Study of Acute Liver Transplant: A study of NSAIDs-exposed acute liver failure in European transplant centres (SALT-I)

First published: 22/09/2011

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS2181

Study ID

40864

DARWIN EU® study

No

Study countries

- ☐ Greece
- ☐ Ireland
- ☐ Italy
- ☐ Netherlands

☐ Portugal

☐ United Kingdom

Study description

The European Medicines Agency (EMA) has expressed concern about the possibility of an increased relative frequency of acute liver failure (ALF) subsequent to nimesulide exposure. The SALT-1 study was initiated to evaluate the risk of ALF in patients exposed to non-steroidal anti-inflammatory drugs (NSAIDs) at the request of the CHMP. The protocol was approved by the CHMP in November 2008 and the final version was sent to the CHMP in December 2008. The SALT-1 study was a multicenter, multinational retrospective case-population study of patients exposed to NSAIDs registered for liver transplantation (LT) because of ALF between 01/01/2005 and 31/12/2007. Seven countries participated, France, Italy, Portugal, Greece, Ireland, Netherlands, UK. The primary objectives were to estimate the absolute frequency and population exposure of ALF leading to registration for LT in patients exposed to the different NSAIDs. Exclusively pediatric (n=4) or oncology centres (n=1) were not eligible, 57 centres were contacted. Criteria for inclusion were: adults ≥18 years of age at the time of registration on LT list with ALF, whether the LT is actually performed or not, and resident of the participating countries. Index date (ID) was the date of initial symptoms of liver disease. Exposure was considered within 90 days prior to ID. ALF cases were classified as “with identified clinical cause”, “possibly drug-exposed/no identified clinical cause" "exposed to NSAIDs" "exposed to drugs without NSAIDs" "without drug exposure and no identified clinical cause" or "acute drug intoxication". A descriptive analysis of all drug-exposed cases of ALF was performed. Per country rates of NSAID-exposed transplantation registered ALF among subjects exposed to NSAIDs within 30 days prior to the index date were estimated along with its corresponding 95% confidence interval (CI) from a Poisson distribution and expressed in cases per million treatment-years.

Estimation was irrespective of any causality.

Study status

Finalised

Research institutions and networks

Institutions

Bordeaux PharmacoEpi, University of Bordeaux

France

First published: 07/02/2023

Last updated: 08/02/2023

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

Pharmacy & Pharmacology, University of Bath

United Kingdom

First published: 30/04/2010

Last updated: 08/04/2019

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

Pharmacologie En Population cohorteS biobanqueS (PEPSS), Hopitaux de Toulouse

☐ France

First published: 31/03/2022

Last updated: 01/07/2024

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**

Bordeaux PharmacoEpi, University of Bordeaux

☐ France

First published: 07/02/2023

Last updated: 08/02/2023

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

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Ezgi Gulmez

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 04/12/2007

Actual: 05/12/2008

Study start date

Planned: 02/01/2009

Actual: 26/01/2009

Data analysis start date

Planned: 21/10/2009

Actual: 26/01/2011

Date of interim report, if expected

Actual: 22/09/2010

Date of final study report

Planned: 27/11/2009

Actual: 23/03/2011

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Helsinn Healthcare S.A.

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

Data collection methods:

Secondary use of data

Main study objective:

To estimate the absolute frequency of ALF leading to registration for transplantation in patients exposed to NSAIDs

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Case-population study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(M01A) ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

Medical condition to be studied

Liver transplant

Population studied

Short description of the study population

Cases were patients ≥18 years of age with acute liver failure (ALF) at the time of registration on the transplant list for liver transplantation who had been exposed to an NSAID within 30 days preceding the initial symptoms of liver disease (index date).

Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Special population of interest

Hepatic impaired

Estimated number of subjects

600

Study design details

Outcomes

- To estimate the absolute frequency of ALF leading to registration for transplantation in patients exposed to NSAIDs,- To compare the population incidence rates of liver transplantation after nimesulide exposure to that after exposure to other NSAIDs. To describe the clinical characteristics of ALF with NSAIDs compared to other drug and to non-drug related ALF, and to test the effects of causality assessment and drug exposure patterns on relative rates of ALF among patients exposed to NSAIDs.

Data analysis plan

A descriptive analysis of all drug-exposed cases of ALF was performed. Per country rates of NSAID-exposed transplantation registered ALF among subjects exposed to NSAIDs within 30 days prior to the index date were estimated along with its corresponding 95% confidence interval (CI) from a Poisson distribution and expressed in cases per million treatment-years. Estimation was made irrespective of any causality assessment.

Documents

Study publications

Gülmez SE, Lignot-Maleyran S, S deVries C, Sturkenboom M, Micon S, Hamoud F, Bl…

Moore N, Gulmez SE, Larrey D, Pageaux GP, Lignot S, Lassalle R, Jové J, Parient…

Gülmez SE, Larrey D, Pageaux GP, Lignot-Maleyran S, de Vries C, Sturkenboom M, …

Gülmez SE, Larrey D, Pageaux GP, Lignot S, Lassalle R, Jové J, Gatta A, McCormi…

Gülmez SE, Moore N, Pageaux GP, Lignot S, Horsmans Y, Stricker B, Bernuau J, Bi…

Data management

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.

Composition of steering group and observers

SALT-Committees.pdf(174.45 KB)

Data sources

Data sources (types)

Disease registry

Other

Data sources (types), other

National liver transplant registries/waiting lists in France (CRISTAL), Ireland and UK (UKTR), and Netherlands,Local liver transplant waiting lists in Greece, Italy, Portugal,Patient medical files at the participating liver transplant centers

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