

Nucleos(t)ide withdrawal in Hepatitis B virus infection (NUC-B)

Submission date 07/11/2016	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 11/11/2016	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 22/07/2025	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Hepatitis B is a type of liver disease, which is caused by the hepatitis C virus (HBV). It can present as either a severe infection with a short duration (acute) or a persistent long term infection (chronic). If a person has a chronic HBV infection, over time the virus causes the liver to become irreversibly scarred (cirrhosis), eventually leading to liver failure. There are two main drug treatments available for treating a chronic HBV infection: interferons or nucleoside/nucleotide analogues. Interferons can have a lot of unpleasant side effects and rarely results in a cure so most patients choose to be treated with nucleoside/nucleotide analogues. Although these daily tablets have no side effects, most people using this treatment will need to continue taking them for the rest of their life. There is evidence from a recent study that if treatment with nucleoside/nucleotide analogues is stopped after a few years of treatment, some patients may be able to eliminate the virus. The aim of this study is to confirm the findings from this earlier study by seeing if stopping nucleoside/nucleotide analogue treatment can be safely stopped and lead to a cure.

Who can participate?

Adults with a long-term Hepatitis B infection who have been undergoing treatment with nucleoside/nucleotide analogues for less than 3 years.

What does the study involve?

Participants are randomly allocated to one of two groups. Those in the first group stop their nucleoside/nucleotide analogue treatment at the start of the study. Those in the second group stop their nucleoside/nucleotide analogue treatment at the start of the study for four weeks, before starting a course of interferon weekly injections for 16 weeks. After this, all treatment is stopped. Participants in both groups attend the clinic at regular intervals over the next three years and provide blood samples to test for signs of HBV.

What are the possible benefits and risks of participating?

There is a chance that stopping nucleoside/nucleotide analogue treatment (with or without interferon treatment) may allow the patient to be cured. There is a risk that participants may experience withdrawal symptoms when stopping their treatment or that they experience a worsening of their hepatitis (hepatitis flare) as the virus starts to replicate again.

Where is the study run from?
Ten NHS hospitals in England (UK)

When is the study starting and how long is it expected to run for?
June 2016 to August 2024

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
nucbtrial@imperial.ac.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2016-001010-17

IRAS number
187932

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
32555

Study information

Scientific Title
Nucleos(t)ide withdrawal in HBeAg negative hepatitis B virus infection to promote HBsAg clearance (NUC-B)

Acronym

NUC-B

Study objectives

The aim of this trial is to explore whether finite treatment with nucleos(t)ide analogues is feasible in patients with HBeAg (Hepatitis B 'e' antigen) negative chronic HBV (Hepatitis B Virus) infection.

Ethics approval required

Old ethics approval format

Ethics approval(s)

London - Central Research Ethics Committee, 26/08/2016, ref: 16/LO/1318

Study design

Randomised; Interventional; Design type: Treatment, Drug

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Specialty: Hepatology, Primary sub-specialty: Hepatology; UKCRC code/ Disease: Infection/ Viral hepatitis

Interventions

Patients will be electronically randomised using the InForm eCRF online custom built database to the two management arms in equal proportions using variable block sizes.

Control Arm: Patients will discontinue their nucleos(t)ide analogue treatment at baseline and be followed up for 3 years from randomisation.

Interferon Arm: Patients will discontinue their nucleos(t)ide analogue treatment at randomisation. No treatment will be given for 4 weeks, and then (i.e after the 4 week gap) patients will start pegylated interferon 180 mcg 2a and continue taking it weekly for a total of 16 weeks. They will then stop ALL treatment and be followed up for 3 years from randomisation.

During the follow-up the patients are required to attend the clinic at specified intervals so that their safety can be monitored throughout the study. At each of the visits, patients will have their vital signs checked and give blood samples. The blood samples will be used to measure levels of certain blood chemicals and thus evaluate the patient's liver function, the levels of HBV in the their body and their body's ongoing response to the HBV infection. The laboratory tests will allow us to evaluate the effects, on both the patient and the HBV levels in their body, of withdrawal from treatment and/or introduction of interferon treatment.

Intervention Type

Other

Phase

Phase II

Primary outcome measure

HBsAg (Hepatitis B surface antigen) is measured using standard laboratory ELISA assays at baseline and 3 years.

Secondary outcome measures

1. Efficacy is assessed at various timepoints after randomisation using various laboratory evaluations including immunology, virology and hepatology assessments. Specifically looking at the following:

1.1. The proportion of patients who achieve HBsAg loss who also have undetectable HBV DNA

1.2. The proportion of patients in each group who become inactive HBV carriers; i.e. achieve a sustained virological response (HBV DNA < 2000 IU/ml & normal ALT values) at 3 years

1.3. Magnitude of reduction in quantitative HBsAg levels at 1, 6, 12, 24 and 36 months

1.4. Magnitude of changes in antiviral T cells response at 1, 5, 6, 12, 24 and 36 months

1.5. Magnitude of changes in NK cells response at 1, 5, 6, 12, 24 and 36 months

2. Safety is assessed at various timepoints after randomisation using various laboratory evaluations. Specifically looking at the following:

2.1. The proportion of patients who achieve HBsAg loss who also have undetectable HBV DNA

2.2. The proportion of patients in each group who become inactive HBV carriers; i.e. achieve a sustained virological response (HBV DNA < 2000 IU/ml & normal ALT values) at 3 years

2.3. Magnitude of reduction in quantitative HBsAg levels at 1, 6, 12, 24 and 36 months

2.4. Magnitude of changes in antiviral T cells response at 1, 5, 6, 12, 24 and 36 months

2.5. Magnitude of changes in NK cells response at 1, 5, 6, 12, 24 and 36 months

Overall study start date

01/06/2016

Completion date

31/08/2024

Eligibility

Key inclusion criteria

1. Aged 18 years and over
2. Chronic HBV infection
3. HBeAg negative
4. Nucleos(t)ide analogues treatment for ≥ 3 years

5. HBV DNA < 400 IU/ml ≥2 years

6. Informed consent

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 240; UK Sample Size: 240

Key exclusion criteria

1. Cirrhosis at any time
2. HBeAg to anti-HBe seroconversion within the last 3 years
3. Interferon use in the last 3 years
4. Contraindications to interferon use
5. Participation in HBV-specific therapeutic vaccine studies within 12 months
6. HCV, HDV or HIV co-infection
7. Immunosuppressant use
8. Clinically significant comorbidities that, in the opinion of the investigator, render the patient unsuitable

Date of first enrolment

30/11/2016

Date of final enrolment

30/07/2018

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

St Mary's Hospital

Department of Hepatology

10th Floor

QEQM Building

London
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W2 1NY

Study participating centre
Kings College Hospital
Institute of Liver Studies
Denmark Hill
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Study participating centre
The Royal London Hospital
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Study participating centre
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Study participating centre
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Study participating centre
St George's Hospital
Blackshaw Road
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Study participating centre
Queen Elizabeth Medical Centre
Edgbaston
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B15 2TH

Study participating centre
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Beckett Street
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Study participating centre
Manchester Royal Infirmary
Oxford Road
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Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle-Upon-Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
Imperial College London

Sponsor details

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Sponsor type

University/education

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

Results will be disseminated at scientific meetings and through publications in relevant scientific journals.

Intention to publish date

28/02/2025

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type

[HRA research summary](#)

Details

Date created

Date added

26/07/2023

Peer reviewed?

No

Patient-facing?

No