in each data source did not exceed 0.3% (CI 0.0-1.9). Similarly, small number of patients had reports of gastrointestinal effects (gastrointestinal stenosis, obstruction, or delayed gastric emptying); the risk in each data source did not exceed 0.1% (CI 0.0-0.2).

The estimated incident risk of arrhythmia ranged from 0.2% (95% CI 0.2-0.4, BIPS cohort) to 0.5% (Messina, M-PEM cohorts), [0.5%; 95% CI 0.1-1.4], and [0.5%; 95% CI 0.4-0.7], respectively).

A calculated average frequency of two or more dulaglutide prescriptions/ dispensings per week in the three databases was identified in <0.1%, and 1.4% of patients in BIPS and PHARMO cohorts, respectively. More than once weekly prescription/ dispensing of dulaglutide was described for 0.2% of the patients in the M-PEM cohort (collected on the DCFs).

Prevalence estimates for pancreatic and thyroid cancer in the BIPS-cohort were 0.1% (95% CI 0.1-0.2) and 0.3% (95% CI 0.2-0.4) respectively, and prevalence estimate amongst the M-PEM-cohort for pancreatic cancer was 0.1% (95% CI <0.1-0.2). Only two cases of thyroid cancer were reported in the M-PEM cohort, resulting in a prevalence of less than 0.1%. There were no cases identified in the PHARMO and Messina cohorts.

Discussion and Conclusion

The majority of patients in this PASS programme were being prescribed dulaglutide according to its licenced indication, and risk estimates for the medical conditions of interest, including acute pancreatitis, were generally in line with known information about dulaglutide.