Risk of Febrile Convulsions after a Second Immunization against Measles, Mumps and Rubella with MMRV as compared to MMR or MMR+V (MMRV 2nd dose)

First published: 24/02/2014

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS5899

Study ID

29012

DARWIN EU® study

No

Study countries

☐ Germany

Study description

The German Standing Vaccination Committee (STIKO) recommends vaccination against measles, mumps, rubella (MMR), and varicella (V) in all children at 11 to 14 months of age (1st dose) and revaccination at 15 to 23 months of age (2nd dose). In July 2006, the combined measles-mumps-rubella-varicella (MMRV) vaccine Priorix-Tetra® (GlaxoSmithKline) was licensed in Germany, which made simultaneous vaccination against all four infectious diseases possible. After licensure of the MMRV vaccine, studies on the safety of the vaccine have suggested an elevated risk for febrile convulsions (FC) in children vaccinated with a 1st dose of MMRV as compared to children vaccinated with separately administered MMR and V vaccines. Concerning the risk of FC after the 2nd dose of MMRV as compared with a 2nd dose of MMR or MMR+V, data was generally limited and no information was available for Germany, where the 2nd dose is recommended for relatively young children as compared to e.g. the US (recommendation for 2nd dose at the age 4 to 6 years). A retrospective matched cohort study was performed on the basis of statutory health insurance claims data from 2004 to 2008. For the determination of the risk of febrile seizures after administration of the 2nd dose of vaccination against measles, mumps and rubella (two doses are recommended at age 11-14 and 15-23 months in Germany), a total of 159,013 children were included in the study, of whom 50,350 (32%) had received the MMRV vaccine. Due to very low incidences of FC in the risk intervals under investigation, the power of the analyses was insufficient to draw reliable conclusions from the generated results and to exclude a risk of FC. Further analyses based on a larger sample size are planned.

Study status

Finalised

Research institutions and networks

Institutions

Leibniz Institute for Prevention Research and Epidemiology - BIPS

Germany

First published: 29/03/2010

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Institution | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Tania Schink

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 26/03/2013

Actual: 03/04/2013

Study start date
Planned: 01/01/2004

Actual: 01/01/2004

Data analysis start date
Planned: 01/04/2013

Actual: 01/04/2013

Date of final study report
Planned: 31/07/2013

Actual: 29/07/2013

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GlaxoSmithKline Biologicals SA

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

Not applicable

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:

Secondary use of data

Main study objective:

The objective of this study was to estimate the risk of febrile convulsions after a first dose vaccination with Priorix-Tetra® in comparison to first dose vaccination with MMR or MMR+V in the pre-specified risk intervals: 0-4 days after immunization, 5-12 days after immunization (main risk interval), 13-30 days after immunization, and the entire risk period, that is 0-30 days after immunization.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J07BD54) measles, combinations with mumps, rubella and varicella, live attenuated

measles, combinations with mumps, rubella and varicella, live attenuated

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Medical condition to be studied

Febrile convulsion

Population studied

Short description of the study population

All insurants born during the study period from January 1st, 2004 through December 31st, 2008, with available date of birth who received a 2nd vaccination with one of the index vaccines measles-mumps-rubella-varicella (MMRV), MMR+V, or MMR.

Age groups

- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)

Estimated number of subjects

159013

Study design details

Outcomes

The primary outcome of this study was the occurrence of febrile convulsions (FC) defined as hospitalization with a diagnosis of FC without any alternative

plausible cause of FC, e.g. an infection or neurological condition, coded as main discharge diagnosis. The secondary outcome was defined as closely as possible to the outcome-criteria specified by the previous study by Jacobsen et al. That is, only hospitalizations for FC with a neurological condition coded as main discharge diagnosis were excluded.

Data analysis plan

A retrospective matched cohort study was performed to provide risk estimates of FC after a 2nd dose of MMRV compared to MMR and MMR+V (index vaccines) in pre-defined risk intervals (RI). Insurants born from 01/01/2004 through 31/12/2008 who received a 2nd vaccination with one of the index vaccines were included in the cohort. Cumulative incidences were calculated. . Relative risks and risk differences for the comparison of exposure groups were calculated with 95% CIs. All children with a 2nd immunization with MMRV were matched 1:1 to children with a 2nd immunization with MMR or MMR+V by statutory health insurance, sex, age in months (± 1 month) and month of cohort entry (± 1 month).Multivariable analyses were performed, adjusted for FC history, hospitalization for an infectious disease, administration of other vaccines, type of 1st dose vaccine, time between 1st and 2nd dose to estimate ORs with 95% CIs using a separate binary logistic regression model for each RI.

Documents

Study results

Abstract.pdf (20.62 KB)

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)

German Pharmacoepidemiological Research Database

Data sources (types)

Administrative healthcare records (e.g., claims)

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