Risk of Febrile Convulsions after 1st dose MMRV vaccination in comparison to MMR and MMR+V vaccination (MMRV 1st dose)

First published: 24/02/2014

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS5896

Study ID

28996

DARWIN EU® study

No

Study countries

☐ Germany

Study description

In July 2006, Priorix-Tetra™, a combined measles-mumps-rubella-varicella (MMRV) vaccine, was licensed in Germany. Since a post-licensure study (Jacobsen et al., 2009) had shown a more than twofold elevated risk of febrile convulsions (FC) after first dose vaccination with the combined MMRV vaccine ProQuad® compared to separately administered MMR and V vaccines (MMR+V), a study investigating the risk of FC for Priorix-Tetra™ was requested by the Paul-Ehrlich Institute, the regulatory agency responsible for vaccine licensing and safety in Germany.A retrospective matched cohort study was performed to provide risk estimates of FC after a first dose of Priorix-Tetra™ (MMRV) compared to MMR and MMR+V in pre-defined risk intervals. All children born between 01.01.2004 and 31.12.2008 who received a first dose of MMRV vaccine were matched to children vaccinated with MMR, MMR+V and MMR or MMR+V, respectively, by sex, age, month of vaccination and statutory health insurance provider.The objective of this study was to estimate the risk of FC after a first dose vaccination with Priorix-Tetra™ compared to first dose vaccination with MMR or MMR+V vaccines 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 status

Finalised

Research institutions and networks

Institutions

Leibniz Institute for Prevention Research and Epidemiology - BIPS

Germany

First published: 29/03/2010

Last updated: 26/02/2024

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: 14/01/2011

Actual: 14/01/2011

Study start date

Planned: 01/01/2004

Actual: 01/01/2004

Data analysis start date
Planned: 14/01/2011

Actual: 14/01/2011

Date of final study report
Planned: 30/09/2011

Actual: 14/03/2012

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)?

EU RMP category 3 (required)

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

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Medical condition to be studied

Febrile convulsion

Population studied

Short description of the study population

All children born between 01.01.2004 and 31.12.2008 who received a first dose of MMRV vaccine were matched to children vaccinated with MMR, MMR+V and MMR or MMR+V, respectively, by sex, age, month of vaccination and statutory health insurance provider.

Age groups

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

Estimated number of subjects

286622

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 febrile convulsion after a first dose of Priorix-Tetra™ (MMRV) compared to MMR and MMR+V in pre-defined risk intervals according to the number of days after immunization (0-4, 5-12, 13-30, and the entire risk period (0-30)).Children born between 01.01.2004 and 31.12.2008 who received a first dose of MMRV were matched to children vaccinated with MMR, MMR+V and MMR or MMR+V, by sex, age, month of vaccination and health insurance provider.Cumulative incidences (=risks) of primary and secondary outcomes with 95% CIs were calculated for all exposure groups within each risk interval. Risk ratios and risk differences of the primary and secondary outcomes were calculated with 95% CIs. Confounder adjusted odds ratios with corresponding 95% CIs were estimated to compare the MMRV exposure group with each of the comparison exposure groups using a separate binary logistic regression model for each risk interval.

Documents

Study results

ShortReport_FCHistory_v1.1.pdf (103.99 KB)

Study_Summary_v1_0.pdf (48.52 KB)

Study publications

Schink T, Holstiege J, Kowalzik F, Zepp F, Garbe E. Risk of febrile convulsions...

Data management

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