EPID Multiple Sclerosis Pregnancy study - Pregnancy outcomes in Multiple Sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries

First published: 15/04/2016

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS13054

Study ID

47377

DARWIN EU® study

No

Study countries

- ☐ Finland
- ☐ Norway

Sweden

Study description

MS disease is the most common chronic neurologic disability in young adult females in their childbearing ages. It is commonly understood that relapses are fewer during pregnancy, but also that medication taken before conception or in early pregnancy could negatively affect pregnancy outcomes. Experience about exposure to MS disease modifying drugs (MSDMDs) during pregnancy has been mostly collected from IFN-βs and glatiramer acetate with no clear association of adverse outcomes such as low birth weight, congenital anomaly or spontaneous abortion. However, it is contraindicated to initiate treatment with IFN-β products during pregnancy. Furthermore, information on newer MSDMD substances such as fingolimod from previous studies is limited. Due to limited evidence being available regarding the association between exposure to IFN-β products and adverse pregnancy outcomes the four marketing authorization holders (MAHs) of IFN-β are conducting a European-wide IFN-β pregnancy registry. Additionally, the Committee for the Medicinal Products for Human Use (CHMP) has requested a study to enable identification of pregnancy outcomes in the MS population unexposed to IFN-β products for comparison with the ongoing European IFN-β Pregnancy Registry. The overall research questions of this study are to determine if exposure to IFN-β before or during pregnancy has an adverse effect on pregnancy outcomes in patients with MS and, as requested by the CHMP, to identify the prevalence of adverse pregnancy outcomes in MS women unexposed to IFN-β products.

Study status

Finalised

Research institutions and networks

Institutions

IQVIA

United Kingdom

First published: 12/11/2021

Last updated: 22/04/2024

Institution | Non-Pharmaceutical company | ENCePP partner

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

Sweden

First published: 24/03/2010

Last updated: 23/04/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Haukeland University Hospital Bergen, Norway

Contact details

Study institution contact

Pasi Korhonen PAS_registrations@iqvia.com

Study contact

PAS_registrations@iqvia.com

Primary lead investigator

Massoud Toussi

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 20/12/2012

Study start date

Planned: 02/05/2016

Actual: 02/05/2016

Data analysis start date

Actual: 31/10/2017

Date of final study report

Planned: 31/12/2018

Actual: 07/06/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Bayer Pharma AG, Biogen Idec Ltd, Merck Serono Europe Ltd, Novartis Pharma AG

Study protocol

ER-9430-EPID Research PASS study protocol_version 2.0 v5_2015-08-18_CLEAN.pdf(1.13 MB)

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 main objectives are to estimate and compare the prevalence of adverse pregnancy outcomes between women with MS exposed to IFN-β only vs. unexposed to any MSDMDs and women with MS exposed to IFN-β only vs. unexposed to IFN-β regardless of exposure to other MSDMDs.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(L03AB07) interferon beta-1a

interferon beta-1a

(L03AB08) interferon beta-1b

interferon beta-1b

(L03AB13) peginterferon beta-1a

peginterferon beta-1a

Medical condition to be studied

Multiple sclerosis

Population studied

Short description of the study population

The target study population consists of Finnish, Swedish and Norwegian women with MS who have been pregnant during the study period. The study population will be identified according to the inclusion and exclusion criteria below.

Inclusion criteria

• Women who have had a pregnancy with a recorded outcome consisting of an induced abortion, spontaneous abortion, ectopic pregnancy, or birth during the study period in FIN, SWE or NOR with the event being documented in the relevant databases.

Exclusion criteria

• None

Age groups

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Special population of interest

Pregnant women

Estimated number of subjects

1671

Study design details

Outcomes

The primary outcome variable is a serious adverse pregnancy outcome defined as a composite endpoint including elective termination of pregnancy due to foetal anomaly (TOPFA), major congenital anomaly (MCA), and stillbirth. Other outcome variables include live births, stillbirths, elective TOPFA or elective termination due to other reasons, MCA, spontaneous abortions, ectopic pregnancies and defect cases. The following perinatal health outcomes are also included: mode of delivery, preterm birth, birth weight and height, sex of the newborn, head circumference and Apgar scores.

Data analysis plan

The characteristics of all pregnancies with respect to relevant covariates are described with number of events, mean, median, standard deviation, minimum, maximum and inter-quartile range for continuous variables and with number and percentage for categorical variables. The descriptive statistics (the number of events and prevalence) will be presented for each pregnancy outcome. Descriptive analyses of the pregnancy outcomes will be further stratified by e.g. maternal age at LMP, chronic diseases, exposure to any teratogenic medication, duration of MS treatment and gestational age. The prevalence of the pregnancy outcomes will be compared between the study cohorts using log-binomial regression with adjustments for relevant confounders. The RR estimates with 95% confidence intervals and associated p-values will be reported for these

comparisons and for confounders used in the model. In indirect comparison between cohort 6 vs. cohort 3, standardized prevalence ratio will be used.

Documents

Study results

ER-9430_Study Report_v2.0_2019-06-07_abstract_for EU PAS register.pdf (252.79 KB)

ER-9430_Study Report_v2.0_2019-06_07_clean_final_fully_executed.pdf(2.83 MB)

Study report

ER-9430_Study Report_v2.0_2019-06-07_abstract_for EU PAS register_clean_2019-10-01.pdf(253.36 KB)

Study, other information

2589353_Avonex and Plegridy additional analyses_abstract_for EU PAS_V1.0_09 Sep 2020.pdf(292.1 KB)

Study publications

Korjagina M, Hakkarainen KM, Burkill S, Geissbühler Y, Sabidó M, Everage N, Suz...

Hakkarainen KM, Juuti R, Burkill S, Geissbühler Y, Sabidó M, Popescu C, Suzart-...

Burkill S, Vattulainen P, Geissbuehler Y, Sabido Espin M, Popescu C, Suzart-Woi...

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.

Conflicts of interest of investigators

ER-9430_Annex5_DoIForm_Korhonen_signed.pdf(1.08 MB)

Data sources

Data source(s)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Data source(s), other

NorPD, Drugs and Pregnancy Finland

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

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