116239 - An observational cohort study to assess the risk of autoimmune diseases in adolescent and young adult women aged 9 to 25 years exposed to Cervarix® in the United Kingdom

First published: 27/09/2013

Last updated: 01/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS4584

Study ID

31665

DARWIN EU® study

No

Study countries

United Kingdom

Study description

This is an observational cohort study to assess the risk of autoimmune disease(s) within 12 months of receiving the first dose of Cervarix® in the exposed cohort and over a comparable period in the unexposed cohorts.This is an alternative study by GSK using the CPRD database in the UK to fulfil the US FDA safety commitment (evaluate the incidence of new neurological and eye-related autoimmune diseases and other pre-specified autoimmune diseases in subjects receiving Cervarix® in the US). Because of the very low Cervarix® uptake in the US, the observational GSK study to address this commitment is due to be stopped, as it will take too long to recruit the target subjects. The UK has had sufficient Cervarix® vaccination coverage during the period mid-September 2008 to 2011 to allow suitable data to be collected.Four cohorts will be defined based on exposure to Cervarix and sex as recorded in the CPRD GOLD data source:1. Cervarix vaccinated (exposed) female cohort2. Unexposed historical female cohort3. Unexposed concurrent male cohort4. Unexposed historical male cohortNOAD represent a heterogeneous group of diseases with different clinical conditions and disease progression. Some NOAD present with a chronic disease pattern of relapse over time e.g. multiple sclerosis or systemic lupus erythematous, or an acute disease pattern (e.g. Guillain Barré Syndrome).In addition to the comparison of the exposed vs. non exposed cohort (cohort design), the confirmed NOAD in the exposed cohort will also be analysed using a self-control case series (SCCS) analysis.In the cohort design, specified NOAD will be collected over a period of one year following the administration of at least one dose of Cervarix in an exposed cohort and over a comparable period in the unexposed cohorts.The unexposed male cohorts will be enrolled in order to assess a possible change over time in the incidence rate of NOAD in CPRD GOLD independent of Cervarix introduction.

Study status

Finalised

Research institutions and networks

Institutions

Clinical Practice Research Datalink (CPRD)

United Kingdom

First published: 15/03/2010

Last updated: 17/01/2025

Institution | Laboratory/Research/Testing facility | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Call Center EU Clinical Trials

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 19/07/2013

Study start date
Actual: 28/10/2013

Data analysis start date
Actual: 26/08/2014

Date of final study report
Actual: 23/03/2015

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GlaxoSmithKline

Study protocol

EPI-HPV-040 VS UK (116239) Protocol (FDA - EMA PASS) (09-Jul-2013)_PASS Registry.pdf (654.31 KB)

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)

Methodological aspects

Study type

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:

Secondary use of data

Main study objective:

To assess the risk of neuroinflammatory/ophthalmic new onset of autoimmune disease(s) (NOAD) and other pre-specified NOAD within 12 months following the administration of the first dose of Cervarix.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Self-controlled case series

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J07BM02) papillomavirus (human types 16, 18)

papillomavirus (human types 16, 18)

Medical condition to be studied

Autoimmune disorder

Population studied

Short description of the study population

Inclusion criteria for the exposed female cohort : Exposed females must satisfy ALL the following criteria at study entry

• Female aged from 9 to 25 years at the reference date (01 September 2008 through 31 August 2010)

• Recorded in the CPRD GOLD for at least 12 months before the reference date

• The first dose of Cervarix received between 01 September 2008 through 31 August 2010, Full date (day/month/year) of Cervarix vaccination(s) available

• Subject defined as acceptable in CPRD GOLD

Inclusion criteria for the unexposed historical female cohort: Unexposed females must satisfy ALL the following criteria at study entry

• Female aged 9 to 25 years at the reference date (01 September 2005 through 31 August 2007)

• Recorded in the CPRD GOLD for at least 12 months before the reference date

• Subject defined as acceptable in CPRD GOLD

Inclusion criteria for the unexposed concurrent male cohort: Unexposed concurrent males must satisfy ALL the following criteria at study entry

• Male aged 9 to 25 years at the reference date (01 September 2008 through 31 August 2010)
• Recorded in the CPRD GOLD for at least 12 months before the reference date
• Subject defined as acceptable in CPRD GOLD

Inclusion criteria for the unexposed historical male cohort: Unexposed historical males must satisfy ALL the following criteria at study entry
• Male aged 9 to 25 years at the reference date (01 September 2005 through 31 August
2007)
• Recorded in the CPRD GOLD for at least 12 months before the reference date
• Subject defined as acceptable in CPRD GOLD

Age groups

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- Adults (18 to < 46 years)

Estimated number of subjects

1.053

Study design details

Outcomes

Occurrence of new onset of confirmed autoimmune disease during the period of one year following administration of the first dose of Cervarix (risk period) among an exposed cohort and during an equivalent time period in the unexposed cohorts for the following two co-primary composite endpoints:1 Neuroinflammatory/ophthalmic autoimmune diseases2 Other autoimmune

diseases, Occurrence of new onset of individual confirmed autoimmune disease within 2 months (Guillain Barré syndrome and autoimmune haemolytic anaemia), within 6 months (idiopathic thrombocytopenic purpura) and within 1 year (e.g. multiple sclerosis, transverse myelitis, optic neuritis, other demyelinating diseases, auto-immune uveitis) following the administration of the first dose of Cervarix.

Data analysis plan

Incidence rates for NOAD will be calculated as the number of cases divided by person-time. A Poisson regression model will estimate the exposed/unexposed risk ratio and its 95% confidence interval. The Poisson model will include the number of cases in each cohort as the dependent variable, the exposure status as a binary independent variable and the log-transformed total person-year as an offset. The same statistical model will be used to compare the two cohorts.The cases of NOAD in exposed subjects will be analysed using Self-control case-series (SCCS) methods.

Documents

Study results

gsk-116239-clinical-study-report_1-redact.pdf (1.12 MB)

Study report

gsk-116239-clinical-study-report_2-redact.pdf (1.52 MB)

gsk-116239-clinical-study-report_3-redact.pdf (1.6 MB)

gsk-116239-clinical-study-report_4-redact.pdf (1.97 MB)

Study, other information

gsk-116239-clinical-study-report_3-redact.pdf (1.6 MB)

gsk-116239-clinical-study-report_4-redact.pdf (1.97 MB)

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), other

Clinical Practice Research Datalink General Practitioner OnLine Database (CPRD GOLD) United Kingdom

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