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A platform study to evaluate investigational therapies in chronic hepatitis B infection

Submission date	Recruitment status	[X] Prospectively registered
25/09/2022	Stopped	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
28/09/2022	Stopped	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
27/03/2024	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The purpose of this research study is to test different experimental study drug(s) in people with chronic hepatitis B virus (HBV) infection. The main goals of the research study are to study if the experimental drugs are safe, how the study drugs interact with the patient's body, do the study drugs cause any side effects, can the study drugs reduce levels of HBV particles in the body, and measure how much study drugs are found in the blood over time.

Who can participate?
Adults with chronic HBV infection

What does the study involve?
The research study duration for each sub-protocol will have a screening period that could be up to 8 weeks, an on-treatment period that will have a minimum of 8 weeks, and a follow-up period that will have a minimum of 24 weeks. The sub-protocols will include different groups (or cohorts) and each group may evaluate different doses, different dosing schedules, and different combinations of the study drugs. Assignment to a cohort within a sub-protocol will be done in order based on available open cohorts. Study procedures include but are not limited to routine blood and urine tests, HBV blood tests, and physical examinations.

What are the possible benefits and risks of participating?
A possible benefit is that the study drugs may reduce viral particles in the participant's blood or help activate the immune system to fight HBV. Potential risks in participating are outlined in the participant's informed consent forms.

Where is the study run from?
Vir Biotechnology Inc (USA)

When is the study starting and how long is it expected to run for?
January 2022 to March 2027

Who is funding the study?
Vir Biotechnology Inc (USA)

Who is the main contact?
Briana (Project Manager) (New Zealand)
Briana.Kawaihae@novotech-cro.com

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2022-002014-16

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
VIR-MHB1-200

Study information

Scientific Title
A platform study evaluating the efficacy and safety of investigational therapies in participants with chronic hepatitis B infection (PREVAIL)

Acronym
PREVAIL

Study objectives
Phase Ib sub-protocols will be exploratory, and no formal hypothesis testing will be conducted. In phase II sub-protocols, the null hypothesis is that the response rate is the same as in NRTI-suppressed patients. It is assumed that ≤ 2% of NRTI-suppressed patients will achieve a response rate. The alternative hypothesis will be described in the sub-protocol.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/09/2022, (Central) Health & Disability Ethics Committee (Ministry of Health, 133 Molesworth Street, PO Box 5013, Wellington, 6011, New Zealand; +64 (0)800 4 38442; hdecs@health.govt.nz), ref: 2022 FULL 12906.

Study design
Multicentre parallel-assignment open-label Phase Ib/II platform study

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 participant information sheet

Health condition(s) or problem(s) studied
Chronic hepatitis B infection

Interventions
Sub-Protocol A (STRIVE): Participants will receive combination therapy with VIR-3434, VIR-2218, PEG-IFNα, and/or TD/TDF up to 48 weeks total
Assigned interventions:
Drug: VIR-3434
VIR-3434 given by subcutaneous injection
Drug: VIR-2218
VIR-2218 given by subcutaneous injection
Drug: TD/TDF
TD/TDF given orally
Drug: PEG-IFNα
PEG-IFNα given by subcutaneous injection

Sub-Protocol B (THRIVE):
Participants will receive combination therapy with VIR-3434, VIR-2218, and/or TD/TDF up to 44 weeks total
Assigned interventions:
Drug: VIR-3434
VIR-3434 given by subcutaneous injection
Drug: VIR-2218
VIR-2218 given by subcutaneous injection
Drug: TD/TDF
TD/TDF given orally

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
VIR-2218, VIR-3434, pegylated interferon alfa-2a (PEG-IFNα or Pegasys®), tenofovir disoproxil /tenofovir disoproxil fumarate (TD/TDF; Viread®)

Primary outcome measure
1. Proportion of participants achieving sustained suppression of HBV DNA (< lower limit of quantification [LLOQ]) at 24 weeks after discontinuation of all treatment
2. Proportion of participants achieving sustained suppression of HBV DNA (< LLOQ) with HBsAg loss (< 0.05 IU/mL) at 24 weeks after discontinuation of all treatment

3. Proportion of participants with Hepatitis B surface antigen (HBsAg) loss (<0.05 IU/ml) at the end of treatment
4. Proportion of participants with HBsAg loss (<0.05 IU/ml) at 24 weeks post-end of treatment
5. Mean change in serum HBsAg from baseline across time points in the study

STRIVE:
6. Proportion of participants with HBsAg loss (< 0.05 IU/ml) at the end of treatment

THRIVE:
7. Proportion of participants with HBsAg loss (<0.05 IU/ml) at the end of treatment

All outcomes measured using drawn blood

Secondary outcome measures

1. Proportion of participants with treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) during the study
2. Proportion of participants with serum HBsAg ≤ 10 IU/ml at end of treatment
3. Proportion of participants with serum HBsAg ≤ 10 IU/ml at 24 weeks post-end of treatment
4. Serum HBsAg levels and change from baseline across time points in the study
5. Serum HBsAg level at nadir during the study
6. Time to achieve nadir of serum HBsAg during the study
7. Time to achieve serum HBsAg loss (< 0.05 IU/ml)
8. Proportion of participants with HBsAg loss with anti-HBs seroconversion at end of treatment and at 24 weeks post-end of treatment

STRIVE:
9. Proportion of participants with HBsAg loss (< 0.05 IU/mL) at 24 weeks post-end of treatment
10. Proportion of participants achieving sustained suppression of HBV DNA (< LLOQ) after discontinuation of all treatment:
10.1. At 24 weeks
10.2. At the F48 Follow-Up visit
11. Proportion of participants achieving sustained suppression of HBV DNA (< LLOQ) with HBsAg loss (< 0.05 IU/ml) after discontinuation of all treatment:
11.1. At 24 weeks
11.2. At the F48 Follow-Up visit
12. For HBeAg-positive participants: proportion of participants with HBeAg loss (undetectable HBeAg) and/or anti-HBe seroconversion
13. Incidence and titers of anti-drug antibodies (ADA; if applicable) to VIR-3434
14. Mean change in serum HBsAg level from baseline across time points in the study
15. Proportion of participants achieving HBV DNA (< LLOQ) across time points in the study
16. Proportion of participants achieving ALT ≤ ULN across time points in the study

THRIVE:
9. Proportion of participants with HBsAg loss (< 0.05 IU/mL) at 24 weeks post-end of treatment
10. Proportion of participants achieving sustained suppression of HBV DNA (< LLOQ) after discontinuation of all treatment:
10.1. At 24 weeks
10.2. At 48 weeks
11. Proportion of participants achieving sustained suppression of HBV DNA (< LLOQ) with HBsAg loss (< 0.05 IU/mL) after discontinuation of all treatment
11.1. At 24 weeks
11.2. At 48 weeks

12. Incidence and titers of anti-drug antibodies (ADA; if applicable) to VIR-3434
13. Mean change in serum HBsAg level from baseline across time points in the study
14. Proportion of participants achieving HBV DNA (< LLOQ)
All outcomes measured using drawn blood

Overall study start date
30/01/2022

Completion date
05/04/2023

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Male or female aged 18 years old and over
2. Chronic HBV infection for >/= 6 months
3. A Body Mass Index (BMI) less than 18 kg/m2 or greater than 35 kg/m2

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Up to 90 (STRIVE) and up to 60 (THRIVE)

Key exclusion criteria
1. History or current suspicion of malignancy diagnosed or treated within 5 years
2. Any clinically significant medical or psychiatric condition that may interfere with study intervention, assessment, or compliance with the protocol or otherwise makes the participant unsuitable for participation in the study
3. History or evidence of drug or alcohol abuse
4. History of hepatic decompensation

Date of first enrolment
18/10/2022

Date of final enrolment
30/04/2025

Locations

Countries of recruitment
New Zealand

Study participating centre
Auckland City Hospital
2 Park Road, Grafton
Auckland
New Zealand
1010

Study participating centre
Middlemore Clinical Trials
Esme, Green Building 100 Hospital Road, Middlemore Hospital
Auckland
New Zealand
2025

Study participating centre
P3 Research Ltd. (Tauranga)
Suite 11, Promed House, 71 Tenth Avenue
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3110

Study participating centre
Waikato Hospital
183 Pembroke Street
Hamilton
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Sponsor information

Organisation
VIR Biotechnology (United States)

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Sponsor type
Industry

Website
https://www.vir.bio/

ROR
https://ror.org/030pjfg04

Organisation
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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Vir Biotechnology

Alternative Name(s)
Vir Biotechnology Inc, Vir Biotechnology, Inc., Vir

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
A clinical study report for each sub-protocol will be written and may be provided to the appropriate regulatory authorities. This clinical study may be registered, and its results posted on public registries in compliance with local and/or regional regulations. Site-specific results of this study may be published or presented at scientific meetings subject to the terms and requirements of the clinical trial agreement.

Intention to publish date
01/03/2022

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date