Immune phenotyping in chronic HCV patients treated with Sofosbuvir and Daclatasvir combination for 12 or 24 weeks * SODA study

Published: 08-10-2014
Last updated: 22-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON44573

Source
ToetsingOnline

Brief title
AI444-281

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
Chronic hepatitis C, Hepatitis C

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bristol-Myers Squibb

Intervention

Keyword: Chronic hepatitis C, Daclatasvir, Sofosbuvir, Treatment

Outcome measures

Primary outcome

Primary endpoint:

- Immune response in patients

o Baseline versus end-of-treatment versus follow-up

o Patients with SVR versus patients with non-SVR

o Patients with genotype 1 versus 3 versus 4

Secondary outcome

1. Proportion of patients with SVR12 in the study population

2. Proportion of patients with HCV RNA < LLOD at 4 and 24 weeks after cessation

of therapy.

3. Proportion of patients with HCV RNA < LLOD at week 4 during treatment.

4. Any AE leading to discontinuation of the study drug.

Study description

Background summary

Hepatitis C virus (HCV) is a single-stranded RNA virus and represents a major causative agent of chronic liver disease. Worldwide, 130-170 million people have a chronic HCV infection and are at risk to develop cirrhosis, leading to clinical complications such as hepatocellular carcinoma. Every year more than 350,000 people die from HCV-related liver diseases.

In all patients with chronic HCV infection, antiviral therapy should be considered. The aim of chronic hepatitis C treatment is to achieve a sustained virological response (SVR), which is associated with reduced occurrence of liver failure and HCC, and with prolonged overall survival. It is possible to completely eradicate the virus and to achieve a sustained virological response (SVR). Until recently, SVR 24 weeks after treatment (SVR24) was the gold standard for successful treatment; this endpoint is predictive of long-term elimination of the virus and correlates with a reduction in symptoms and a reduction in the risk for patients. However, there are strong indications that most patients with SVR at week 12 maintain this response through week 24. Based on these data, the FDA concluded that regulatory approval SVR12 is suitable as a primary endpoint.
The ultimate goal of the therapy is the disappearance of the inflammation of the liver, fibrosis of stop to cirrhosis formation and the prevention of liver cancer.

There are several different genotypes of hepatitis C (1 t/m 7), of which especially the genotypes 1, 2, 3, and 4 appear in the Netherlands. The current standard of care for patients with HCV genotype 1 is triple therapy with pegylated interferon (Peg-IFN), ribavirin (RBV) and a HCV protease inhibitor * Telaprevir or Boceprevir. The current standard treatment for chronic HCV genotype 2-6 is Peg-IFN plus RBV for 24-48 weeks.

Recently, interferon-free treatment regimens with a combination of 2 DAA's are available for chronic hepatitis C patients with advanced liver fibrosis (fibrosis stadium > F3) and HCV genotype 1 or 4.

Study objective

Primary objective
The primary objective for this study is to analyse the impact of inhibition of viral replication by interferon-free therapy consisting of Sofosbuvir and Daclatasvir (±Ribavirin) on the phenotype and function of the innate immune cells and HCV-specific T-cells, in treatment-naive or previously relapsed chronic hepatitis C patients with chronic HCV GT-1, -3 or -4 infection.

Secondary objectives
- To evaluate if a shortened treatment duration of 12 weeks with Sofosbuvir and Daclatasvir (±Ribavirin) also results in high sustained virological response rates in subjects infected with HCV genotype 3 and 4;
- Rapid viral response (RVR) on-treatment with SOF + DCV ± RBV.
- Sustained virological response at 4 weeks after treatment and at 24 weeks after treatment.
- Evaluation of tolerability and safety as measured by the frequency of discontinuations due to adverse events (AEs) and serious adverse events (SAEs).

Study design

This study will be conducted in a maximum of 32 subjects with chronic HCV GT-1, -3 or -4 infection. This is an open-label study. All subjects will be treatment-naïve to or relapsed after any previous antiviral therapy other than combination of sofosbuvir + NS5A inhibitor ± ribavirin. Ribavirin will be added to the treatment regimen of patients infected with genotype 3.

Intervention

Sofosbuvir 400 mg daily + daclatasvir 60 mg daily ± RBV (1000 or 1200 mg / day) for 12 or 24 weeks

Study burden and risks

N.A.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed written informed consent
- Willingness to sign the written ICF.
2. Target population
- Previous documentation of positive HCV serology (HCV antibody or HCV RNA) at least 24 weeks prior to enrollment to study, OR Positive HCV serology (HCV antibody or HCV RNA) with a prior remote risk factor (more than 24 weeks prior to Screening) for the acquisition of hepatitis C.
- Subjects infected with HCV genotype 1, 3 or 4 on screening laboratory test OR previous availaible documentation of HCV genotype 1,3 or 4 genotype.
- Treatment-naïve to or relapsed after any previous antiviral therapy other than combination of sofosbuvir + NS5A inhibitor ± ribavirin. Relapse is defined as the recurrence of HCV RNA following the termination of a full course of treatment and after having achieved an undetectable HCV RNA during treatment.
3. Age and reproductive status
- Age: 18 - 65 years
- Subjects must agree to use birth control (condoms) from the time of dosing until 90 days after the follow-up visit; male or female patients who are surgically sterile need not to employ a method of contraception
4. Laboratory test findings
- Screening hematology, clinical chemistries, coagulation and urinalysis are not clinically significant and the following criteria are met:
o Platelets >50x10^9/L
o Total white blood cells >3.0x10^9/L and absolute neutrophil count >1.5x10^9/L
o Hemoglobin >6.8 mmol/L for females and >7.4 mmol/L for males
o Total and direct bilirubin < 2 x ULN
o ALT < 10 x ULN
o Serum creatinine within normal limits and estimated creatinine clearance rate as calculated by the Cockcroft-Gault formula >50 mL/min
- Negative results on the following screening laboratory tests: HBsAg and HIV antibody OR previous availaible documentation within 1 year before screening of HBsAg and HIV antibody negativity.

Exclusion criteria

- Other known cause of liver disease except for CHC
- History or symptoms of decompensated liver disease: Child-Pugh Class B or C, including ascites, hepatic encephalopathy, esophageal variceal bleeding, or other signs of hepatic insufficiency or portal hypertension

- History of hepatocellular carcinoma
- Concurrent clinically significant medical diagnosis (other than hepatitis C-related conditions) that would potentially interfere with the subjects study compliance or confound study results
- History of relevant drug and/or food allergies

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2014
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	copegus
Generic name:	ribavirin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	daklinza
Generic name:	daclatasvir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	sovaldi
Generic name:	sofosbuvir

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-002808-25-NL
CCMO	NL50128.018.14