Association between glucagon-like peptide 1 receptor agonist (GLP1-RA) and sodium glucose co-transporter 2 inhibitor (SGLT2i) use and COVID-19 outcomes: A national retrospective cohort study

First published: 01/11/2020

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Study Planned

Administrative details

EU PAS number

EUPAS37860

Study ID

40044

DARWIN EU® study

No

Study countries

☐ United States

Study description

Emerging evidence from the COVID-19 pandemic suggest that patients with type 2 diabetes comprise a significant portion of the affected population and are at higher risk for severe outcomes including hospitalization and death, yet it remains largely unknown how pre-morbid medication may impact outcomes of COVID-19 in patients with type 2 diabetes. Several medications have biologically plausible mechanisms with relevance for patients with diabetes among others including ACE inhibitors, metformin, and DPP4-inhibitors. Recent large cardiovascular outcome trials and subsequent metanalyses have demonstrated that some glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose-linked cotransporter 2 inhibitors (SGLT2i) are associated with a reduction of cardiovascular events and all-cause mortality among the same high-risk populations who show higher susceptibility to severe COVID-19 and increased mortality. Yet, no studies have examined the class effect of these newer anti-hyperglycemic of mortality and other outcomes in the setting of COVID-19 infection. These data are critical because therapeutics represent a highly actionable intervention point to improve outcomes from both the inpatient and outpatient setting for a large population of patients with inherently high risk for COVID-19 associated mortality. To address this gap and inform evolving care guidelines for patients with medication-managed type 2 diabetes during the COVID-19 pandemic, this study aims to characterize the association of use of GLP1-RA and SLGT2i with COVID-19 outcomes using real world data from the National COVID Cohort Collaborative (N3C). We will consider the well-studied and commonly used class of dipeptidyl peptidase-4 inhibitors (DPP4i) as the active comparator drug to avoid confounding by indication.

Study status

Planned

Research institutions and networks

Institutions

University of North Carolina at Chapel Hill

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Institution

Networks

National COVID Cohort Collaborative (N3C)

Contact details

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Primary lead investigator

John Buse

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 01/06/2020

Study start date
Planned: 01/06/2020

Date of final study report
Planned: 01/04/2020

Sources of funding

- Other

More details on funding

National Institutes of Health (National Center for Advancing Translational Sciences)

Study protocol

N3C_DM_Meds_Covid_Outcomes_Protocol_301020_Locked.pdf(166.17 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Main study objective:

This study aims to characterize the association of use of GLP1-RA and SLGT2i with COVID-19 outcomes among adults with diabetes and COVID-19 infection, using real world data from the National COVID Cohort Collaborative (N3C).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A10BJ) Glucagon-like peptide-1 (GLP-1) analogues

Glucagon-like peptide-1 (GLP-1) analogues

(A10BK) Sodium-glucose co-transporter 2 (SGLT2) inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

(A10BH) Dipeptidyl peptidase 4 (DPP-4) inhibitors

Dipeptidyl peptidase 4 (DPP-4) inhibitors

Medical condition to be studied

Diabetes mellitus

COVID-19

Population studied

Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

5000

Study design details

Outcomes

The outcome is 60-day mortality following a COVID-19 diagnosis. Secondary outcomes will include markers of illness severity including hospital admission and level of respiratory support required.

Data analysis plan

The aim of the analysis is to estimate the relative odds of mortality 60 days following a COVID-19 diagnosis for patients with type 2 diabetes and a history of SGLT2i/GLP1-RA use vs DPP4i use among eligible patients with COVID-19 in the N3C database. The primary estimand is the odds of mortality following 60 days from diagnosis with COVID-19. The ratio of the odds (OR) between the two drugs will be estimated using targeted maximum likelihood estimation (TMLE).

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Disease registry

Other

Data sources (types), other

Prospective patient-based data collection

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No