A study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (De Novo DAA PASS)

First published: 05/05/2020

Last updated: 14/03/2024

Study Finalised

Administrative details

EU PAS number

EUPAS30818

Study ID

44706

DARWIN EU® study

No

Study countries

United States

Study description

Evaluate the potential risk of de novo hepatocellular carcinoma following direct-acting antiviral treatment in hepatitis C virus infected patients with compensated cirrhosis without a history of hepatocellular carcinoma.

Study status

Finalised

Contact details

Study institution contact

Clinical Trial Disclosure AbbVie CT.Disclosures@abbvie.com

Study contact

CT.Disclosures@abbvie.com

Primary lead investigator

Clinical Trial Disclosure AbbVie

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 07/04/2020

Study start date

Actual: 06/04/2020

Date of final study report

Planned: 14/12/2021

Actual: 19/11/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AbbVie; Gilead Sciences; Merck Sharp & Dohme

Study protocol

denovo-daa-pass-protocol_v3_abstract_01Aug2019.pdf (158.39 KB)

denovo-daa-pass-protocol_v3_redacted.pdf (328.84 KB)

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)

Other study registration identification numbers and links

B20-146

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:

This analysis examines the following research question: among compensated cirrhotic patients, does DAA therapy for chronic HCV infection increase the risk of incident HCC compared to no treatment or treatment with IFN-based regimens?

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

DAKLINZA

EPCLUSA

EXVIERA

HARVONI

MAVIRET

SOVALDI

VIEKIRAX

VOSEVI

ZEPATIER

Medical condition to be studied

Chronic hepatitis C

Population studied

Short description of the study population

The analysis will be conducted among US veterans, aged 18 years or older, with chronic HCV who sought care at any of the medical centers and ambulatory care and community-based outpatient clinics that comprise the national VA healthcare system. This analysis will be restricted to HCV mono-infected (i.e., no hepatitis B virus or human immunodeficiency virus coinfection) patients with compensated liver cirrhosis.

Inclusion criteria:

1. Patients with chronic HCV defined as a positive test for HCV ribonucleic acid (RNA) in plasma by qualitative or quantitative assays or genotype test between January 01, 2005 and December 31, 2017.

2. For the first primary objective (DAA only treated and untreated patients): a clinical encounter (i.e., office visit, procedure, lab result, prescription, etc.) recorded in the 6 months preceding and including January 01, 2013 or between January 01, 2013 and December 31, 2017.

3. For the second primary objective: for IFN treated patients, the IFN based treatment was initiated after the above HCV diagnosis, but between January 01, 2005 and December 31, 2013. If DAA-only exposed, the DAA treatment was initiated after the above HCV diagnosis, but between January 01, 2014 and December 31, 2017.
4. Patients with data in VA sources to establish a diagnosis of compensated cirrhosis as follows: • At least 1 fibrosis-4 (FIB-4) > 3.25 within 24 months before or 6 months after the index date but before any HCV treatment (and with all measurements for FIB-4 calculation within 6 months of each other) or at least 1 ICD-9 (571.2, 571.5) or ICD-10 (K70.30, K70.31, K74.60, K74.69, K74.3, K74.4 and K74.5) code indicating cirrhosis, and • No diagnosis codes for hepatic decompensation defined as ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, or hepatorenal syndrome based on inpatient or outpatient ICD-9 codes of 789.5, 456.0–2, 572.4, 572.2, 348.3×, 070.0, 070.2×, 070.4×, 070.6, 070.71, or corresponding ICD-10 codes d

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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

16000

Study design details

Outcomes

1. Estimate the risk of de novo HCC associated with DAA therapy exposure in cirrhotic HCV patients compared to no anti-HCV therapy exposure in cirrhotic HCV patients. 2. Estimate the risk of de novo HCC in cirrhotic HCV patients treated with DAA therapy compared to those treated with IFN-based therapy. To compare, in a subset of patients with available data recorded in the VA CCR, tumor characteristics (i.e. tumor size, tumor number, tumor stage, tumor type) of the de novo HCC cases observed following initiation of DAA therapy to those of de novo HCC cases observed (a) following initiation of IFN-containing regimens and (b) in untreated patients.

Data analysis plan

For the first primary objective, a multivariable Cox proportional hazards regression model will be used to examine the risk of HCC associated with DAA exposed time compared to untreated time using DAA exposure as a time-varying covariate and adjusting for values of potential confounders ascertained at index date or most recently prior to index date and updated at 12-month time intervals until DAA exposure start or through untreated person time if no DAA start. For the second primary objective, another multivariable proportional hazards model will be used to examine the risk of HCC in the DAA treated patients compared to the IFN-based therapy treated patients. For the secondary objective, in all patients with HCC recorded in the VA CCR, the first occurrence of de novo HCC during the observation period will be identified by any instance of primary site code C220 and histology codes 817XX through 818XX.

Documents

Study results

b20146-abstract.pdf (185.62 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 sources (types)

Other

Data sources (types), other

Veterans Affairs system databases

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