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: 23/04/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/49075

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 institution and networks

Institutions

IQVIA
United Kingdom
First published: 12/11/2021
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Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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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
100000095899
human menopausal gonadotrophin
100000095902
follitropin alfa

Medical condition to be studied
Infertility female

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.

Data management

ENCePP Seal

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)

Data sources

Data source(s)
Danish registries (access/analysis)
National Prescribed Drugs Register / Läkemedelsregistret

Data source(s), other
Danish Registries (access/analysis), The Swedish prescribed drug register

Data sources (types)
Administrative data (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