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

Submission date
11/04/2016

Recruitment status
No longer recruiting

Registration date
14/04/2016

Overall study status
Completed

Last Edited
19/05/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 a 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?
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Contact information

Type(s)
Public

Contact name
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Contact details
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Additional identifiers

EudraCT/CTIS number
2015-005004-28

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
See additional file

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/paritaprevir /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 measure
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

Secondary outcome measures
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

Overall study start date
01/03/2016

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 ≤7.1kPa, equivalent to F0-F134, within 180 days prior to planned randomisation or biopsy consistent with mild fibrosis (Ishak score <=2/6) within 180 days prior to planned randomisation)
5. BMI >=18kg/m2
6. Laboratory tests: platelets >=60x109/l, haemoglobin >12g/dl (male) or >11g/dl (female), creatinine clearance (estimated glomerular filtration rate (eGFR) (Cockcroft-Gault)) >=60ml/min, international normalised ratio (INR) <1.5xULN
7. Screening HCV viral load <10,000,000IU/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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 408; UK Sample Size: 408

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 know 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
England

United Kingdom

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

Sponsor details
AHSC Joint Research Compliance Office
Imperial College London
510 C, 5th Floor, Lab block
Charing Cross
London
England
United Kingdom
W6 8RF

Sponsor type
Hospital/treatment centre

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

Publication and dissemination plan
It is intended that the final study results will be published in a major medical journal. Investigators will ensure the wide dissemination of the results within the NHS and ensure

maximal influence on clinical care. Results will also be disseminated to the public and patients through the Hepatitis Trust.

Intention to publish date
31/12/2019

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?
Plain English results	version 1.0	24/03/2020	30/03/2020	No	Yes
Results article		29/04/2021	19/08/2021	Yes	No
Participant information sheet		26/01/2021	23/09/2021	No	Yes
Results article		01/10/2021	19/05/2023	Yes	No
HRA research summary			28/06/2023	No	No