Pregnancy outcome after rheumatologic methotrexate (MTX) treatment prior to or during early pregnancy: a prospective multicenter cohort study (Rheumatologic MTX treatment and pregnancy outcome)

First published: 25/04/2012

Last updated: 01/04/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/28099

EU PAS number

EUPAS2566

Study ID

28099

DARWIN EU® study

No

Study countries

- [ ] Canada
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Israel
- [ ] Italy
- [ ] Netherlands
- [ ] Switzerland
- [ ] United States

Study description

Methotrexate (MTX) is known as a teratogen that causes a specific embryopathy. This is based on several retrospective case reports (e.g. Seidahmed 2006, Yedlinski 2005, Adam 2003, Chapa 2003, Krähenmann 2002, Wheeler 2002, Bawle 1998, and Milunsky 1968.). MTX has been used as an abortifacient, in cancer therapy, and beginning in the 90th for rheumatoid arthritis and some autoimmune diseases. The dose of MTX varies depending on the treatment indication and is lower in rheumatic diseases. There is still uncertainty concerning the risk of low-dose methotrexate therapy during pregnancy. As there is only one small prospective study, which observed no major birth defects in 28 pregnancies (Lewden 2004), no precise risk evaluation can be made so far. Furthermore, it has been debated how long prior to conception MTX therapy should be stopped. Recently, a broad international panel of rheumatologists recommended stopping MTX at least 3 months before conception (Visser 2009). Study Target: To assess the risk of low-dose MTX exposure in early pregnancy. Primary Outcome:Rate of major birth defects, rate of specific MTX embryopathy (time frame up to approximately 8 weeks after birth), rate of spontaneous abortion, intrauterine growth retardation (IUGR) in malformed and non malformed newborns (criterion: birth weigth), rate of

prematurity. There are three prospectively ascertained groups to be compared:1) Exposed group with maternal exposure of low-dose MTX for rheumatic/autoimmune diseases, 2) Control group 1 (“disease group”): Pregnant women with rheumatic /autoimmune diseases without MTX during pregnancy, 3) Non-exposed control group 2 (“general control”): No MTX, no rheumatic / autoimmune diseases.

Study status

Finalised

Research institutions and networks

Institutions

Pharmakovigilanzzentrum Embryonaltoxikologie (Embryotox Berlin), Charité-Universitätsmedizin

Germany

First published: 22/02/2010

Last updated: 30/12/2013

Institution **Educational Institution** **ENCePP partner**

Networks

European Network of Teratology Information Services (ENTIS)

Austria

- [ ] Czechia
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Greece
- [ ] Italy
- [ ] Netherlands
- [ ] Spain
- [ ] Switzerland
- [ ] United Kingdom

First published: 31/05/2010

Last updated: 13/05/2024

Network **ENCePP partner**

Contact details

Study institution contact

Christof Schaefer

Study contact

christof.schaefer@charite.de

Primary lead investigator

Corinna Weber-Schoendorfer

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 06/02/2012

Study start date
Actual: 06/02/2012

Data analysis start date
Actual: 09/08/2012

Date of final study report
Planned: 31/12/2012

Actual: 21/12/2012

Sources of funding

- Other

More details on funding

Bundesministerium für Gesundheit, Senatsverwaltung Berlin

Study protocol

Arthritis Rheumatol_abstract.pdf(145.4 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:

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:

Primary data collection

Main study objective:

To assess the risk of low-dose methotrexate (MTX) exposure in early pregnancy.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

METHOTREXATE

Population studied

Short description of the study population

Women on MTX (≤30mg/week) either in the post-conception period or within 12 weeks before conception.

Age groups

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Special population of interest

Pregnant women

Estimated number of subjects

1450

Study design details

Outcomes

Rate of major birth defects, rate of specific MTX embryopathy, rate of spontaneous abortion, rate of elective terminations of pregnancies, birth weight, rate of prematurity, Definition of a "teratogenic time window", Evaluation of teratogenic dose-effect relationship.

Data analysis plan

Birth defect rates include live births and anomalies in elective terminationsof pregnancies (ETOPs) and miscarriages. For calculating rates ofmajor birth defects possibly associated with a teratogen, welldefinedgenetic syndromes are excluded. See: Schaefer C, Ornoy A, Clementi M, Meister R, Weber-Schoendorfer C. Using observational cohort data for studying drug effects on pregnancy outcome--methodological considerations. Reprod Toxicol. 2008,26:36-41. For calculation spontaneous abortion rate see Meister R, Schaefer C. Statistical methods for estimating the probability ofspontaneous abortion in observational studies--analyzing pregnancies exposed to coumarin derivatives. Reprod Toxicol. 2008,26:31-5

Documents

Study publications

Weber-Schoendorfer C, Chambers C, Wacker E, Beghin D, Bernard N, Network ofFren…

Data management

Data sources

Data sources (types)

Other

Data sources (types), other

ENTIS provides drug risk assessment for pregnant patients and/or physicians. Exposed pregnancies are documented and after the expected date of delivery, follow-up is conducted both using a structured questionnaire or phone interview.

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