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

First published: 15/01/2016

Last updated: 16/04/2026

Study Finalised

Administrative details

EU PAS number

EUPAS12116

Study ID

49352

DARWIN EU® study

No

Study countries

- ☐ Netherlands
- ☐ United Kingdom
- ☐ United States

Study description

This is a multinational cohort database study to estimate the incidence of female breast cancer and bladder cancer, by insulin use at cohort entry, 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 a large populations.

The study will be implemented in four administrative health care data sources in three countries: in the United Kingdom, the Clinical Practice Research Datalink (CPRD), in the United States, the Centers for Medicare and Medicaid Services (CMS) Medicare databases and the Healthcare Integrated Research Database (HIRD), and, in the Netherlands, the PHARMO Database Network.

Individuals in the databases will be included in the study if they meet the following age criteria, 40 years or older (CPRD and PHARMO), 40 to 64 years (HIRD) or 65 years or older (Medicare), and if they did not have type 1 diabetes, were treated with 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 November 13, 2012 in CPRD, November 1, 2013 in PHARMO 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

HealthCore

First published: 01/02/2024

Last updated: 01/02/2024

Institution

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

- [ ] Netherlands

First published: 07/01/2022

Last updated: 19/12/2025

Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Planned: 12/02/2015

Actual: 12/02/2015

Study start date

Planned: 29/01/2016

Actual: 01/02/2016

Date of interim report, if expected

Planned: 30/12/2016

Actual: 22/11/2016

Date of final study report

Planned: 31/12/2025

Actual: 12/12/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Astra Zeneca

Study protocol

DAPA Protocol MB102118_Cancer_ 27June 2014_final_redacted.pdf (852.94 KB)

Dapa Cancer Protocol MB102118__v3.1_06Jun2023_final_signed_Redacted.pdf (6.69 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

NCT02695121

Link to Clinicaltrials.gov

Methodological aspects

Study topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Cohort study with an active-comparator, new-user design.

Main study objective:

To compare, among patients with type 2 diabetes, who are new users of dapagliflozin and patients who are new users of ADs (1) the incidence of invasive breast cancer and (2) the incidence of in situ and invasive bladder cancer.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

FORXIGA

XIGDUO

Medicinal product name, other

Farxiga, Xigduo XR

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

DAPAGLIFLOZIN

Anatomical Therapeutic Chemical (ATC) code

(A10BD15) metformin and dapagliflozin

metformin and dapagliflozin

(A10BD21) saxagliptin and dapagliflozin

saxagliptin and dapagliflozin

(A10BD25) metformin, saxagliptin and dapagliflozin

metformin, saxagliptin and dapagliflozin

(A10BK01) dapagliflozin

dapagliflozin

Medical condition to be studied

Breast cancer

Bladder cancer

Population studied

Short description of the study population

Patients newly initiating dapagliflozin (with or without concomitant use of any other antidiabetic drugs [AD]) or newly initiating an eligible comparator AD (with or without concomitant use of any other AD) during the study period,

evaluated for selection into the study cohorts individually for study from each data source.

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

1800000

Study design details

Setting

The study is being conducted in four population-based health care data sources:

• CPRD in the UK, specifically, CPRD GOLD

• PHARMO in the Netherlands

• The HIRD in the US

• Medicare in the US

Comparators

New users of ADs in classes other than SGLT2 inhibitors, insulin monotherapy, metformin monotherapy, or sulfonylurea monotherapy.

Outcomes

Primary outcomes: Female breast cancer and bladder cancer.

Secondary outcomes: Composite incidence of selected cancers among males

(prostate, colon/rectum, lung, stomach, non-Hodgkin lymphoma (NHL), and melanoma of skin) and among females (colon/rectum, lung, corpus uteri, ovary, stomach, NHL and melanoma of skin). Frequency of health care utilization measures during follow up.

Data analysis plan

Descriptive statistics will be calculated to compare baseline characteristics at cohort entry between dapagliflozin users versus comparator antidiabetic users separately for each outcome.

Propensity scores will be estimated by using logistic regression, with measured potential predictors of the cancer outcome as independent variables in the regression model and actual exposure group (dapagliflozin or comparator) as the outcome.

Incidence rates of each outcome will be estimated during exposure time at risk for dapagliflozin initiators and comparators.

Unadjusted incidence rate ratios (IRRs) of the outcomes 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 report

Dapa Cancer Final Study Report_12Dec2025_Redacted.pdf (12.56 MB)

Study, other information

Dapa Cancer Protocol MB102118_28Feb2017_redacted.pdf (899.62 KB)

Study publications

Gutierrez L, Beachler D, Overbeek J, McQuay L, Yin R, Kuiper J, McGrath L, Jemi…

Zhou CK, Dinh J, Danysh HE, Johannes C, Gutierrez L, Schmid R, Arana A, Kaye JA…

Gutierrez L, Danysh HE, Aguado J, Hunt PR, Kaye JA, Garcia-Albeniz X, Gilsenan …

Danysh HE, Gilsenan A, Beachler DC, Kaye JA, Garcia-Albeniz X, Schmid R, Hunter…

Dinh J, Danysh HE, Johannes C, Gutierrez L, Schmid R, Arana A, Kaye JA, Pladeva…

Danysh HE, Gilsenan A, Kaye JA, Garcia-Albeniz X, Schmid R, Bartsch J, Calingae…

Danysh HE, Khan AM, Daniels K, Gilsenan A, Beachler DC, Bartsch J, Quimbo T, Ga…

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

PHARMO Data Network

Data source(s), other

Healthcare Integrated Research Database

Medicare Research Database

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug prescriptions

Electronic healthcare records (EHR)

Pharmacy dispensing records

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after data extraction