Post-licensure observational safety study after meningococcal B vaccine 4CMenB (Bexsero®) vaccination in routine UK care

First published: 30/11/2015

Last updated: 26/03/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/41061

EU PAS number

EUPAS11728

Study ID

41061

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

The objective is to assess the safety of 4CMenB vaccination within the UK National Immunisation program (NIP). The study design is an observational descriptive study followed by a comparative self-controlled case series (SCCS) for primary outcomes based on THIN database of UK primary care records. The primary outcomes are seizures (all and febrileseizures), and Kawasaki disease. Acute disseminated encephalomyelitis (ADEM), Guillain-Barré syndrome (GBS), and anaphylaxis are secondary outcomes. The exposure of interest is meningococcal B vaccine 4CMenB (Bexsero®). The incidence of each outcome will be estimated during an outcome specific post-exposure risk period. The incidence after any immunisation dose in total and after each immunization dose (recommended as 2, 4 and 12-13 months) will be estimated. The risk period is the time frame when an outcome might be expected to occur if it was caused by the exposure based on known mechanisms, published studies or case reports. A plot will be produced to show the temporal distribution of episodes of outcomes around the date of the exposure.Relative incidence and 95% confidence intervals will be estimated using the self-controlled case series (SCCS) method. Within the SCCS, person time and outcomes for each individual will be assigned to the outcome specific post-exposure risk period or a control period outside this time. A relative incidence will then be calculated.

Study status

Finalised

Research institutions and networks

Institutions

Gillian Hall

United Kingdom

First published: 01/04/2022

Last updated: 05/04/2022

Institution | Other | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Gillian Hall

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 11/11/2014

Actual: 02/11/2011

Study start date

Planned: 31/12/2015

Actual: 08/12/2015

Date of interim report, if expected
Planned: 31/12/2017

Actual: 30/01/2018

Date of final study report
Planned: 12/06/2020

Actual: 12/03/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GSK Vaccines s.r.l.

Study protocol

V72_36OB-04 Trial Registration Form-ENCePP Registration-2015-08-24-76747267.pdf(966.42 KB)

V72_36OB-04 Revised Protocol-v3-2015-11-13-77293343 pdf.pdf(556.43 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:

Combined primary data collection and secondary use of data

Main study objective:

The objective is to assess the safety of 4CMenB vaccination within the UK National Immunisation program.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Self-controlled case series

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J07AH09) meningococcus B, multicomponent vaccine

meningococcus B, multicomponent vaccine

Medical condition to be studied

Seizure

Febrile convulsion

Acute disseminated encephalomyelitis

Guillain-Barre syndrome

Anaphylactic reaction

Kawasaki's disease

Population studied

Short description of the study population

The baseline population will be those children permanently registered at a UK primary care practice which contributes data to The Health Information Network (THIN) database between a start date and an end date (observation period). The start date for each child will be the most recent of 1st May 2015 (earliest data included), date of birth plus one month, or transfer from another practice plus three months. The first month of life is not included as part of this time is usually spent in secondary care. The three months after transfer in is not included so that prevalent events recorded at a registration visit during this period are not mistaken for incident episodes. The end date will be the earliest of date of birth plus 18 months, transfer out of the practice, last data collection or the study end.

There are no exclusion criteria.

Descriptive analysis – The study population will be all children in the baseline population who receive one or more vaccination with 4CMenB in their observation period.
SCCS – For both primary outcomes the study population will be children in the baseline population who had a diagnosis of that outcome and had received at least one dose of 4CMenB vaccine.

Age groups

Preterm newborn infants (0 – 27 days)
Term newborn infants (0 – 27 days)
Infants and toddlers (28 days – 23 months)

Estimated number of subjects

70000

Study design details

Outcomes

Seizures (all and febrile seizures) and Kawasaki disease. Acute disseminated encephalomyelitis, Guillain-Barré syndrome, and anaphylaxis

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Data analysis plan

A post-exposure risk period has been assigned for each outcome as the time following vaccination during which an outcome would be expected to occur if it were caused by the vaccination. The incidence of each outcome in the post-exposure risk periods will be estimated for all vaccination doses and each dose. Plots will be produced for outcomes with at least one event to show the temporal distribution around exposure. Age-sex distributions will be reported. The self-controlled case series will analyse the primary outcomes of seizures and KD (first episodes). GBS, ADEM and anaphylaxis will be analysed if

sufficient events are observed in the risk period to provide 80% power, relative incidence of 10. All exposures to 4CMenB will be treated as equivalent risk periods. Outcomes and person-time during pre-defined pre-exposure periods will be excluded from baseline and analysed as a separate risk window.SCCS subgroup and sensitivity analyses have been outlined in a Statistical Analysis Plan.

Documents

Study results

EPI-MENB REC 2ND GEN (V72)-007 EPI VS GB DB (205512) V72_36OB (205512) Redacted Report (20-Feb-2020).pdf(2.33 MB)

Study publications

Hall, G. C., Douglas, I., Heath, P. T., Prabhakar, P., Rosillon, D., Khan, J. e...

Data management

Data sources

Data source(s)

THIN® (The Health Improvement Network®)

Data sources (types)

Electronic healthcare records (EHR)

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

No