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Selecting treatment duration based on early response to Epclusa in patients with type 3 hepatitis C virus infection – is longer therapy worthwhile?

Submission date
13/03/2017

Recruitment status
No longer recruiting

Registration date
16/03/2017

Overall study status
Completed

Last Edited
06/10/2022

Condition category
Infections and Infestations

[X] Prospectively registered

[X] 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. Treatment for long-term (chronic) HCV has evolved rapidly in the last few years, with licensing of new oral treatments (pills) which are highly successful at clearing the virus and enabling a cure. Despite this however, some patients remain relatively more difficult to cure. These include patients infected with type 3 HCV and with advanced liver disease. In the UK, up to half of all people infected with HCV have type 3 virus. Standard treatment in the UK for patients with type 3 HCV and advanced liver disease is a 12 week course of sofosbuvir/velpatasvir (trade name Epclusa). It is known that such patients may require an additional drug, ribavirin, to improve cure rates. However, ribavirin is associated with many unpleasant side effects such as anaemia (low blood count), tiredness, and cough. International guidelines recommend extending Epclusa treatment to 24 weeks in order to avoid ribavirin in patients who may not tolerate such side effects. Given the high costs of Epclusa it is important to have ways to identify which patients are best treated with the extended 24 weeks rather than standard 12 weeks. There is increasing evidence that early response on treatment predicts the likelihood of cure for some HCV therapies in type 3 virus infected patients – patients who clear the virus slowly during therapy are more likely to fail treatment. The aim of this study is to find out whether 24 weeks of Epclusa treatment improves cure rates compared to the standard duration of 12 weeks in patients who are slow responders to Epclusa treatment.

Who can participate?
Adults with genotype 3 HCV cirrhosis and a slow early response to Epclusa.

What does the study involve?
Patients who agree to participate are randomly allocated (by computer programme) to receive standard treatment (12 weeks of Epclusa) or extended treatment (24 weeks of Epclusa). The study looks at which treatment leads to a higher proportion of HCV cure. Participants are

reviewed monthly with blood tests monitoring, until three months after end of treatment, to determine through blood tests if HCV cure has been achieved.

What are the possible benefits and risks of participating?
Participants allocated to the extension treatment may benefit from an improved chance of cure, however this is not known for sure. There is a small risk of pain or bruising from blood testing.

Where is the study run from?
1. Royal London Hospital (UK)
2. King's College Hospital (UK)
3. St George's Hospital (UK)
4. Royal Free Hospital (UK)
5. North Manchester General Hospital (UK)
6. Chelsea & Westminster Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2015 to July 2019 (as of 08/10/2018)

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

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Additional identifiers

Clinical Trials Information System (CTIS)
2016-000599-87

Protocol serial number
33488

Study information

Scientific Title
Response guided therapy with sofosbuvir and velpatasvir for 12 or 24 weeks in patients with genotype 3 chronic hepatitis C virus: is longer therapy worthwhile?

Acronym
Extend-3

Study objectives
The aim of this study is to evaluate cure rates in patients with genotype 3 HCV cirrhosis and a slow early response to Epclusa, to evaluate if 24 weeks is better than 12 weeks of treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-West London & GTAC REC, 22/11/2016, ref: 16/LO/0879

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Drug

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Specialty: Hepatology, Primary sub-specialty: Hepatology; UKCRC code/ Disease: Infection/ Sequelae of infectious and parasitic diseases, Infection/ Viral hepatitis

Interventions
A total of 60 patients will be randomized (between weeks 8-12) to receive a total of 12 weeks of sofosbuvir/velpatasvir treatment (standard therapy) or 24 weeks of sofosbuvir/velpatasvir (extended therapy which is being studied in the trial). There will be 30 patients in each treatment group (1:1). Block randomization will be performed and participants stratified by compensated or decompensated cirrhosis at baseline.

Follow up is the same for both treatment groups – patients will be seen once/ month until 3 months after treatment end. At this point, SVR rates will indicate if the patient has been cured of hepatitis C virus infection.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Sofosbuvir, velpatasvir

Primary outcome(s)
Proportion of patients in each group (12 or 24 weeks of sofosbuvir/velpatasvir) with undetectable HCV RNA (below limit of quantification up to 15 IU/mL) in serum at 12 weeks (+ 4 weeks) after end of treatment (SVR12).

Key secondary outcome(s)
1. Proportion of patients in each group requiring premature treatment discontinuation, reported in patient notes, throughout the treatment period
2. Proportion of patients in each group who developed serious adverse events, reported in patient notes, throughout the trial period
3. Quality of life, measured as SF36 questionnaire scores, in each treatment group at end of study treatment and end of study follow-up (12 weeks post-treatment end)

Completion date
04/07/2019

Eligibility

Key inclusion criteria
1. Voluntarily signed informed consent form
2. Aged 18 years or older
3. Chronic HCV infection, defined by anti-HCV antibody or HCV RNA detection for greater than 6 months
4. Infected with genotype 3 HCV (identified by referring hospital)
5. Meets NHS England treatment criteria to commence sofosbuvir/velpatasvir
6. Pre-treatment HCV RNA >10,000 iu/mL (can be any time before treatment week 0)

7. HCV RNA > or equal to 30 iu/mL at treatment week 2 (+/- 3 days)
8. Has cirrhosis defined by: evidence of portal hypertension, OR APRI >2 plus AST:ALT ratio >1, OR radiological evidence of cirrhosis, OR fibroscan score >11.5kPa, OR liver biopsy showing cirrhosis
9. Patients with decompensated cirrhosis (variceal bleeding, ascites and encephalopathy) can be included
10. Patients with malignancy including hepatocellular carcinoma can be included
11. Patients with liver transplant can be included
12. Patients coinfected with chronic hepatitis B virus or human immunodeficiency virus can be included
13. Female subjects of childbearing potential must have documented negative pregnancy test prior to enrolment (negative urinary pregnancy test), and if engaged in heterosexual intercourse must use protocol specified method of contraception (see below) during study drug treatment and for 30 days after last dose
14. Male subjects engaged in heterosexual intercourse with a female of childbearing potential should protocol specified method of contraception during study drug treatment and for 30 days after last dose

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
25

Key exclusion criteria
1. Any of the above inclusion criteria not met
2. Any of the following criteria excludes a subject from enrolling into this study
3. Clinically-significant medical or psychiatric illness (other than chronic HCV) in the past, present, or being evaluated, that may interfere with participant treatment, safety, assessment or compliance with the protocol.
4. Severe renal impairment with eGFR <30 mL/min/1.73m2 or requiring dialysis
5. Alcohol consumption or illicit drug abuse likely to interfere with participant treatment, safety, assessment or compliance with protocol, as deemed by the investigator
6. Previous exposure to sofosbuvir (or other NS5B inhibitor) or NS5A inhibitor
7. Severe allergy to study drugs, its metabolites or formulation excipient (see SmPC for details)
8. Any investigational medicinal product ≤ 6 weeks prior to treatment start
9. Pregnant or nursing female, or males wishing to conceive during the period of study treatment + 30 days after
10. Patients who adhered to less than 90% of prescribed sofosbuvir/velpatasvir at screening

11. In accordance with the SmPC of sofosbuvir/velpatasvir concomitant use of the following medications are contraindicated:
11.1. Anticonvulsants - carbamazepine, phenytoin, phenobarbital, oxcarbazepine
11.2. Antimycobacterials – rifampicin, rifabutin, rifapentine
11.3. Antiretrovirals - efavirenz
11.4. St John's wort
11.5. Modafinil
11.6. Proton-pump inhibitors should be avoided and if necessary, should be administered 4 hours after at maximum doses equivalent to 20mg omeprazole per day
11.7. Amiodarone should be avoided and if necessary, close monitoring is required
12. Using effective contraception if of child-bearing potential

Date of first enrolment
05/04/2017

Date of final enrolment
01/10/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal London Hospital
Whitechapel Road
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Study participating centre
King's College Hospital
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SE5 9RS

Study participating centre
St George's Hospital
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Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
North Manchester General Hospital
Delaunays Road
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M8 5RB

Study participating centre
Chelsea & Westminster Hospital
369 Fulham Road
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SW10 9NH

Sponsor information

Organisation
Queen Mary University of London

ROR
https://ror.org/026zzn846

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
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository: Discovere (available at www.discoverecert.cerner.co.uk). Access can be granted to representatives from the Sponsor, host institution and regulatory authorities.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		05/07/2020	18/01/2021	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version v1.4	23/11/2016	16/03/2017	No	Yes
Protocol file	version 2.9.3	13/11/2016	05/10/2022	No	No