Nested case-control study evaluating effectiveness of immunization of girls and women of childbearing potential with GARDASIL(TM)/GARDASIL(TM) 9 against juvenile-onset recurrent respiratory papillomatosis (JoRRP) in Sweden, Denmark, and Norway (V503-095)

First published: 23/08/2024

Last updated: 17/12/2024

Study Ongoing

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000286

EU PAS number

EUPAS1000000286

Study ID

1000000286

DARWIN EU® study

No

Study countries

- ☐ Denmark
- ☐ Norway
- ☐ Sweden

Study description

Recurrent respiratory papillomatosis (RRP) is a medical condition where HPV types 6 and 11 cause wart-like growths in the larynx. The condition is rarely fatal but associated with high morbidity. Current treatment only offers temporary symptomatic relief. There is an expectation that HPV vaccination of mothers, targeting types 6 and 11, will reduce incidence of RRP in their children.

The primary objective of this study is to assess if the odds of JoRRP are lower among children whose biologic mothers were fully vaccinated with GARDASIL/GARDASIL 9 at least one year prior to delivery versus unvaccinated mothers.

Study status

Ongoing

Research institutions and networks

Institutions

Merck & Co.

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Karolinska Institutet

Sweden

First published: 01/02/2024

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Institution | Educational Institution

Cancer Registry of Norway

Danish Cancer Society

Contact details

Study institution contact

Clinical Trials Disclosure Merck Sharp & Dohme LLC

Study contact

ClinicalTrialsDisclosure@merck.com

Primary lead investigator

Clinical Trials Disclosure Merck Sharp & Dohme LLC

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 23/11/2021

Study start date
Actual: 03/03/2023

Data analysis start date
Planned: 15/05/2025

Date of final study report
Planned: 15/10/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck Sharp & Dohme LLC

Study protocol

V503-095-00-v3-Protocol_final-redaction.pdf(675.47 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Population-based nested case-control study

Main study objective:

To assess if the odds of juvenile-onset recurrent respiratory papillomatosis (JoRRP) are lower among children whose biologic mothers were fully vaccinated with GARDASIL/GARDASIL 9 at least one year prior to delivery versus unvaccinated mothers.

Study Design

Non-interventional study design

Case-control

Other

Non-interventional study design, other

Population-based nested case-control

Study drug and medical condition

Name of medicine

GARDASIL

GARDASIL 9

Name of medicine, other

Gardasil 4

Anatomical Therapeutic Chemical (ATC) code

(J07BM01) papillomavirus (human types 6, 11, 16, 18)

papillomavirus (human types 6, 11, 16, 18)

(J07BM03) papillomavirus (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)

papillomavirus (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)

Medical condition to be studied

Respiratory papilloma

Additional medical condition(s)

juvenile-onset recurrent respiratory papillomatosis

Population studied

Short description of the study population

Inclusion Criteria:

-Birth cohorts 2008 to 2020
- The study subject (child) must be born and resident in Sweden, Denmark or Norway as defined through the Total Population Registry for their entire life.
- The study subject must be between 0 to 9 years of age
- The child's mother had the opportunity to be fully vaccinated with GARDASIL/GARDASIL 9 at least one year prior to delivery.

Exclusion Criteria:
- Children whose mother immigrated to Sweden, Denmark, or Norway both after 2006 and after age 9 years
- Adopted children, as the vaccination status of the actual, biological mother will be missing.
- Children whose mother received the bivalent vaccine Cervarix, since it provides no effectiveness against the causative HPV types (6 and 11) in RRP.
- Any child (case or control subject) who previously received any HPV vaccine

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Age groups

Paediatric Population (< 18 years)

Estimated number of subjects

200

Study design details

Setting

Nordic population, patient, and vaccine registries.

Comparators

Random selection of up to 100 controls per case from the underlying population at risk, using incidence density sampling procedures. Matching criteria will be age of mother (+/- 1 year), sex of child, calendar year of case diagnosis, and region where case was diagnosed.

Outcomes

A subject will be defined as having JoRRP if he/she has > or =1 hospitalization or outpatient record with diagnosis registered as D14.1, with appropriate topography/morphology codes (where possible to obtain from pathology/cancer registry), between 0-9 years of age

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Data analysis plan

Conditional logistic regression will be used for estimation of odds ratios (ORs) and corresponding 95% confidence intervals in the pooled analysis using 1-step approach, with adjustment for clustering and adjustment for relevant covariates; all measured with similar high accuracy in each country.

Data management

Data sources

Data source(s)

Landspatientregisteret (National Patient Register)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

The Cancer Registry of Norway

Norwegian Health Registers

Data source(s), other

Denmark Central Population Registry

Denmark Pregnancy/Birth Registry

Denmark Prescription Registry

Denmark- The National Health Insurance Service Registry

Denmark Family database

Statistics Denmark

Denmark Pathology Register

Sweden Total Population Registry

Sweden National Patient Registry

Sweden Medical Birth Registry

SVEVAC/National Vaccination Registry

Sweden Multi-generation registry

LISA (Swedish Longitudinal integrated database for health insurance and labour market studies)

The National Population Registry of Norway (“Folkeregisteret”)

The National Patient Registry in Norway (NPR)

The Medical Birth Registry of Norway (MBRN)

Norwegian Prescribed Drug Registry

The Norwegian Immunization Registry (SYSVAK)

Statistics Norway (SSB)

Data sources (types)

Disease registry

Drug dispensing/prescription data

Non-interventional study

Population registry

Pregnancy registry

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Unknown

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes