

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

**First published:** 20/01/2023

**Last updated:** 19/04/2024

Study

Planned

## Administrative details

### EU PAS number

EUPAS50643

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### Study ID

50644

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### DARWIN EU® study

No

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### Study countries

☐ Australia

☐ Germany

☐ Israel

☐ Italy

☐ Switzerland

☐ United Kingdom

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## **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.

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## **Study status**

Planned

## **Research institutions 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

**Last updated:** 13/05/2024

Network

ENCePP partner

## Contact details

### Study institution contact

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Study contact

[ursula.winterfeld@chuv.ch](mailto:ursula.winterfeld@chuv.ch)

### Primary lead investigator

Ursula Winterfeld

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 01/08/2023

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**Study start date**

Planned: 03/10/2022

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**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

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

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study type:**

Non-interventional study

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**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

Glucagon-like peptide-1 (GLP-1) analogues

## Population studied

**Age groups**

Adults (18 to < 46 years)

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## **Special population of interest**

Pregnant women

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## **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.

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## **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

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

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### 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

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### Check completeness

Unknown

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### **Check stability**

Unknown

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### **Check logical consistency**

Unknown

## **Data characterisation**

### **Data characterisation conducted**

No