

# Comparative risk of the incident cancer between histamine-2 receptor antagonists (Risk of cancer between H2RAs)

**First published:** 19/04/2021

**Last updated:** 23/04/2024

Study

Planned

## Administrative details

### EU PAS number

EUPAS38902

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### Study ID

42946

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### DARWIN EU® study

No

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### Study countries

- ☐ France
- ☐ Germany
- ☐ Korea, Republic of
- ☐ Spain

☐ United Kingdom

☐ United States

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## Study description

Dietary N-nitrosodimethylamine (NDMA) has been shown to be carcinogenic in animals, however, evidence from population-based studies is inconclusive. The U.S. Food and Drug Administration has issued a statement on ranitidine because they may contain unacceptable levels of NDMA in 2019. To date, there have been several studies regarding association between NDMA exposure and risk of cancer, however, real-world evidence of cancer risk in relation with ranitidine is scarce. We aim to evaluate the comparative risk of incident cancer in patients exposed to various H2 receptor antagonists (H2RAs). We will conduct systematic, multinational study to estimate the relative risk of primary outcome (overall cancer except non-melanoma skin cancer) and secondary outcomes (overall cancer, overall cancer except thyroid cancer, 16 types of cancer, and cancer mortality) in ranitidine cohort. We will compare the target cohort with the comparator cohort for the hazards of outcome during the time-at-risk by applying a Cox proportional hazards model after propensity score adjustment.

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## Study status

Planned

# Research institutions and networks

## Institutions

Yonsei University

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

**IQVIA**

☐ United Kingdom

**First published:** 12/11/2021

**Last updated:** 22/04/2024

**Institution**

**Non-Pharmaceutical company**

**ENCePP partner**

**Ajou University**

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

**IQVIA**

☐ United Kingdom

**First published:** 12/11/2021

**Last updated:** 22/04/2024

**Institution**

**Non-Pharmaceutical company**

**ENCePP partner**

NHIS South Korea, Hanyang University South Korea, Ajou University South Korea, Kangdong Sacred Heart Hospital South Korea, Columbia University US, Stanford University US, IQVIA US

## Contact details

### Study institution contact

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Study contact

[seng.chan.you@ohdsi.org](mailto:seng.chan.you@ohdsi.org)

### Primary lead investigator

Seng Chan You

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 01/01/2021

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### Study start date

Planned: 18/01/2021

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### Date of final study report

Planned: 01/11/2021

## Sources of funding

- Other

## More details on funding

Ministry of Health & Welfare, Republic of Korea. grant number: HI19C0143

## Study protocol

[H2RACancerRisk\\_Protocol\\_V0.5.pdf](#)(679.44 KB)

[H2RACancerRisk\\_Protocol\\_V0.5.1.pdf](#)(691.94 KB)

## Regulatory

### **Was the study required by a regulatory body?**

No

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

Non-EU RMP only

## Other study registration identification numbers and links

<https://github.com/ohdsi-studies/ranitidinecancerrisk>

## Methodological aspects

### Study type

### Study type list

**Study type:**

Non-interventional study

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**Scope of the study:**

Effectiveness study (incl. comparative)

**Main study objective:**

To generate evidence for comparative safety of incident cancer of ranitidine compared with other H2 blockers

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(A02BA) H2-receptor antagonists

H2-receptor antagonists

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**Medical condition to be studied**

Neoplasm malignant

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**Additional medical condition(s)**

The primary outcome was overall cancer except non-melanoma skin cancer.

The secondary outcomes were overall cancer, 16 subtypes of cancer.

## 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)

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## **Estimated number of subjects**

200000

# **Study design details**

## **Outcomes**

Occurrence of malignant neoplasm except non-melanoma skin cancer for the first time in the person's history, The secondary outcomes include overall cancer, 16 subtypes of cancer (lip, oral cavity and pharynx cancer, esophageal cancer, stomach cancer, colorectal cancer, liver cancer, pancreatic cancer, lung cancer, breast cancer, cervical cancer, uterine cancer, ovary cancer, prostate cancer, bladder cancer, leukemia, thyroid cancer, gall bladder and biliary tract cancer) and death

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## **Data analysis plan**

We use propensity score model to reduce potential confounding due to imbalance between the target and comparator cohorts in baseline covariates. The following covariates are used in the large-scale propensity score matching: demographics including age, gender and race, all recorded medication, medical history, exposed procedures, Charlson comorbidity index in the year prior to the index date in each database. We construct matched cohorts using 1:1 propensity score matching with a caliper of 0.2 on the logit scale. The

propensity scores were estimated by L1 regularized logistic regression, tuned by 10-fold cross validation. Cox proportional hazard models will be used to assess the hazard ratios with associated 95% confidence intervals (CIs) between the two cohorts using the CohortMethod R package (<https://github.com/OHDSI/CohortMethod>). Random-effect model meta-analysis will be performed to calculate summary hazard ratio for pooling effect estimates across databases.

## 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)

THIN® (The Health Improvement Network®)

The Information System for Research in Primary Care (SIDIAP)

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### Data source(s), other

THIN, SIDIAP

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### Data sources (types)

[Administrative healthcare records \(e.g., claims\)](#)

[Electronic healthcare records \(EHR\)](#)

## Use of a Common Data Model (CDM)



**CDM mapping**

No

Data quality specifications

**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

Data characterisation

**Data characterisation conducted**

No