Observational Study Description H6D-MC-LVHQ(b) A Prospective Case-Crossover Study to Evaluate the Possible Association Between the Use of PDE5 inhibitors and the Risk of Acute Nonarteritic Anterior Ischaemic Optic Neuropathy (NAION)

First published: 13/04/2017

Last updated: 30/03/2024

Study Finalised

Administrative details

EU PAS number

EUPAS13266

Study ID

18651

DARWIN EU® study

No

Study countries

United States

Study description

This is an observational multicentre, case-crossover study design to evaluate the possible association between PDE5 inhibitor exposure and the risk of acute NAION in adult males. All subjects included in the analysis populations had adjudication-confirmed NAION and intermittent PDE5 inhibitor use. A subject was considered an exposed case if their exposure occurred in the predefined time period immediately preceding NAION symptom onset (hazard period). The remaining time was the control period, that time in which exposure occurred without subsequent NAION onset. The exposure window was defined as 5 times the half-life of the PDE5 inhibitor (4 days for tadalafil and 1 day for sildenafil and vardenafil). In the primary analysis, the person-time method was used to calculate a Mantel Haenszel rate ratio for the risk of NAION, comparing PDE5 inhibitor exposure in the 30 days before NAION onset by exposed case definition (ie, exposure within the hazard period). Secondary analyses conducted as part of this study evaluated the Mantel Haenszel rate ratio for person-time for NAION comparing PDE5 inhibitor exposure in the 12 months before NAION onset by exposed case definition. A matched interval analysis method was also conducted assessing PDE5 inhibitor exposure occurring in the hazard periods and matched control periods during the 42 days prior to the acute NAION onset.The study did not examine the risk of NAION in association wtih any particular PDE5 inhibitor individually, therefore results can be considered applicable to the class.

Study status

Finalised

Research institutions and networks

Institutions

Syneos Health

United Kingdom

First published: 23/04/2015

Last updated: 06/03/2024

Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Eva Flahavan

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 02/12/2009

Study start date

Planned: 19/04/2010

Actual: 05/05/2010

Date of final study report

Planned: 18/05/2016

Actual: 26/05/2016

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Eli Lilly and Company

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

https://clinicaltrials.gov/show/NCT01131104

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Primary data collection

Main study objective:

The objective of this noninterventional, case-crossover, observational study was to evaluate whether there is a possible association between exposure to PDE5 inhibitors and the risk of acute NAION in adult males.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Case-crossover

Study drug and medical condition

Medicinal product name

CIALIS

LEVITRA

VIAGRA

Medical condition to be studied

Optic ischaemic neuropathy

Optic neuropathy

Optic neuritis

Population studied

Short description of the study population

Adult subjects from US who experienced abrupt visual loss (defined as visual loss typically occurring during less than a 1-day period or visual loss noted upon awakening) in one eye and presented to an ophthalmologist within 45 days of onset of NAION symptoms for an initial visit that resulted in a diagnosis of suspected NAION by the investigator.

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

350

Study design details

Outcomes

The primary objective of this case-crossover study examined the rate of acute NAION occurring in patients with PDE5 inhibitor exposure in the hazard periods (immediately preceding NAION onset) compared with exposure occurring over the 30 days before NAION onset, expressed as a Mantel Haenszel rate ratio for person-time. Secondary analyses included (1) a person-time analysis evaluating acute NAION occurring in patients with PDE5 inhibitor exposure in the hazard periods compared with exposure over the 12 months prior to NAION onset, and (2) a matched interval analysis method assessing PDE5 inhibitor exposure during hazard periods and matched controlled periods the 42 days prior to NAION onset.

Data analysis plan

This case-crossover study was conducted to evaluate the possible association between PDE5 inhibitor exposure and the risk of acute NAION in adult males. Exposure was based on the PDE5 inhibitor effect period (5 times the half-life). The primary analysis used the person-time method, including subjects with adjudication-confirmed NAION who had intermittent exposure to PDE5 inhibitors. In this analysis, a Mantel Haenszel rate ratio for the risk of NAION was calculated, comparing PDE5 inhibitor exposure in the 30 days before NAION onset by exposed case definition (ie, exposure within the hazard period). A secondary analysis, using the person-time method examined this risk using PDE5 inhibitor exposure over the 12 months prior to NAION onset. Other secondary analyses, used the matched interval method to evaluate the association between PDE5 inhibitor exposure in the 42 days prior to acute NAION, evaluated using a 4-day hazard period and a series of 4 preceding 4-day control intervals.

Documents

Study results

LY450190 H6D-MC-LVHQ PASS full CSR redacted.pdf (3.79 MB)

Study publications

Flahavan EM, Li H, Gupte-Singh K, Rizk RT, Ruff DD, Francis JL and Kinchen KS. ...

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 sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

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

Unknown