Comparison of the Risk of Acute Liver Injury Between Patients With Type 2 Diabetes Exposed to Dapagliflozin and Those Exposed to Other Antidiabetic Treatments

First published: 15/01/2016

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS12110

Study ID

50493

DARWIN EU® study

No

Study countries

- [ ] United Kingdom
- [ ] United States

Study description

The overall goal of this research study is to estimate the risk of hospitalization for acute liver injury in patients who are prescribed dapagliflozin compared to patients prescribed other specific oral antidiabetic drugs. Dapagliflozin and other antidiabetic drugs are used to treat type 2 diabetes mellitus. Because of the mechanism of action for dapagliflozin and results from small safety monitoring studies, there is interest in further evaluating the safety of dapagliflozin in large populations. The study will be implemented in three administrative health care data sources in two countries: in the United Kingdom, the Clinical Practice Research Datalink (CPRD), and in the United States, the Centers for Medicare and Medicaid Services (CMS) Medicare databases and the HealthCore Integrated Research Database (HIRDSM). Individuals in the databases will be included in the study if they meet the following age criteria, 18 years and older (CPRD and HIRD), or 65 years or older (Medicare), and if they did not have type 1 diabetes, are new users of one of the study drugs and meet the criteria of at least 180 days of electronic data before their first prescription of the study drug. The study period starts July 1, 2013 in CPRD and January 9, 2014 in the United States data sources, and will end at the latest available data at each database at the time of analysis.

Study status

Finalised

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)

- [ ] France
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom
- [ ] United Kingdom (Northern Ireland)
- [ ] United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | ENCePP partner

RTI Health Solutions (RTI-HS)

- [ ] France
- [ ] Spain
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- [ ] United States

First published: 21/04/2010

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Institution | Not-for-profit | ENCePP partner

Healthcore United States

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Catherine Johannes

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 12/02/2015

Actual: 12/02/2015

Study start date

Planned: 29/01/2016

Actual: 02/02/2016

Date of interim report, if expected

Planned: 30/12/2016

Actual: 22/11/2016

Date of final study report

Planned: 30/11/2020

Actual: 23/12/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Astra Zeneca

Study protocol

DAPA ALI Protocol_ final 23 June 2014_redacted.pdf (1.15 MB)

DAPA ALI_Protocol_Revisions 28Feb2017_redacted.pdf (1.26 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Other study registration identification numbers and links

D1690R00005

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

To compare, by insulin use at the index date, the incidence of hospitalization for acute liver injury (ALI) among patients with type 2 diabetes mellitus who are new users of dapagliflozin to those who are new users of ADs in classes other than sodium-glucose cotransporter 2 (SGLT2) inhibitors, insulin monotherapy, metformin monotherapy, or sulfonylurea monotherapy.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

XIGDUO

Medicinal product name, other

Farxiga

Study drug International non-proprietary name (INN) or common name

DAPAGLIFLOZIN

Anatomical Therapeutic Chemical (ATC) code

(A10BD14) metformin and repaglinide

metformin and repaglinide

Medical condition to be studied

Acute hepatic failure

Population studied

Short description of the study population

The study focused on risk of acute liver injury in patients with type 2 diabetes aged 18 years or more exposed to dapagliflozin and other antidiabetic (ADs) treatments identified from CPRD, HIRD and Medicare database in the US.
Inclusion criteria:
(1) receive newly prescribed dapagliflozin (with or without other ADs) or a newly prescribed AD (with or without other ADs) in a class other than SGLT2 inhibitors, insulin monotherapy, metformin monotherapy, or sulfonylurea monotherapy;
(2) do not have evidence of type 1 diabetes;
(3) are aged 18 years or older at the index date for CPRD patients, 18-64 years for HIRDSM patients, or 65 years or older for Medicare patients; and
(4) have been enrolled in the data source for at least 180 days before the first

prescription or dispensing for dapagliflozin or comparator AD.

Exclusion criteria:
Patients with a previous diagnosis of ALI; liver, biliary, or pancreatic disease; hepatobiliary or pancreatic neoplasm; or congestive heart failure will be excluded.

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)

Special population of interest

Other

Special population of interest, other

Patients with type 2 diabetes mellitus

Estimated number of subjects

459636

Study design details

Outcomes

acute liver injury

Data analysis plan

Descriptive statistics will be calculated to compare baseline characteristics at cohort entry between dapagliflozin users versus comparator antidiabetic users. Propensity scores will be estimated by using logistic regression, with measured potential predictors of acute liver injury as independent variables in the regression model and actual exposure group (dapagliflozin or comparator) as the outcome. Incidence rates of acute liver injury will be estimated during exposure time at risk for dapagliflozin initiators and comparators. Unadjusted incidence rate ratios (IRRs) of the outcome of interest with 95% confidence intervals in dapagliflozin users versus other AD users will be calculated, and adjusted using propensity score–stratified analysis. Analyses will be conducted in each data source separately, and a pooled estimate will be calculated if deemed appropriate.

Documents

Study results

0304030_Dapa ALI Final Report_Final_9Nov2020_Abstract_Redacted.pdf (185.54 KB)

Study publications

Danysh HE, Johannes CB, Beachler DC, Layton JB, Ziemiecki R, Arana A, Dinh J, L…

Johannes C, Layton JB, Beachler DC, Ziemiecki RM, Li L, Danysh HE, Dinh J, Hunt…

Johannes C, Beachler D, Ziemiecki R, Yin R, McGrath L, Jemison J, Lanes S, Gils…

Layton JB, Zhou CK, Danysh HE, Beachler DC, Ziemiecki R, Dinh J, Yin R, Calinga…

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 source(s)

Clinical Practice Research Datalink

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Electronic healthcare records (EHR)

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