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An efficacy and safety study of a combination of JNJ-73763989, nucleos(t)ide analogs (NA), and a programmed cell death protein receptor-1 (PD-1) inhibitor in chronic hepatitis B participants

Submission date
04/03/2022

Recruitment status
No longer recruiting

Registration date
24/05/2022

Overall study status
Completed

Last Edited
14/05/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims:
The purpose of this study is to look at if treating people with hepatitis B virus (HBV) infection with the study drugs JNJ-73763989 ('JNJ-3989' for short, a liver targeted antiviral for chronic hepatitis B), nivolumab (a PD-1 inhibitor) and nucleos(t)ide analogs (NUC) is safe and will increase your chance of losing hepatitis B surface antigen (HBsAg) (a sign of your hepatitis B infection).
JNJ-3989 is not approved for use by any Regulatory Authority. Nivolumab is approved for the treatment of some cancers and other indications at higher doses than in this study. It is not approved for the treatment of HBV infection. NUC is approved for the treatment of chronic hepatitis B. JNJ-3989 is given in clinic as an injection. Nivolumab is given in clinic as an infusion into the vein. NUC is your current hepatitis B treatment tablet.

Who can participate?
This study will include adults with chronic hepatitis B between the ages of 18 and 55 years.

What does the study involve?
This study consists of a Screening Phase, a Treatment Phase and a Follow-up Phase. Participants will receive several JNJ-3989 injections during the treatment period. Nivolumab will be given either once or several times depending on the treatment group. Participants will continue their current NUC daily throughout the study. Treatment groups will be randomly assigned which means that the chance of being assigned to each treatment group is 1 in 2 (50%).
At study visits a participant will have procedures such as blood and urine tests, physical examinations, ECGs, fibroscans and ultrasounds. Study participation is expected to last between 76-80 weeks.

What are the possible benefits and risks of participating?
Taking part in this study may improve a participant's hepatitis B. However, this cannot be guaranteed because JNJ3989 and the PD1 inhibitor are still under investigation as treatments. Not all possible side effects and risks related to JNJ3989 and the PD1 inhibitor are known. It is possible that unexpected side effects may arise or may be life threatening. To minimise the risk associated with this, participants are frequently reviewed at every visit for side effects and adverse events. Participants are educated to report any such problems to the study staff without delay. Any serious adverse events that a reported to the sponsor are reviewed by a specialist drug safety team.
The participant information sheet, which will be signed by every participant agreeing to participate in the study, includes a detailed section with all known risks to participating in the study.

Where is the study run from?
Janssen-Cilag International NV is the sponsor for this study. The study will be run at multiple healthcare locations both within the UK and around the world.

When is the study starting and how long is it expected to run for?
March 2022 to May 2024

Who is funding the study?
Janssen Research and Development LLC (USA)

Who is the main contact?
Lucy Marshall, JanssenUKRegistryQueries@its.jnj.com

Contact information

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Additional identifiers

EudraCT/CTIS number
2021-005132-33

IRAS number
1005023

ClinicalTrials.gov number
NCT05275023

Secondary identifying numbers
73763989PAHPB2008, IRAS 1005023, CPMS 51860

Study information

Scientific Title
A phase 2 open-label trial to evaluate safety, efficacy, tolerability, and pharmacodynamics of a combination of JNJ-73763989, nucleos(t)ide analogs, and a PD-1 inhibitor in chronic hepatitis B patients

Acronym
OCTOPUS-1

Study objectives
To evaluate efficacy of the study treatment, based on HBsAg (hepatitis B surface antigen, a protein produced by the Hepatitis B virus) levels in the blood at Follow Up.
1. To determine the safety and tolerability of the study treatment.
2. To evaluate efficacy in terms of changes in HBsAg levels from baseline over time during the study treatment and follow-up periods.
3. To evaluate efficacy in terms of HBsAg seroclearance (the removal of HBsAg from the blood) /seroconversion (the development of antibodies against HBsAg in the blood) during the study treatment and follow-up periods.

4. To evaluate the efficacy as measured by blood markers, including hepatitis B DNA (HBV DNA) in the blood (the viral load) during the study treatment and follow-up period.
5. To measure the proportion of participants who experience an increase in their hepatitis B viral load throughout the study.
6. To evaluate the pharmacokinetics (what the body does to the drug) of JNJ-3989 and optionally of NA (also known as NUC) and/or nivolumab.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/05/2022, Wales Research Ethics Committee (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 1686 252101; Wales.REC5@wales.nhs.uk), ref: 22/WA/0077

Study design
Interventional double blind randomized parallel group controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Chronic Hepatitis B Virus Infection

Interventions
The total duration of the study is 76 – 80 weeks which includes a screening period, a treatment period and a follow-up period. Participants will be randomly assigned to one of two treatment arms by an online interactive web randomisation system tool.

Arm 1 will receive JNJ-73763989 subcutaneous (SC) injections and single dose of programmed cell death protein receptor-1 (PD-1) inhibitor as intravenous (IV) infusion. Participants will also receive background treatment with NA (either tenofovir disoproxil, tenofovir alafenamide [TAF] or entecavir [ETV])
Arm 2 will receive Participants will receive JNJ-73763989 SC injections and multiple doses of PD-1 inhibitor as IV infusion. Participants will also receive background treatment with NA (either tenofovir disoproxil, TAF or ETV).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
JNJ-73763989

Primary outcome measure
Percentage of Participants who Achieve Hepatitis B Surface Antigen (HBsAg) Seroclearance determined at follow up week 24.

Secondary outcome measures
1. Percentage of Participants who Experience Adverse Events (AEs) of Interest, monitored up to week 72. An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. AEs of interest are significant AEs that are judged to be of special interest because of clinical importance, known class effects or based on nonclinical signals.
2. Number of Participants with Adverse Events (AEs) by Severity, monitored up to week 72. An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Severity of adverse event will be graded by using Division of AIDS (DAIDS) grading scale ranges from Grade 1 to Grade 5. Grade 1 indicates a mild event, Grade 2 indicates a moderate event, Grade 3 indicates a severe event, Grade 4 indicates a potentially life-threatening event, Grade 5 indicates death.
3. Number of Participants with Immune Related Adverse Events (AEs) by Severity, monitored up to week 72. An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/ biological agent under study. Severity of immune related AEs will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0. Severity scale ranges from Grade 1 (Mild) to Grade 5 (Death). Grade 1= Mild, Grade 2= Moderate, Grade 3= Severe, Grade 4= Life-threatening and Grade 5= Death related to adverse event.
4. Number of Participants with Abnormalities in Vital Signs, Physical Examinations, Clinical Laboratory Tests, 12-lead Electrocardiograms (ECGs), monitored up to week 72. Number of participants with abnormalities in vital sign measurements (including pulse rate and blood pressure, both systolic and diastolic); physical examinations (including height at screening, body weight, skin examination, general appearance, eyes, ears, nose, throat, cardiovascular system, respiratory system, gastro-intestinal system and mucous; clinical laboratory tests (including hematology, clinical chemistry and urinalysis); 12-lead ECGs (heart rate, PR, QRS, QT) will be reported.
5. Change From Baseline in Hepatitis B Surface Antigen (HBsAg) Levels, measured from baseline up to week 72.
6. Percentage of Participants with Change in HBsAg Levels Below/Above Different Cut-offs Over Time, monitored up to week 72.
7. Time to Achieve HBsAg Seroclearance/ Seroconversion measured up to week 72.
Change from Baseline in Hepatitis B Virus (HBV) Deoxyribonucleic Acid (DNA) Levels, measured from baseline up to week 72.
8. Percentage of Participants with HBV DNA and Hepatitis B e Antigen (HBeAg) Levels Below /above Different Cut-offs, monitored up to Week 72.
9 Percentage of Participants with Virologic Breakthrough, monitored up to week 72.
10. Percentage of participants with virologic breakthrough (confirmed on-treatment HBV DNA increase by greater than [>]1 log10 international unit per milliliter [IU/mL] from nadir or

confirmed on-treatment HBV DNA level >200 IU/mL in participants who had HBV DNA level less than [<] lower limit of quantification [LLOQ] of the HBV DNA assay) will be reported.
11. Plasma Concentrations of JNJ-3989 and its Metabolites (JNJ-3924 and JNJ 3976) measured up to week 24.
12. Plasma Concentrations of NA (Tenofovir disoproxil, Tenofovir Alafenamide [TAF] or Entecavir [ETV]) (Optional) measured up to week 24. Plasma concentrations of NA (tenofovir disoproxil, TAF or ETV) will be reported.
13. Serum Concentrations of PD-1 Inhibitor (Optional) measured up week 24.

Overall study start date
01/03/2022

Completion date
29/05/2024

Eligibility

Key inclusion criteria
1. Participants must have chronic hepatitis B virus (HBV) infection
2. Participants must have fibroscan liver stiffness measurement less than or equal to (<=) 9.0 kilopascal (KpA) or a liver biopsy result classified as metavir F0-F2

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
44

Total final enrolment
37

Key exclusion criteria
1. Participants with evidence of hepatitis A virus infection (hepatitis A antibody immunoglobulin IgM), hepatitis C virus (HCV) infection (HCV antibody), hepatitis D virus (HDV) infection (HDV antibody), hepatitis E virus (HEV) infection (Hepatitis E antibody IgM) or human immunodeficiency virus type-1 (HIV-1) or human immunodeficiency virus type-2 (HIV-2) infection (laboratory confirmed) at screening
2. History or evidence of clinical signs or symptoms of hepatic decompensation, including but not limited to portal hypertension, ascites, hepatic encephalopathy, esophageal varices
3. Participants with history or signs of cirrhosis or portal hypertension or signs of hepatocellular carcinoma (HCC) or clinically relevant renal abnormalities
4. Participants with personal/familial history/indicative of immune-mediated disease risk

Date of first enrolment

25/05/2022

Date of final enrolment
25/11/2022

Locations

Countries of recruitment
Canada

Czech Republic

England

France

Italy

Malaysia

Russian Federation

Scotland

Spain

Taiwan

Türkiye

United Kingdom

Study participating centre
Glasgow Royal Infirmary
16-20 Alexander Parade New Lister Building Clinical Research Facility
Glasgow
United Kingdom
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Study participating centre
Imperial College London and Imperial College Healthcare NHS Trust
Liver & Anti-Viral Unit, 10th Floor, QEQM
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Study participating centre
Kings College Hospital
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Janssen-Cilag International N.V.

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development LLC

Alternative Name(s)
Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals

Intention to publish date
11/03/2025

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson & Johnson is available at www.janssen.com/clinicaltrials/transparency . As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No