The safety of anti-tumor necrosis factor-α (TNF-α) agents in pregnancy. An observational prospective multicenter study (TNF-α Blocker in Pregnancy)

First published: 28/01/2013

Last updated: 23/11/2018

Study Ongoing

Administrative details

EU PAS number

EUPAS3435

Study ID

26688

DARWIN EU® study

No

Study countries

Australia

Finland

France

Germany
Italy
Netherlands
Switzerland
Türkiye
United Kingdom

Study description

The five TNF-alpha inhibitors adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are not labeled for use in pregnancy. Existing experience during pregnancy does not suggest teratogenicity, but varies between the different substances and altogether is still limited. Furthermore, there are concerns against the use of TNF-α inhibitors in late pregnancy, because at least some of them exhibit an increasing placental transfer during the course of pregnancy. This results in therapeutic fetal/neonatal plasma concentrations. A case report of a newborn raises concern. The mother was treated with infliximab throughout pregnancy. The 3-months old infant received BCG live-vaccination resulting in disseminated BCG infection and ultimately in the death of the child (Cheent 2010). Our prospective multicenter cohort study enrolls women who have spontaneously contacted a teratology information service (TIS) within the European Network (ENTIS). The sample of exposed pregnancies includes women who were treated with a TNF-alpha inhibitor during the first trimester (part 1). The comparison group consists of non-exposed women matched for year of enrollment and TIS. The focus lies on the risk of birth defects (BD), spontaneous abortion, and low birth weight. Part 2 evaluates potential impacts of maternal TNF-α inhibitors on the infant’s immune system during the 1st year of life. It is an explorative cohort study including infants born ≥ 34.0 weeks without major BD. Prerequisite are access to data regarding the pregnancy course within 8 weeks after delivery and no information on the further development of the child. Exposed women may have

been treated at any time during pregnancy, but special interest lies on an exposure period > 20 weeks of gestation. Exposed infants are compared to non-exposed children matched for sex, gestational week at birth, birth weight, and year of birth. Cases exposed to major teratogens or fetotoxicants are excluded from all groups of both parts.

Study status

Ongoing

Research institutions and networks

Institutions

Charité-Universitätsmedizin

First published: 01/02/2024

Last updated: 01/02/2024

Institution

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

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Study contact

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Primary lead investigator

Corinna Weber-Schoendorfer

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 02/01/2012

Actual: 29/05/2012

Study start date
Planned: 23/09/2013

Actual: 02/09/2013

Data analysis start date
Planned: 03/03/2014

Actual: 20/03/2014

Date of final study report
Planned: 31/12/2014

Sources of funding

- Other

More details on funding

Bundesministerium für Gesundheit, Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)

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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Main study objective:

Part I: To evaluate the risk of major birth defects after first tirmester TNF-α inhibitor exposure-Part II: To analyze if there is an effect on infant’s immune system during the first year of life

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(L04AB) Tumor necrosis factor alpha (TNF-alpha) inhibitors

Tumor necrosis factor alpha (TNF-alpha) inhibitors

Population studied

Age groups

- Preterm newborn infants (0 – 27 days)
- Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)

Estimated number of subjects

2665

Study design details

Outcomes

Study part I: Rate of major birth defects (major birth defect classification according to the Eurocat classification), risk of spontaneous abortion, birth weight.Study part II: Severity and frequency of infections, infant’s weight gain, Study part I: rate of electively terminated pregnancies, risk of preterm birthStudy part II: allergic diseases and adverse vaccine effects, achievement of developmental milestones

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Data analysis plan

Part I: Birth defect rates (BD) include live births and anomalies in elective terminations of pregnancies and miscarriages. Classification of major BD excluding genetic disorders according to the EUROCAT-classification. Cumulative incidences used for calculating spontaneous abortion rates (Meister R 2008). Propensity score method for bias reduction using boosted regression trees including maternal age, parity, previous spontaneous abortions, previous

children/fetuses with major birth defects, alcohol, tobacco, other immunosuppressant medication including systemic corticosteroids.Part II: mainly descriptive

Documents

Study publications

Weber-Schoendorfer C, Oppermann M, Wacker E, Bernard N, Network of French Pharm...

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 sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

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