Birth defects after maternal exposure to GLP1 agonists in early pregnancy: a comparative ENTIS cohort study

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Study | Planned

Administrative details

PURI
https://redirect.ema.europa.eu/resource/50644

EU PAS number
EUPAS50643

Study ID
50644

DARWIN EU® study
No

Study countries
Australia
Germany
Israel
Italy
Switzerland
United Kingdom

Study description
The aim of this study is to assess the risks linked to Glucagon-like peptide 1 (GLP1) agonists' exposure during pregnancy for which safety data is absent. There are indeed until today no published available human exposure data on GLP1 agonists during pregnancy.

Only one case of exposure to liraglutide in the 1st trimester was published with favourable outcome of the newborn and 7 cases in a registry for exenatide, however without information on follow-up. To fill this gap of knowledge, an observational cohort study is planned among participating centres of the European Network of Teratogen Information Services (ENTIS). Prospectively ascertained patients that received a GLP1 agonist during the first trimester of pregnancy will be eligible for the study. For each case, patients will be selected for the reference groups including diabetic patients treated with metformin and obese patients without diabetes, identified within the same TIS prospective cohort and similar for year of TIS contact. The association between GLP-1 agonist exposure and the risk of major birth defects will be the primary objective and evaluated using multivariate logistic regression analysis to estimate odds ratios with 95% CI. The risks for pregnancy terminations will also be considered competing risks and their frequency will be presented as cumulative incidence functions. A Cox regression model will be used to estimate the adjusted hazard ratios of these pregnancy outcomes associated with GLP-1 agonist exposure during the first trimester.

Study status
Planned

Research institution and networks

Institutions

Swiss Teratogen Information Service
First published: 01/02/2024
Last updated 01/02/2024
Institution

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
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Network
ENCePP partner

Contact details

Study institution contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
01/08/2023

Study start date
Planned:
03/10/2022

Date of final study report
Planned:

30/06/2023

Sources of funding

- Other

More details on funding

Swiss National Science Foundation

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:
The aim of the study is to assess the risks linked to GLP1 agonists' exposure during pregnancy. The primary objective is to prospectively evaluate the risk of major birth defects and to evaluate risks of spontaneous pregnancy losses (abortions and stillbirths) and pregnancy terminations after first trimester exposure to one GLP1 agonist compared to two reference groups.

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(A10BJ) Glucagon-like peptide-1 (GLP-1) analogues

Population studied

Age groups
Adults (18 to < 46 years)

Special population of interest
Pregnant women

Estimated number of subjects
200

Study design details

Outcomes
The primary outcome of interest include the risk of major birth defects and the risks of spontaneous pregnancy losses (abortions or stillbirths) and pregnancy terminations. Secondary outcomes include: minor birth defects, neonatal outcomes including gestational age at birth and birth weight (sex and gestational age adapted) and preterm births.

Data analysis plan
Dataset description: Baseline demographic data will be presented using numbers and proportions for each group of key characteristics. Inferential measure such as standard errors, confidence intervals or significance tests will be avoided, since even small differences in a confounder may have a strong effect on the outcome. Primary outcome: The association between GLP-1 agonist exposure and the risk of major birth defects will be evaluated using multivariate logistic regression analysis to estimate odds ratios (OR) with 95% CI. The risks for pregnancy terminations will be considered competing risks and their frequency will be presented as cumulative incidence functions. A Cox regression model will be used to estimate the adjusted hazard ratios of these pregnancy outcomes associated with GLP-1 agonist exposure during the first trimester.

Data management

Data sources

Data sources (types)
Other

Data sources (types), other
Participating centres of the European Network of Teratogen Information Services (ENTIS).

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