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# Step-down affordable treatment for chronic HEPatitis B infection in Africa

**Submission date**
07/01/2014

**Recruitment status**
No longer recruiting

**Registration date**
31/03/2014

**Overall study status**
Completed

**Last Edited**
10/05/2021

**Condition category**
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

## Plain English summary of protocol

Background and study aims
Hepatitis B virus (HBV) is a virus which causes long term liver damage in people all over the world. It is very common in much of sub-Saharan Africa and southeast Asia. Some countries have more than 10% of the entire population with the virus. Zambia is a country with a high HBV prevalence approximately 10%. HBV causes liver cirrhosis and liver cancer after several decades of infection, but now this is preventable. It is known that the best way to treat people who have active HBV infection is to give them powerful drugs that stop the virus replicating. The old drugs that used to be used to treat hepatitis B (such as lamivudine) are very cheap but they are not very powerful and many people develop resistance to them so that they stop working after a period of time. The new drugs that are used to treat hepatitis B are more powerful and most people do not develop resistance. However, the new drugs may have more side effects in the long term and they are much more expensive. In many infections we know that starting treatment with a powerful drug and then reducing the treatment to a weaker drug is very effective. In London a small study of this approach has been tried in patients with hepatitis B with success in most cases. Specifically people who had been treated with the expensive new drug tenofovir and who were responding to treatment were changed to treatment with the weaker, cheaper, probably safer drug lamivudine. The great majority responded very well. The aim of this study is to find out whether this way of treating hepatitis B works in Lusaka, Zambia.

Who can participate?
80 Zambian adults, both sexes and aged 18 years or more, with HBV infection, already with evidence of some liver damage (using a marker in blood called ALT).

What does the study involve?
Participants take tenofovir, the best single drug currently available, for 12 months to suppress the virus, then step down to lamivudine treatment. The evidence suggests that after a period of complete viral suppression lamivudine failure may be much less likely. Participants are monitored very closely during the 6 months after stepping down to lamivudine.

What are the possible benefits and risks of participating?
The main benefit is that participants receive at least 18 months of powerful antiviral therapy. The principal risks are associated with the liver biopsy (bleeding, but only 1 in 3000 have this

problem), and the possibility that the infection may flare up aggressively at the end of the study. Past experience suggests that this is very uncommon. If successful, this approach could lead to a much more affordable treatment approach for Africans with HBV infection, of whom there are many tens of thousands.

Where is the study run from?
University Teaching Hospital, Lusaka (Zambia)

When is the study starting and how long is it expected to run for?
January 2014 to September 2017

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
1. Prof. Graham Foster, principal investigator
2. Prof. Paul Kelly and Dr Bright Nsokolo, chief investigators in Lusaka

# Contact information

### Type(s)
Scientific

### Contact name
Prof Graham Foster

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
Step HEP

# Study information

### Scientific Title

Step-down affordable treatment for chronic hepatitis B infection in Africa: feasibility of treatment strategy

## Acronym
Step HEP

## Study objectives
That a treatment regime of tenofovir for 48 weeks followed by lamivudine for 24 weeks effectively suppresses hepatitis B virus (HBV) replication in more than 50% of patients.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
University of Zambia Biomedical Research Ethics Committee, 24/05/2013, ref: 005-02-13

## Study design
Single group evaluation of feasibility of treatment strategy

## Primary study design
Interventional

## Secondary study design
Non randomised study

## Study setting(s)
Hospital

## Study type(s)
Treatment

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

## Health condition(s) or problem(s) studied
Hepatitis B infection

## Interventions
Patients will be given Tenofovir 300mg daily (orally) for 52 weeks and then lamivudine 100mg (orally) daily for 26 weeks. Patients will be followed up for 6 months after starting lamivudine.

## Intervention Type
Drug

## Phase
Not Applicable

## Drug/device/biological/vaccine name(s)
Tenofovir, lamivudine

### Primary outcome measure
Proportion of patients who successfully step down to lamivudine monotherapy with virological control of replication throughout

### Secondary outcome measures
1. Proportion of patients who, even if there is virological rebound, achieve successful control on re-introduction of tenofovir
2. Accuracy of ALT monitoring in comparison with viral load monitoring
3. Accuracy of HBsAg quantification compared to viral load monitoring

The primary and secondary outcomes will be assessed by virological measurements in blood samples obtained every 3 months.

### Overall study start date
06/01/2014

### Completion date
01/09/2017

## Eligibility

### Key inclusion criteria
1. HBV viral load >105 copies/ml
2. Alanine aminotransferase (ALT) >1.3 times upper limit of normal (which sets the criterion at 45 i.u./l)
3. Evidence of inflammation on liver biopsy
4. May be either e antigen negative (n=40) or positive (n=40)

### Participant type(s)
Patient

### Age group
Adult

### Sex
Both

### Target number of participants
80

### Key exclusion criteria
1. Histological or radiological evidence of cirrhosis
2. HIV infection
3. History of alcohol abuse or histological evidence of alcoholic liver disease
4. History of any long-term drug ingestion
5. Histological evidence of metabolic liver disease (haemochromatosis, Wilsons disease, a1-antitrypsin deficiency) or autoimmune liver disease [antibodies to M2 antigen, Perinuclear antineutrophil cytoplasmic antibodies (p-ANCA), nuclear antigens, microsomes or smooth muscle]
6. Histological or radiological evidence of schistosomiasis

7. Histological evidence of hepatitis D virus (HDV) infection
8. Virological evidence of active hepatitis C virus (HCV) or hepatitis E virus (HEV) infection

### Date of first enrolment
06/01/2014

### Date of final enrolment
31/12/2015

## Locations

### Countries of recruitment
Zambia

### Study participating centre
**University Teaching Hospital**
Lusaka
Zambia
-

## Sponsor information

### Organisation
Queen Mary University of London (UK)

### Sponsor details
Barts & The London School of Medicine Joint R&D office
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### Sponsor type
University/education

### ROR
https://ror.org/026zzn846

## Funder(s)

**Funder type**
Research council

**Funder Name**
Medical Research Council (MR/K007394/1)

**Alternative Name(s)**
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

# Results and Publications

**Publication and dissemination plan**
Not provided at time of registration

**Intention to publish date**

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

**IPD sharing plan summary**
Not provided at time of registration

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Other publications | baseline liver pathology | 01/09/2017 | 10/05/2021 | Yes | No |