

STOP HCV-1 – Stratified Treatment Optimisation for HCV-1

Submission date 11/04/2016	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 14/04/2016	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 19/05/2023	Condition category Infections and Infestations	☐ Individual participant data

Plain English summary of protocol

Background and study aims

Hepatitis C is a type of liver disease, which is caused by the hepatitis C virus (HCV). Over time, the virus causes the liver to become irreversibly scarred (cirrhosis), eventually leading to liver failure. Traditional treatments for HCV involved long-term (6-12 months) treatment with drugs called interferons, which often caused severe side-effects. Newer treatments for HCV however can be taken for shorter periods of time, with much less severe side-effects. Almost all people are cured with 12 weeks of treatment, however it is not known what the minimum length of time treatment needs to be taken for to achieve a cure. The aim of this study is to establish what the minimum duration of treatment required is to have a high chance of curing patients with HCV.

Who can participate?

Adults with HCV who do not have significant liver disease.

What does the study involve?

Participants are randomly allocated to one of two groups, one group receive a varying length of treatment between 4-6 weeks of the study drugs depending on the amount of virus in their blood, people with more virus will get more days of treatment. The second group receive a fixed treatment course of 8 weeks regardless of the amount of virus in their blood. Within each group, participants are also randomly allocated to either take ribavirin or not twice a day (the dosage is dependent on the participant's weight). Participants attend study visits on day 3, 7, 14 and 28 after randomisation, every other week until 4 weeks after the end of the (first-line) treatment, 4 weekly until 12 weeks after the end of treatment, and then 24 weeks after end of treatment. At each visit a blood sample is taken in order to test for the levels of the HCV virus in order to see if they are cured. In addition participants are assessed by the clinic team and blood tests will be taken for standard safety tests. If the first line treatment is found to have failed at any time after 4 weeks of treatment, participants stop first line therapy and are treated with a fixed dose combination of sofosbuvir/ledispavir (Harvoni) once a day and ribavirin twice daily for 12 weeks. This is called the retreatment phase. For retreatment, participants attend on the day of retreatment, on week 2 and 4 of treatment, and then every 4 weeks until 24 weeks after the end

of treatment. At each retreatment visit a blood sample is taken in order to test for the levels of the HCV virus, in addition participants are assessed by the clinic team and blood tests are taken for standard safety tests.

What are the possible benefits and risks of participating?

Participants may benefit from having their hepatitis C infection cured (either from first line or second round treatment) without the use of old treatments (injectable interferon-based) and their associated severe side effects and their much lower chances of cure. There are no notable risks involved with taking part in the study.

Where is the study run from?

At least 16 NHS Trusts in England and Wales (UK)

When is the study starting and how long is it expected to run for?

March 2016 to November 2019

Who is funding the study?

National Institute for Health Research (UK)

Who is the main contact?

Ms Nafisah B Atako

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Contact information

Type(s)

Public

Contact name

Ms Nafisah. B Atako

Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)

2015-005004-28

Protocol serial number

20686

Study information

Scientific Title

The impact of Hepatitis C viral load determined short-course treatment vs fixed duration treatment on Hepatitis C cure for patients with mild genotype-1 Hepatitis C disease

Acronym

STOPHCV-1

Study objectives

Primary study aim:

To determine if short-course (4-6 weeks) first line treatment with ombitasvir/paritaparevir /dasabuvir/ritonavir (Viekirax), where the duration depends on the levels of the Hepatitis C virus in the patient's body, will cure similar proportions of participants with chronic, mild genotype 1a /1b Hepatitis C disease as compared to a fixed 8 week first-line course, once any patients failing initial treatment have been retreated (with a longer 12 week regimen).

Secondary study aim:

To determine whether adding ribavirin to first-line treatment improves the cure rates within the short course duration and the fixed 8 week duration arms

Ethics approval required

Old ethics approval format

Ethics approval(s)

East of England - Cambridge South Research Ethics Committee, 29/12/2015, ref: 15/EE/0435

Study design

Randomised controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Specialty: Infectious diseases and microbiology, Primary sub-specialty: Infectious diseases and microbiology (migration; UKCRC code/ Disease:

Interventions

The main intervention being compared in all patients is varying (4-6 weeks) duration of treatment (ombitasvir/paritaparevir/dasabuvir/ritonavir (Viekirax)) determined by the participant's screening viral load with or without ribavirin Vs fixed (8 weeks) duration of the same treatment with or without ribavirin. All the treatments in this study are taken orally and are approved for treatment of chronic Hepatitis C. First-line treatment ombitasvir/paritaparevir /ritonavir (two tablets once daily) plus dasabuvir (one tablet twice daily) with or without ribavirin (2 or 3 tablets twice daily) will be taken for:

1. 8 weeks
2. 4-6 weeks

The duration of treatment will be chosen based on a computerised randomisation program. One group of people will all get 8 weeks initial treatment. In the other group, people with less virus

in their blood will get less treatment. Because there is less virus in the blood, less drug should be needed to kill it all – this is what the study is testing. If participants fail first-line treatment they will be offered 12 week treatment with sofosbuvir/ledipasvir (Harvoni) with ribavirin. Follow-up of all treatment arms will be 24 weeks post end of treatment first line or retreatment.

Intervention Type

Other

Primary outcome(s)

1. Sustained Virological Response, measured by HCV viral load through 12 weeks after the end of combined first-line and any retreatment phases
2. Sustained Virological Response measured by HCV viral load through 12 weeks of first line treatment for the ribavirin comparison

Key secondary outcome(s)

1. Sustained virological response, measured by HCV viral load through 24 weeks after the end of combined first-line and any retreatment phases
2. Sustained virological response, measured by HCV viral load through 24 weeks after first-line treatment only
3. Lack of any virological response, measured by HCV viral load at any time point in the study
4. Viral load rebound after becoming undetectable at any time point in the study
5. Serious Adverse Events at any time point during the study
6. Grade 3 or 4 adverse events at any time point during the study
7. Adverse events of any grade judged to be definitely or probably related to the study interventions at any time point during the study
8. Any toxicity which leads to a modification of study treatment at any time point during the study
9. Development of grade 3 or 4 anaemia at any time point during the study
10. Emergence of resistance-associated HCV variants in participants in the duration of the study

Completion date

01/11/2019

Eligibility

Key inclusion criteria

1. Aged ≥ 18 years
2. Infected with HCV genotype 1a or 1b with HCV RNA $>$ LLOQ (lower limit of quantification) on more than one occasion at least six months previously with no intervening results showing undetectable viraemia
3. Plasma HCV RNA $>$ LLOQ at screening
4. No evidence of significant liver fibrosis resulting from any aetiology (defined as Fibroscan* score ≤ 7.1 kPa, equivalent to F0-F134, within 180 days prior to planned randomisation or biopsy consistent with mild fibrosis (Ishak score $\leq 2/6$) within 180 days prior to planned randomisation)
5. BMI ≥ 18 kg/m²
6. Laboratory tests: platelets $\geq 60 \times 10^9$ /l, haemoglobin > 12 g/dl (male) or > 11 g/dl (female), creatinine clearance (estimated glomerular filtration rate (eGFR) (Cockcroft-Gault)) ≥ 60 ml/min, international normalised ratio (INR) $< 1.5 \times$ ULN
7. Screening HCV viral load $< 10,000,000$ IU/ml
8. Written informed consent obtained from the patient

If HIV infected, then an additional eligibility criteria is:

9. On antiretroviral therapy with HIV viral load <50 copies/ml for >24 weeks at the screening visit

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

202

Key exclusion criteria

1. Previous direct acting antivirals (DAA) exposure (previous treatment with pegylated-interferon and/or ribavirin allowed)
2. Malignancy within 5 years prior to screening
3. Any condition in the judgement of the investigator which might limit the patient's life expectancy
4. Currently receiving medication known to interact with study medication (ombitasvir, paritaprevir, dasabuvir, ritonavir, sofosbuvir, ledipasvir, ribavirin; see relevant prescribing information)
8. Disorder which may cause ongoing liver disease including, but not limited to, active hepatitis B, ongoing alcohol misuse
5. Any disorder which in the opinion of the investigator may have a significant negative impact on the ability of the patient to adhere to the trial regimen
6. Use of other investigational products within 60 days of screening
7. Known hypersensitivity to any active ingredient and/or excipients of the study medicines, namely Microcrystalline cellulose, Lactose monohydrate, Croscarmellose sodium, Magnesium stearate, Gelatine, Shellac, Propylene glycol, Polyethylene glycol, Ammonium hydroxide, Pregelatinised maize starch, Sodium starch glycolate (type A), Maize starch, Hypromellose, Talc, Ethylcellulose aqueous dispersion, Triacetin, Copovidone, Colloidal anhydrous silica, Polyvinyl alcohol, Macrogol 3350, Sunset yellow FCF aluminium lake (E110), Colouring agent (E132), Titanium dioxide (E171), Yellow iron oxide (E172), Red iron oxide (E172), Black iron oxide (E172).
8. History of severe pre-existing cardiac disease, including unstable or uncontrolled cardiac disease, in the previous six months
9. Haemoglobinopathies (e.g., thalassemia, sickle-cell anaemia)

Female participants only:

1. Lactating, or pregnant, or planning to become pregnant during the study or within 4 months of the end of the study, or not willing to use effective contraception during the study and for

four months after last dose of study medication

2. Currently taking ethinyl-oestradiol-containing medicinal products such as those contained in most combined oral contraceptives or contraceptive vaginal rings

Male participants only:

Planning pregnancy with female partner during the study or within 7 months of the end of the study, or not willing to use effective contraception during the study and for seven months after last dose of study medication

Date of first enrolment

01/03/2016

Date of final enrolment

01/11/2017

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Central and North West London NHS Foundation Trust

Mortimer Market Centre

Off Caper Street

London

United Kingdom

WC1E 6AU

Sponsor information

Organisation

Imperial College London

ROR

<https://ror.org/041kmwe10>

Funder(s)

Funder type

Government

Funder Name

National Institute for Health Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		29/04/2021	19/08/2021	Yes	No
Results article		01/10/2021	19/05/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet		26/01/2021	23/09/2021	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results	version 1.0	24/03/2020	30/03/2020	No	Yes