Association between hydrochlorothiazide exposure and skin and lip cancer: a series of populationbased nested case-control studies

First published: 31/05/2018

Last updated: 12/03/2020

Study Finalised

Administrative details

EU PAS number

EUPAS24154

Study ID

34087

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

Observational studies to assess the association between hydrochlorothiazide exposure and lip cancer, non-melanoma skin cancer and melanoma skin cancer.

Study status

Finalised

Research institutions and networks

Institutions

European Medicines Agency (EMA)

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Daniel Morales

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 05/02/2018

Actual: 05/02/2018

Study start date
Planned: 05/02/2018

Actual: 05/02/2018

Date of final study report
Planned: 06/08/2018

Actual: 25/03/2019

Sources of funding

- EMA

Study protocol

EUPAS24154.protocol.pdf (65.08 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 topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Data collection methods:

Secondary use of data

Main study objective:

a) Assessing the association between hydrochlorothiazide exposure and each skin and lip cancer outcome using patients in THIN.b) Assessing if the association is influenced by adjusting for additional confounders such as smoking status and body mass index.

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C09DX01) valsartan, amlodipine and hydrochlorothiazide
valsartan, amlodipine and hydrochlorothiazide
(C09BX03) ramipril, amlodipine and hydrochlorothiazide
ramipril, amlodipine and hydrochlorothiazide
(C09DX03) olmesartan medoxomil, amlodipine and hydrochlorothiazide
olmesartan medoxomil, amlodipine and hydrochlorothiazide
(C03AX01) hydrochlorothiazide, combinations
hydrochlorothiazide, combinations
(C03EA01) hydrochlorothiazide and potassium-sparing agents
hydrochlorothiazide and potassium-sparing agents
(C03AB03) hydrochlorothiazide and potassium
hydrochlorothiazide and potassium
(C03AA03) hydrochlorothiazide
hydrochlorothiazide
(C09XA54) aliskiren, amlodipine and hydrochlorothiazide
aliskiren, amlodipine and hydrochlorothiazide
(C09XA52) aliskiren and hydrochlorothiazide
aliskiren and hydrochlorothiazide

Medical condition to be studied

Skin cancer

Population studied

Short description of the study population

Patients were required to have no previous cancer diagnosis before the index date, i.e. the date of the first skin cancer event occurring after cohort entry for case subjects. For the lip cancer and oral cavity cancer analysis, patients were allowed to have a prior history of nonmelanoma skin cancer (BCC or SCC), in

keeping with the Danish study. Patients were required to have no prior record of organ transplantation, human immunodeficiency virus diagnosis or use of immunosuppressant drugs such as azathioprine, cyclosporine or mycophenolate mofetil, at any time before the index date that may predispose to skin cancer risk.

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

50000

Study design details

Outcomes

1. Lip cancer2. Squamous cell carcinoma skin cancer3. Basal cell carcinoma skin cancer4. Melanoma

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Data analysis plan

Cases will be identified through Read codes recorded in THIN and the incidence of these conditions calculated among the population. Incidence density sampling will be used to randomly select controls to each matched on age, sex, general practice and follow up time and will repeated for each cancer case. Up to 100 controls will be selected for lip cancer and up to 20 controls for the other cancer outcomes. Odds ratios will be estimated for the association between ever use and cumulative use of hydrochlorothiazide exposure prior to the index

date, using a primary lag time of exposure of two years.

Documents

Study results

bcp.14245.pdf (279.11 KB)

Study publications

Morales DR, Pacurariu A, Slattery J, Kurz X. Association between hydrochlorothi…

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®)

Data sources (types)

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