VAG-4602: Vaginal estradiol tablets (Vagifem®) and endometrial cancer risk in the treatment of postmenopausal vaginal atrophy: A register-based cohort study in postmenopausal women

First published: 17/01/2022

Last updated: 15/01/2025

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/50379

EU PAS number

EUPAS44951

Study ID

50379

DARWIN EU® study

No

Study countries

☐ Denmark

☐ United States

Study description

The study will include data from a nationwide Danish cohort of postmenopausal women and the United States of America (US) cohort of postmenopausal women. The Danish nationwide cohort will be established through linkage of Danish national patient registries. The US cohort will be established based on data from US claims database, Truven. The aim of this study is to evaluate whether exposure to Vagifem® increases the rate of endometrial cancer in postmenopausal women.

Study status

Finalised

Research institutions and networks

Institutions

Novo Nordisk

First published: 01/02/2024

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Institution

North Zealand hospital Denmark, Truven Health MarketScan United States

Contact details

Study institution contact

Clinical Transparency (dept. 2834) Novo Nordisk A/S

Study contact

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Primary lead investigator

Clinical Transparency (dept. 2834) Novo Nordisk A/S

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 10/12/2021

Actual: 10/12/2021

Study start date

Planned: 31/05/2022

Actual: 15/01/2022

Date of final study report

Planned: 31/12/2023

Actual: 04/03/2024

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Novo Nordisk A/S

Study protocol

VAG-4602 16-1-01 protocol eu-pas-reg redacted.pdf(616.05 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 type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Main study objective:

The aim of this study is to evaluate whether exposure to Vagifem® increases the rate of endometrial cancer in postmenopausal women.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

Vagifem, Other LDVE product

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

ESTRADIOL

Anatomical Therapeutic Chemical (ATC) code

(G03CA03) estradiol

estradiol

Population studied

Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Estimated number of subjects

500000

Study design details

Outcomes

The primary objective is to investigate the hypothesis that there is no difference in risk of endometrial cancer between women using low dose vaginal estrogens (LDVE) (split into Vagifem® and other LDVE products) and women using no hormone replacement therapy to manage symptoms related to the postmenopausal phase. The secondary objective is to compare the rate of endometrial cancer for women exposed to Vagifem® 10 mcg and 25 mcg, respectively, with women that have been exposed to systemic cyclic HRT (defined as estrogen taken daily and progestogen taken in a cyclic pattern for 10 to 14 days of the month) or oral, transdermal and opposed injectable systemic HRT products.

Data analysis plan

The main statistical analysis will compare patients initiating LDVE (new users), split into Vagifem® and other LDVE, in the study period in a 1:2 ratio with non-users, in an intention to treat fashion, i.e. the patient will be considered at risk after initiation of treatment regardless of treatment discontinuation. Propensity score matching methods will be employed involving the available risk factors, including previous use of HRT. The IR and the 95% confidence intervals will be presented both for the exposure groups and the comparator group. Hazard

Ratio and 95% confidence interval will be estimated using a Cox proportion hazard rate model. For the secondary objective, the same methods will be used, with users of systemic cyclic HRT and oral, transdermal and opposed injectable systemic HRT products in the comparator group rather than non-users. A range of sensitivity analyses will be performed.

Documents

Study report

4602 nsr eu-pas-reg redacted.pdf(1.28 MB)

Data management

Data sources

Data source(s)

Danish registries (access/analysis)

Data source(s), other

Truven health marketscan United States

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Other

Data sources (types), other

Prescription event monitoring

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