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First-in-Human study of a medication called ALG-020572 to determine how it works in people with Chronic Hepatitis B

Submission date
14/01/2022

Recruitment status
No longer recruiting

Registration date
01/03/2022

Overall study status
Completed

Last Edited
01/04/2022

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
Chronic Hepatitis B (CHB) infection affects the liver and is a global public health problem associated with significant disease and death. The study drug, ALG-020572, is being developed as a potential new treatment for CHB infection. This is the first time that ALG-020572 will be administered to humans. The study aims to investigate whether ALG-020572 is safe and well-tolerated when given at different doses, and will also measure the levels of the drug in the blood at different times.

Who can participate?
Adult healthy volunteers will be invited to participate in Part 1 of the study and adult patients with Chronic Hepatitis B will be invited to participate in Part 2 of the study.

What does the study involve?
The study is comprised of two parts: Part 1, and Part 2.

Part 1 will involve healthy volunteers who will be divided into up to 8 different cohorts. Each cohort will be comprised of 8 participants who will receive a single dose of either the study drug or a placebo (an identical-looking drug with no active medicine) administered as an injection below the skin (subcutaneously). Within each cohort, 6 participants will receive the study drug and 2 will receive the placebo, which will be determined at random, without the participants knowing which they have received. The dose of the study drug in cohort 1 will be 50 mg, and the subsequent doses for later cohorts will be determined based on the safety and tolerability of the preceding data. Within each Part 1 cohort, at least 4 Asian participants (50%) will be enrolled in order to evaluate the potential effect of ethnicity on drug metabolism.

Part 2 will consist of up to 48 patients with Chronic Hepatitis B. Patients will be randomised to receive 7 doses of either the study drug or placebo (with 3 of every 4 participants receiving the study drug, and 1 of every 4 participants receiving the placebo) via subcutaneous injection. The Part 2 doses will be confirmed following analysis of the data from Part 1, and ongoing data from Part 2.

What are the possible benefits and risks of participating?
The purpose of this study is not to provide a treatment for Chronic Hepatitis B. Participants may or may not receive any benefits from participation in this study. However, by taking part in this study, they may contribute new information that will help benefit other people who have a medical problem similar in the future. Participants may experience side effects while participating in the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen. Medicines may be given to help lessen side effects. For example, participants may be given a pain medication such as ibuprofen if they develop pain. Many side effects may be mild and go away soon after stopping the test drug. In some cases, side effects can be serious, long-lasting, or may never go away. The study doctor will review all the potential risks associated with this study with the participants.

Where is the study run from?
Aligos Therapeutics, Inc. (USA)

When is the study starting and how long is it expected to run for?
From June 2021 to June 2023

Who is funding the study?
Aligos Therapeutics, Inc. (USA)

Who is the main contact?
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Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003904-42

Integrated Research Application System (IRAS)
1004256

ClinicalTrials.gov (NCT)
NCT05001022

Protocol serial number
ALG-020572-401, IRAS 1004256, CPMS 50373

Study information

Scientific Title
A phase 1, double-blind, randomized, placebo-controlled, first-in-human study of subcutaneously administered ALG-020572 to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics after single ascending doses in healthy volunteers (part 1) and multiple doses in subjects with Chronic Hepatitis B (part 2)

Study objectives
The study drug, ALG-020572, is safe and well-tolerated in patients with Chronic Hepatitis B.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/12/2021North East - York Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ; +44 (0)207 1048091; york.rec@hra.nhs.uk), ref: 21/NE/0203

Study design
Phase I, multicentre, randomized, placebo-controlled, dose-escalation study

Primary study design
Interventional

Study type(s)
Screening

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

Interventions
This Phase 1 study consists of two parts: Part 1, and Part 2.

Part 1 will consist of up to 64 healthy participants, enrolled in up to 8 different cohorts, including two optional cohorts (cohorts 7 and 8). Each cohort will be comprised of 8 participants who will receive a single dose of ALG-020572 or placebo in a 3:1 ratio (ALG-020572:placebo), administered subcutaneously (SC). The starting dose in cohort 1 will be 50 mg, and subsequent doses will be determined based on the safety and tolerability of the preceding data. Within each Part 1 cohort, at least 4 Asian participants (50%) will be enrolled in order to evaluate the potential effect of ethnicity on drug metabolism.

Part 2 will consist of up to 48 Chronic Hepatitis B (CHB) patients, approx. 24 patients who are Hepatitis B e-antigen (HBeAg) negative and 24 patients who are HBeAg positive. Patients that

are HBeAg negative will enroll into cohorts 1, 2, or 3, and patients that are HBeAg positive or negative will enroll into cohorts 4, 5, or 6. Patients will be randomised to receive 7 doses of ALG-020572 or placebo in a 3:1 ratio (ALG-020572:placebo) via SC injection. The Part 2 doses will be confirmed following analysis of the data from Part 1, and ongoing data from Part 2.

Randomization will be used to minimize bias in the assignment of subjects to study medication groups, to increase the likelihood that known and unknown subject attributes (e.g., demographic and baseline characteristics) are evenly balanced across study medication groups, and to enhance the validity of statistical comparisons across study medication groups. Optional cohorts in Part 2 may be conducted in an open-label manner and are intended to build upon the safety database established in HV and HBeAg negative subjects by evaluating the clinical profile of ALG-020572 in other CHB populations.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ALG-020572

Primary outcome(s)
Safety and tolerability will be measured using the number and severity of treatment emergent adverse events as assessed by DAIDS v2.1 for up to 60 days for Part 1, and up to 120 days for Part 2

Key secondary outcome(s))
1. Pharmacokinetic parameters of ALG-020572 in plasma will be measured using blood samples collected between 0 and 1080 h (between predose and 45 days) to calculate the following:
1. 1. Maximum Plasma Concentration (Cmax)
1. 2. Area under the concentration time curve (AUC)
1. 3. Time to maximum plasma concentration (Tmax)
1. 4. Half-time (t1/2)
1. 5. Minimum Plasma Concentration (Cmin)
2. Change in HBsAg from baseline through Day 120 in multiple-dose HBV-infected patients measured using blood samples collected at screening and 1, 2, 4, 8, 11, 15, 22, 29, 36, 45, 60, 90, and 120 days

Completion date
20/06/2023

Eligibility

Key inclusion criteria
Parts 1 and 2:
1. Signed informed consent form (ICF) indicating that the participants understand the purpose of, and procedures required for, the study, and are willing to participate in the study
2. In the Investigator’s opinion, the participant is able to understand and comply with protocol requirements, instructions, and protocol stated restrictions and is likely to complete the study as planned

3. Female participants must have a negative serum (β human chorionic gonadotropin) pregnancy test at screening and a negative urine pregnancy test at Day -1 (Part 1) or Week -1 Screening (Part 2)
4. Female participants must not be a woman of childbearing potential (WOCBP) defined as either:
4.1. Postmenopausal. A postmenopausal state is defined as no menses for 12 months without an alternative medical explanation. A high follicle-stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). In the absence of 12 months of amenorrhea, 2 FSH measurements at least 3 months apart and in the postmenopausal range must be documented. If there is a question about menopausal status in women on HRT, the woman will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if she wishes to continue HRT during the study.
4.2. Permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy.
5. Male participants must agree to wear a condom during sexual intercourse and their female sexual partners must agree to use highly effective means of contraception. These contraceptive measures must be implemented, at a minimum, from the start of dosing until at least 120 days after the last dose. Contraceptive use should be consistent with local regulations regarding the use of contraceptive methods for subjects participating in clinical studies.
6. Participants must have a 12-lead electrocardiogram (ECG) that meets the following criteria (ECG intervals will be based on the mean value of triplicate ECGs collected at screening):
6.1. Heart rate ≥40 bpm and ≤100 bpm
6.2. QT interval corrected for heart rate (QTc) according to Fridericia's formula (QTcF) ≤450 ms (males) or ≤470 ms (females)
6.3. QRS interval <120 ms
6.4. PR interval ≤200 ms (Part 1) or ≤220 ms (Part 2)
6.5. In addition to fulfilling the above ECG criteria, ECG morphology must have no clinically significant abnormalities observed.
Retesting of an apparently exclusionary ECG will be allowed once without prior approval from the Sponsor. Participants with a retest (triplicate) ECG without clinically significant abnormalities as per this inclusion criterion may be included.
7. Participants must be deemed to be in good overall health by the Investigator on the basis of a medical evaluation that reveals the absence of any clinically significant abnormality and includes a physical examination, medical history, vital signs, and the results of blood chemistry, blood coagulation and hematology tests, and a urinalysis performed at screening
8. Participants must be willing and able to adhere to the Prohibited Medications and Special Precautions specified in the study protocol

Part 1 only:
1. Healthy volunteers
2. Aged ≥18 years and ≤55 years
3. Body mass index (BMI) of ≥18.0 and ≤32.0 kg/m²
4. Asian participants must be of Chinese, Japanese, Taiwanese, Korean, or Hong Kong ancestry. Asian participants should preferably be of first-generation Asian ancestry.

Part 2 only:
1. Aged ≥18 years and ≤75 years
2. Body mass index (BMI) of ≥18.0 and ≤35.0 kg/m²
3. Virally suppressed (VS) participants must have each of the following:
3.1. On a stable HBV treatment regimen. Defined as currently receiving HBV NA (any commercially available oral formulation of entecavir, tenofovir disoproxil fumarate, or tenofovir

alafenamide fumarate) treatment for ≥6 months prior to screening and have been on the same treatment regimen for ≥3 months at the time of screening
3.2. Screening HBV DNA level <20 IU/ml
3.3. Screening serum HBeAg <LLOQ (for HBeAg negative participants) and ≥LLOQ (for HBeAg positive participants)
3.4. Serum alanine aminotransferase (ALT) values ≤1.2× upper limit of normal (ULN) during screening
4. Currently not treated (CNT)/treatment naïve (TN) participants must have each of the following (if applicable):
4.1. Screening HBV DNA level ≥2000 IU/ml
4.2. Screening serum HBeAg <LLOQ (for HBeAg negative participants) and ≥LLOQ (for HBeAg positive participants)
4.3. Serum ALT values ≤5× ULN during screening
4.4. Either TN (have never received treatment with HBV antiviral medicines (NA, interferon) or investigational anti-HBV agents) or CNT (have not been on treatment with approved (NA, interferon-based treatment) or investigational HBV antiviral medicines within 6 months prior to randomization)
5. Participants must have serum HBsAg ≥100 IU/ml at screening

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Parts 1 and 2:
1. Any current or previous illness that, in the opinion of the Investigator, might confound the results of the study or pose an additional risk in administering study drug to the participant, or that could prevent, limit, or confound the protocol-specified assessments or study results' interpretation. This may include, but is not limited to, renal, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, dermatologic, hematologic, rheumatologic, psychiatric, neoplastic, or metabolic disturbances.
2. Past history of cardiac arrhythmias, risk factors for Torsade de Pointes syndrome (e.g. hypokalemia, family history of long QT Syndrome), or history or clinical evidence of significant or unstable cardiac disease at screening (such as angina, congestive heart failure, myocardial infarction, diastolic dysfunction, significant arrhythmia, coronary heart disease, clinically significant ECG abnormalities, moderate to severe valvular disease or uncontrolled hypertension)
3. History of clinically significant drug allergy such as, but not limited to, sulfonamides or drug allergy witnessed in previous studies with experimental drugs
4. Personal or family history of chronic inflammatory skin disease (e.g. psoriasis, atopic dermatitis, drug-related rash, chronic urticaria)

5. Recent (within 1 year of randomization) history or current evidence of use of amphetamines, barbiturates, narcotics or other drugs of abuse/recreational drug use. Use of these drugs under physician supervision (e.g. prescription narcotics for known pain disorder) and cannabis use is not exclusionary.
6. Excessive use of alcohol. Defined as regular consumption of ≥14 standard drinks/week for women and ≥21 standard drinks/week for men. For a current definition of a standard drink, please refer to the National Institute on Alcohol Abuse and Alcoholism website (https://www.niaaa.nih.gov/what-standard-drink).
7. Positive alcohol test at screening and Day -1 (Part 1) and Week -1 Screening (Part 2)
8. Current Hepatitis A (HAV) infection, confirmed by hepatitis A antibody immunoglobulin M (IgM) at screening
9. Current Hepatitis C virus (HCV) infection (confirmed by HCV antibody and/or HCV RNA). Participants who have been treated and achieved sustained virologic response >1 year prior to screening with HCV RNA LLOQ, target not detected, remain eligible.
10. Current Anti-HEV IgM positive and/or detectable HEV RNA level (only applies to participants with a history of living or traveling to an HEV epidemic area)
11. Current Human immunodeficiency virus type 1 (HIV-1) or HIV-2 infection, confirmed by antibodies at screening
12. Acute infection at the time of randomization. If an acute infection is considered resolved prior to randomization, the participant remains eligible.
13. Received an unapproved investigational agent or vaccine within 4 weeks (or 5 half-lives, whichever is longer) prior to randomization
14. Currently participating in another clinical or medical interventional research study
15. Any Grade >1 laboratory abnormality (as defined by the Division of AIDS Toxicity Grading Scale) that is considered clinically significant by the Investigator at screening
16. Clinically significant abnormal vital signs (evaluated in the (semi) recumbent position after 5 min of rest) confirmed with retesting after at least 5 min of additional rest
17. Physical examination findings that are considered clinically significant and likely to adversely impact study conduct and/or interpretation are exclusionary
18. Major surgery (e.g. requiring general anesthesia) within 12 weeks before screening, or will not have fully recovered from surgery, or have surgery planned during the time the participant is expected to participate in the study, or within 12 weeks after the last dose of study drug. Participants with planned surgical procedures to be conducted under local anesthesia may participate.
19. Unwilling to undergo repeat SC study drug administrations (Part 2)
20. Employees of the Sponsor, Investigator, or study site, with direct involvement in the proposed study or other studies under the direction of that Investigator or study site, as well as family members of the employees or the Investigator.
21. Note:
21.1. Retesting of abnormal laboratory or vital sign values that appear to be exclusionary will be allowed once without requiring prior approval from the Sponsor. Retesting must take place under appropriate conditions during an unscheduled visit in the screening phase. Participants with a retest value that is no longer exclusionary may be included.
21.2. Isolated, asymptomatic laboratory abnormalities without apparent clinical correlates are not necessarily exclusionary. The Investigator and Sponsor will determine if such abnormalities fulfill exclusion criterion 15.
21.3. Investigators should ensure that all study eligibility criteria, and none of the exclusion criteria, have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after the screening, but before the first dose of the study drug is given, such that they no longer meet all criteria, then they should be excluded from participation in the study.

Part 1 only:
1. Unwilling to abstain from alcohol use for 48 h prior to the start of, and through the end of study follow up
2. Evidence of heart block or bundle branch block on ECG
3. Any clinically significant hepatologic disease, including Hepatitis B infection. Defined as the presence of any antigen or antibody associated with CHB (i.e. qualitative HBsAg and HBcAb).
4. Renal dysfunction. Defined as estimated creatinine clearance <90 ml/min/1.73 m^2 at screening, calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. CKD-EPI should not be corrected for participants of African ancestry.

Part 2 only:
1. Positive for anti-HBs antibodies.
2. Hepatitis D virus (HDV) infection (confirmed by serum anti-HDV antibodies and/or HDV RNA)
3. Any history or current evidence of hepatic decompensation such as variceal bleeding, spontaneous bacterial peritonitis, ascites, hepatic encephalopathy, or active jaundice (within the last year)
4. History or current evidence of cirrhosis
5. Participants with liver fibrosis that is classified as Metavir Score ≥F3 liver disease based on either a liver biopsy result within 1 year prior to screening, or at the time of screening, or FibroScan™ liver stiffness measurement ≥8.5 kPa within 6 months prior to screening, or at the time of screening.
Conventional imaging procedures (e.g. liver ultrasound, computed tomography, or magnetic resonance imaging) and serum marker panels are not allowed to rule out severe fibrosis or cirrhosis.
A prior history of cirrhosis (i.e. F4) that has improved (≤F2) on long-term treatment for CHB remains exclusionary.
6. Signs of hepatocellular carcinoma (HCC) on an abdominal ultrasound performed within 6 months prior to screening or at the time of screening. In case of suspicious findings on conventional ultrasound, the participant may still be eligible if HCC has been ruled out by a more specific imaging procedure (e.g. contrast-enhanced ultrasound, computed tomography, or magnetic resonance imaging).
7. Any evidence of liver disease of non-HBV etiology. This includes, but is not limited to, hepatitis virus infections mentioned in exclusion Criterion 8, drug- or alcohol-related liver disease, autoimmune hepatitis, hemochromatosis, Wilson's disease, α-1 antitrypsin deficiency, primary biliary cirrhosis, primary sclerosing cholangitis, or any other non-HBV liver disease considered clinically significant by the Investigator. Gilbert's disease is not exclusionary.
8. Any evidence of heart block or bundle branch block is exclusionary except 1st-degree heart block or incomplete right bundle branch block, if not clinically significant in the opinion of the Investigator and does not require monitoring or treatment
9. Any of the following laboratory values:
9.1. Platelet count ≤120,000 /mm^3
9.2. Bilirubin (total, direct) >1.2× ULN (unless Gilbert's is suspected)
9.3. International Normalization Ratio (INR) >1.2× ULN
9.4. Serum albumin less than the lower limit of normal
9.5. Serum alpha feto-protein (AFP) >ULN. If serum AFP >ULN but <50 ng/ml, the participant remains eligible if CT/MRI with contrast excludes evidence of HCC.
9.6. Estimated creatinine clearance <70 ml/min/1.73 m^2 at screening, calculated by the CKD-EPI formula. CKD-EPI should not be corrected for participants of African ancestry.
9.7. HgbA1c >8%

Date of first enrolment

14/12/2021

Date of final enrolment
14/11/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College Hospital
Denmark Hill
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Study participating centre
St George's Hospital
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Sponsor information

Organisation
Aligos Therapeutics, Inc.

Funder(s)

Funder type
Industry

Funder Name
Aligos Therapeutics, Inc.

Results and Publications

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes