A non-interventional register-based comparative effectiveness study of rhFSH-alfa reference product vs. highly purified human menopausal gonadotropin or rhFSH-alfa biosimilar products for ovarian stimulation in in vitro fertilization or intracytoplasmic sperm injection treatment in Denmark and Sweden – The Nordic Follitropin Alfa Comparative Effectiveness Study (NORD-FACE)

First published: 23/06/2021

Last updated: 12/03/2025

Study Finalised

Administrative details

EU PAS number

EUPAS41175

Study ID

49075

DARWIN EU® study

No

Study countries

- [ ] Denmark
- [ ] Sweden

Study description

The urinary gonadotropins had been used universally until the introduction of recombinant technology. Even if this technology had shown improvement in purity, consistency, and specific activity of gonadotropin products, both types of products, urinary and recombinant gonadotropins, are on the market at the present. From a clinical perspective, the decision regarding what kind of gonadotropin to give to a woman undergoing a treatment for fertility is still challenging. One of the points to consider is the possible differences in effectiveness among the different gonadotropins. This non-interventional study is based on secondary data from national population-based registers with prospective data collection in Denmark and Sweden. The study uses a cohort design and is conducted as a comparative effectiveness and safety study with head-to-head comparisons of drugs used for treatment of infertility and in assisted reproductive technology (ART). The study drugs are rhFSH-alfa reference product (drug of interest), HP-hMG and rhFSH-alfa biosimilar products (comparator drugs). The primary objective is to compare rhFSH-alfa reference product with HP-hMG or rhFSH-alfa biosimilar products regarding live birth outcomes. The overall study population includes women, aged 18 years or older, who initiated IVF/ICSI stimulation cycle with rhFSH-alfa reference product, HP-hMG, or rhFSH-alfa biosimilar product monotherapy for controlled ovarian stimulation (COS), 2010-2020. Different study periods are applied for the comparison of rhFSH-alfa reference product with, respectively, HP-hMG (2010-2020) and rhFSH-alfa biosimilar products (2014-2020).

Study status

Finalised

Research institutions and networks

Institutions

IQVIA

United Kingdom

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Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Mickael Arnaud

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 25/11/2020

Actual: 25/11/2020

Study start date
Planned: 27/05/2021

Actual: 27/05/2021

Data analysis start date
Planned: 20/09/2021

Actual: 01/04/2022

Date of interim report, if expected
Planned: 01/04/2022

Date of final study report
Planned: 29/07/2022

Actual: 05/10/2023

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck Healthcare KGaA

Study protocol

Protocol-Merck_NORD-FACE_Study_v1.0_27May2021.pdf (6.22 MB)

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

Effectiveness study (incl. comparative)

Main study objective:

To compare rhFSH-alfa reference product with HP-hMG or rhFSH-alfa biosimilar products regarding live birth outcome measures.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(G03GA02) human menopausal gonadotrophin

human menopausal gonadotrophin

(G03GA05) follitropin alfa

follitropin alfa

Population studied

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)

Estimated number of subjects

79000

Study design details

Outcomes

The primary outcome is live birth, measured as live birth rate (LBR) per initiated in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) stimulation cycle, cumulative live birth rate (CLBR) per initiated IVF/ICSI stimulation cycle, and CLBR in up to five initiated IVF/ICSI stimulation cycles (termed multiple-cycle MC-CLBR). The secondary outcomes are clinical pregnancy, ongoing pregnancy, oocytes retrieved, embryos transferred, embryos cryopreserved, utilizable embryos, implantation, pregnancy loss, multiple pregnancy, cycle cancellation, OHSS, and treatment-associated costs.

Data analysis plan

The analysis will be conducted in two stages: (i) construction of inverse probability of treatment weighted (IPTW) study cohorts, by modelling rhFSH-alfa reference product vs. HP-hMG treatment initiation and rhFSH-alfa reference product vs. rhFSH-alfa biosimilar product treatment initiation, (ii) estimation of the effect of rhFSH-alfa reference product on the outcomes, compared with the respective comparator drugs. Descriptive analysis will be conducted to describe the baseline characteristics of the study cohorts. For outcomes, rates per 100 units of observations will be estimated with 95% CIs. Adjusted odds ratios with 95% CIs will be estimated from the statistical model weighted with IPTWs and any variables included in the propensity score (PS) that are still unbalanced between the study cohorts after weighting. The analyses will be conducted for each data source separately and combined using meta-analyses, providing a summary estimate for all data sources.

Documents

Study report

EUPAS_EUPAS41175_NORDFACE Study_Abbreviated Study Report_Redacted For Publication.pdf (215.29 KB)

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.

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

DoIForm_v1.6_Investigators.pdf (3.28 MB)

Composition of steering group and observers

NORD-FACE EU PAS 41175_No Steering Group and Observers.pdf (59.93 KB)

Signed code of conduct

empty_file.pdf (11.35 KB)

Signed code of conduct checklist

empty_file.pdf (11.35 KB)

Signed checklist for study protocols

empty_file.pdf (11.35 KB)

Data sources

Data source(s)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Data source(s), other

Danish Registries (access/analysis), The Swedish prescribed drug register

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

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