# 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:** 06/05/2025

Study  Ongoing

## 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**

Ongoing

# 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:** 24/07/2024

**Institution** Laboratory/Research/Testing facility ENCePP partner

## Contact details

**Study institution contact**

Lia Gutierrez lgutierrez@rti.org

Study contact

[lgutierrez@rti.org](lgutierrez@rti.org)

**Primary lead investigator**

Lia Gutierrez 0000-0001-6280-1119

Primary lead investigator

**ORCID number:**

0000-0001-6280-1119

## 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

## 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 type

# Study type list

**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 insitu and invasive bladder cancer.

# Study Design

**Non-interventional study design**

Cohort

# Study drug and medical condition

**Name of medicine**

FORXIGA

XIGDUO

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**Name of medicine, other**

Farxiga, Xigduo XR

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

DAPAGLIFLOZIN

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**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

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**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.

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**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, 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...

# 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

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**Data characterisation moment**

after data extraction