Study of Acute Liver Transplant-III: Prospective study of drug-exposed acute liver failure (ALF) in European liver transplant centers (SALT-III)

First published: 13/06/2014

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS6769

Study ID

49929

DARWIN EU® study

No

Study countries

☐ France

Study description

The first SALT (Study of Acute Liver Transplant) study was a retrospective, multicentre, multi-country study of drug-exposed ALF registered for liver transplantation (ALFT), over the years 2005-2007. In the 52 contributing centres in seven participating European countries, 9479 patients were registered for transplantation, 600 for ALF, of which 302 without clinical aetiology were exposed to a drug within 30 days, the most commonly found being paracetamol, even without overdose. The SALT-I study created a network of these liver transplant centres in seven European countries. It also accumulated a considerable body of data on drug-exposed acute liver failure in Europe. The main objective of SALT-I concerned only the risks associated with NSAIDs. The SALT-II study extended the retrospective part of SALT to 2008-2013, thus increasing its power. In the 21 French contributing centres, 559 ALFT patients were identified, of which 214 without clinical aetiology exposed to a drug within 30 days, the most commonly found being paracetamol, even without overdose (as for SALT-I). This SALT-III study took advantage of this network of liver transplantation centres to do a prospective case-population surveillance of liver transplantations for drug-related ALF. The prospective nature of the SALT-III study had to allow for better quality data acquisition for drug-related liver transplantation, within a systematic alert system. The objective was to build a surveillance network of liver transplant centres in France that provide real-time assessment of emerging risks related to drugs newly introduced to the market, allowing for earlier signal identification of a major drug-related public health issue. SALT-III was conducted in 17 French liver transplantation centres over the years 2015-2016. Because of difficulties for including prospectively eligible patients (emergency medical care), it was decided to retrospectively include eligible ALFT patients not identified in time.

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**

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Multiple centres: 17 centres are involved in the study

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Nicholas MOORE

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 20/12/2013

Study start date

Planned: 01/07/2014

Actual: 03/12/2014

Data analysis start date

Actual: 31/01/2018

Date of interim report, if expected

Actual: 26/05/2015

Date of final study report

Planned: 30/11/2017

Actual: 29/05/2018

Sources of funding

- Non-for-profit organisation (e.g. charity)

More details on funding

L’Agence nationale de sécurité du médicament et des produits de santé (ANSM)

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 topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Combined primary data collection and secondary use of data

Main study objective:

To develop the network of liver transplant centres for the prospective identification of drug-related ALFT,To estimate the risk of drug-exposed ALFT in adults, in the 30 days prior to index date (ID, date of first symptoms), according to the population exposure to the same drugs provided by the national healthcare insurance system.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Case-population study

Study drug and medical condition

Medical condition to be studied

Acute hepatic failure

Liver transplant

Population studied

Short description of the study population

The study involved adult patients undergone acute liver transplantation registered in the Study of Acute Liver Transplant (SALT) study identified from the European countries.

The first SALT study, conducted from 2005-2007, involved 9479 patients with drug-exposed acute liver failure (ALFT) in seven European countries. The study gathered data on drug-exposed ALF and NSAID risks. The SALT-I and SALT-II studies expanded the network, identifying 559 ALFT patients in 21 French centers. The SALT-III study aimed to build a surveillance network for drug-related ALF, allowing real-time assessment of emerging risks and early signal identification of major public health issues. The study was conducted in 17 French liver transplantation centers from 2015-2016.

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

120

Study design details

Outcomes

The population event rate for all ALFT cases "without defined clinical cause" exposed to the drug(s) of interest within 30 days prior to ID, expressed as number of cases per million exposed patients over the 2-year study period. Event rates for ALFT “without defined clinical cause” exposed to the drug(s) of interest within 7, 15, or 90 days prior to ID.Event rates for ALFT “with a defined clinical cause”, exposed to drugs within 30 days prior to ID, compared to the previous event rates.Description of cases registered for hepatic transplantation after acute drug overdose.Identification of paracetamol adducts.

Data analysis plan

Descriptive analysis,Exposure rates in ALFT were compared to the population exposure to the same drugs, provided by the national healthcare insurance system.The population event rate for all ALFT cases "without a defined clinical cause for ALFT" exposed to the drug(s) of interest within 30 days prior to index date were computed, globally and for each molecule of interest, with reference to person-time exposed (total population drug exposure) or to number of patients exposed for the 2-year period. The estimated rates (with 95% CI) were expressed in cases per million patient-years.

Documents

Study publications

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

Moore N, Gülmez SE, Larrey D, Pageaux GP, Lignot S, Lassalle R, Jove 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…

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

Data management

Data sources

Data sources (types)

Drug registry

Other

Data sources (types), other

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