EURopean Active Surveillance study - Comparing Regimens of Administration in combined hormonal contraception (EURAS - CORA)

First published: 14/09/2015

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS9818

Study ID

29837

DARWIN EU® study

No

Study countries

- [ ] Austria
- [ ] France
- [ ] Germany

☐ Hungary

☐ Italy

☐ Poland

☐ Spain

Study description

Lisvy (FC Patch Low) is a transdermal contraceptive patch releasing 60mcg gestodene/24 hours and 13 mcg ethinyl estradiol/24 hours. FC Patch Low is applied once a week for three consecutive weeks followed by a break of one week (21/7). One patch contains 2.1mg gestodene and 0.55mg ethinyl estradiol. The most relevant adverse clinical outcomes that have been linked to the use of COCs is venous thromboembolism (VTE). EURAS-CORA is a large, prospective, controlled, long-term active surveillance study to investigate the safety of FC Patch Low with regard to venous thromboembolism, arterial thromboembolism, cancer, long and short term fertility and pregnancy outcomes and application site reactions. The study follows the EURAS design methodology with some modifications due to country and product-specific characteristics. EURAS-CORA was suspended on 17th October 2016. FC Patch Low was withdrawn from the market. Under certain conditions the stability tests showed out of specification results. Data from in vitro dissolution tests showed altered dissolution profile for the gestodene component. Furthermore, visually observable quality defect of crystallization due to the progesterone component (gestodene) had been detected. The clinical relevance of the quality issue was not proven. Based on the company’s safety database, no increase in the frequency of reported adverse events or in the number of unwanted pregnancies were observed in association with the quality issue of the patch. The Pearl Index calculated based on this post-marketing data and taking into account the possible under-reporting (Pearl Index: 0.50) was considerably lower than the Pearl Index based on the data from clinical trials (Pearl Index: 1.19). The market authorization of the product was withdrawn in all European

countries between May 2018 and January 2019. The EURAS-CORA study closed on 22nd May 2019.

Study status

Finalised

Research institutions and networks

Institutions

Berlin Center for Epidemiology & Health Research, ZEG Berlin

Germany

First published: 06/08/2019

Last updated: 20/06/2024

Institution **Laboratory/Research/Testing facility** **ENCePP partner**

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Klaas Heinemann

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 01/04/2015

Actual: 07/09/2015

Study start date
Planned: 01/11/2015

Actual: 27/11/2015

Data analysis start date
Planned: 01/07/2016

Date of final study report
Planned: 30/04/2022

Actual: 18/12/2017

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Gedeon Richter

Study protocol

EURAS-CORA_Study Protocol_ENCePP Submission.pdf(891.5 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 1 (imposed as condition of marketing authorisation)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Effectiveness study (incl. comparative)

Data collection methods:

Primary data collection

Main study objective:

To characterise and compare the risks of short- and long-term use of FC Patch Low with levonorgestrel-containing combined oral contraceptives (COC-LNG) in a study population that is representative of the actual users of the individual preparations. This includes an estimate of the absolute risk of rare serious adverse outcomes (e.g. venous thromboembolism, arterial thromboembolism).

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Intensive monitoring schemes

Study drug and medical condition

Name of medicine, other

Lisvy

Medical condition to be studied

Deep vein thrombosis

Pulmonary embolism

Arterial thrombosis

Skin reaction

Pregnancy

Population studied

Short description of the study population

Lisvy (FC Patch Low users) and users of COCLNG (including adolescents).
All starters and restarters (see above) of FC Patch Low or COCLNG who were willing to participate in the study were eligible for enrollment into the study.

Age groups

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Estimated number of subjects

101000

Study design details

Outcomes

The main clinical outcomes of interest for short- and long-term follow-up are venous thromboembolisms (VTEs), specifically 1. Deep Venous Thrombosis of the lower extremities 2. Pulmonary Embolism. For FC Patch Low and LNG-COC users, describe, measure and compare 1. All VTE 2. Arterial thromboembolism incidence rate (IR) 3. All cancers IR 4. Application site reactions IR 5. Effect on short-/long-term fertility 6. Drug utilisations patterns and baseline risks for clinical outcomes 7. Pregnancy outcomes

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Data analysis plan

Sample size considerations are based on the expected VTE incidence of COC-LNG (10 VTE per 10,000 woman years as requested by CHMP). It is expected that FC Patch Low is associated with a VTE risk that is not higher than with COC-LNG. A non-inferiority approach will be used to test hypotheses. Crude and adjusted hazard ratios will be calculated, with stratification of women into user

categories (first-ever user, re-starter). The final decision on confounding variables will be made by the Safety Monitoring and Advisory Council. Similar analyses will be performed for all VTE, arterial thromboembolism (which includes acute myocardial infarction and cerebrovascular accidents), other secondary variables and other serious adverse events. A detailed analysis plan will be developed by the Principal Investigator during the first year after study start. The final analysis plan will be approved by the Safety and Monitoring Advisory Council before the first interim analysis of follow-up data.

Documents

Study results

ECORA_SynopsisOfStudyStatus_EUPAS_20190522.pdf(76.75 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

EURAS-CORA_DoI_signed.pdf(138.78 KB)

Composition of steering group and observers

EURAS-CORA_SMAC Members_201509.pdf(90.92 KB)

Signed code of conduct

2015_0033_CoC Declaration-SDPP-9818.pdf(62.8 KB)

Signed code of conduct checklist

2015_0033_CoC Checklist-SDPP-9818.pdf(275.42 KB)

Signed checklist for study protocols

2015_0033_Study Protocol Checklist-SDPP-9818.pdf(318.93 KB)

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

Unknown