Safety of Paxlovid Among Patients with Moderate or Severe Hepatic or Renal Impairment

First published: 14/12/2022

Last updated: 19/08/2024

Study Ongoing

Administrative details

EU PAS number

EUPAS50123

Study ID

50124

DARWIN EU® study

No

Study countries

- ☐ France
- ☐ Spain
- ☐ United Kingdom

Study description

This study aims to answer the 2 research questions what is the comparative safety of liver, abdominal, anaphylactic reactions, and other outcomes, in patients with moderate or severe hepatic impairment exposed to Paxlovid and what is the comparative safety of abdominal, anaphylactic reactions, and other outcomes, in patients with moderate or severe renal impairment exposed to Paxlovid?

The primary objective is to assess the safety of Paxlovid relative to the comparator populations who used molnupiravir for COVID-19 and to unexposed patients with COVID-19 with respect to hospitalisations or emergency room visits for the following outcomes among individuals with moderate or severe renal impairment: severe vomiting, nausea, diarrhoea, or abdominal pain, dysgeusia, headache, or hypertension, anaphylactic reactions, and for the same outcomes in addition to hepatic transaminase elevations, clinical hepatitis, or jaundice among individuals with moderate or severe hepatic impairment. The study will focus on the target populations. Within each population, there will be a descriptive analysis and comparative analyses. Molnupiravir, an antiviral with a similar recommended usage, will be used as an active comparator in the data sources for which it is available, other drugs may be incorporated as active comparators as more information becomes available. A second comparator group is included in the study: individuals who were at increased risk for progression to severe COVID-19 but had not received Paxlovid or molnupiravir. This PASS will make secondary use of several data sources from electronic health records and/or claims data in European countries that have the ability to capture Paxlovid exposure and where the target populations, study outcomes, and key covariates can be ascertained.

Study status

Ongoing

Research institutions and networks

Institutions

Pfizer

First published: 01/02/2024

Last updated: 01/02/2024

Institution

University Medical Center Utrecht (UMCU)

☐ Netherlands

First published: 24/11/2021

Last updated: 22/02/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility | ENCePP partner

RTI Health Solutions (RTI-HS)

☐ France
☐ Spain
☐ Sweden
☐ United Kingdom
☐ United Kingdom (Northern Ireland)
☐ United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | ENCePP partner

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

First published: 05/10/2012

Last updated: 23/05/2025

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Bordeaux PharmacoEpi, University of Bordeaux

France

First published: 07/02/2023

Last updated: 08/12/2025

Institution | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Agenzia regionale di sanità della Toscana (ARS)

- [ ] Italy

First published: 01/02/2024

Last updated: 12/03/2024

Institution | EU Institution/Body/Agency | ENCePP partner

Networks

The SIGMA Consortium (SIGMA)

- [ ] Denmark
- [ ] European Union
- [ ] France
- [ ] Germany
- [ ] Italy
- [ ] Netherlands
- [ ] Norway
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom

First published: 10/02/2013

Last updated: 16/12/2024

Network | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Muhammad Younus

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 18/03/2022

Actual: 18/03/2022

Study start date

Planned: 01/03/2024

Actual: 01/03/2024

Date of final study report

Planned: 31/03/2026

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer Inc

Study protocol

C4671047_PROTOCOL_V1_16NOV2022.pdf (3.98 MB)

C4671047_PROTOCOL AMENDMENT 2_V3_21JUN2023_SIGNED.pdf (1.32 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Safety study (incl. comparative)

Main study objective:

Assess the safety of Paxlovid among 1) individuals with moderate or severe hepatic impairment and 2) individuals with moderate or severe renal impairment; compared to users of molnupiravir or to unexposed.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

PAXLOVID

Study drug International non-proprietary name (INN) or common name

NIRMATRELVIR

RITONAVIR

Anatomical Therapeutic Chemical (ATC) code

(J05AE) Protease inhibitors

Protease inhibitors

(J05AE30) nirmatrelvir and ritonavir

nirmatrelvir and ritonavir

Medical condition to be studied

Jaundice

Vomiting

Nausea

Diarrhoea

Abdominal pain

Dysgeusia

Headache

Anaphylactic reaction

Additional medical condition(s)

Hepatic transaminase elevations, clinical hepatitis

Population studied

Age groups

- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Special population of interest

Hepatic impaired

Renal impaired

Study design details

Outcomes

Hepatic transaminase elevations, clinical hepatitis, or jaundice, severe vomiting, nausea, diarrhoea, or abdominal pain, dysgeusia, headache, or hypertension, anaphylactic reactions.

Data analysis plan

The study will have a cohort design, the design is retrospective, and the data were collected prospectively. Focusing on the target populations, the descriptive component will include tabulations of age, sex, comorbidities, selected concurrent medications, COVID-19 vaccination status, history of COVID-19, current COVID-19 status and setting of Paxlovid use (among Paxlovid users). Comparative analyses will be based on the estimation of risk/prevalence, risk/prevalence ratios, and risk/prevalence differences. Comparative analyses will control for measured confounding within each data source. Aggregated results from each data source will be combined using meta-analytic techniques as numbers allow. If a study population is too small, analyses will be only descriptive, pooling of results from various data sources will be undertaken only if at least 3 independent data points are available.

Documents

Study, other information

1047_DeclarationofInterests_combined.pdf (2.79 MB)

1047_DeclarationofInterests-Annex5_template _Muhammad Younus.pdf (104.35 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.

Data sources

Data source(s)

The Information System for Research in Primary Care (SIDIAP)

Système National des Données de Santé (French national health system main database)

Clinical Practice Research Datalink

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

ConcepTION CDM

CDM website

https://www.imi-conception.eu/

CDM release frequency

6 months

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No