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Study of the efficacy and safety of parsaclisib in participants with primary warm autoimmune hemolytic anemia

Submission date
15/11/2022

Recruitment status
No longer recruiting

Registration date
03/02/2023

Overall study status
Ongoing

Last Edited
07/02/2024

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
Primary warm autoimmune hemolytic anaemia (wAIHA) is a rare acquired condition where your body attacks its own red blood cells.
The purpose of this Study is to compare the effects and safety of parsaclisib versus placebo in people with wAIHA.

Who can participate?
Approximately 100 adults with wAIHA from all over the world will participate in this study.

What does the study involve?
Participants will be in this study for a total of 15 months from Screening to be able to participate in a 24 week Extension Period and the final 12 week Follow-up Period.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
Risks associated with taking parsaclisib are not yet fully known. As of 30 March 2021, 601 participants received to parsaclisib as a monotherapy (33 participants for AIHA or Sjogren's syndrome; 561 for advanced malignancies). AEs seen 33 participants who received parsaclisib for AIHA or Sjogren's syndrome include: Very Common (fever (21%), diarrhea (18%), headache (15%), nausea (12%), common (cough, neutropenia, peripheral edema, rash, and vomiting). Detailed AEs are included in the IB and ICF. The ICF will be reviewed with the patient. Safety checks will be performed. Sites are trained on reporting of AEs. Study drug interruption and discontinuation guidelines is based on AEs. The investigator may decrease dose from 2.5 mg QD to 1 mg QD for intolerable AEs. Remote visits are scheduled to eliminate travel burden. Participants must agree to take PJP prophylaxis during the study and for 2- 6 months after the last dose. Risks are mitigated by ensuring site staff have the training and qualifications to perform procedures. Risks are: blood collection -discomfort, bleeding or bruising at the collection site, fainting, swelling, infection or very rare a blood clot and if a participant is fasting

hunger or dizziness. ECG electrode pads may cause temporary irritation/itchiness. Participants may not achieve an improvement in Hgb levels and levels may even continue to decrease. If a participant does not achieve and improvement in Hgb by Week 6 the investigator may prescribe rescue therapy. Participants may remain on prednisone (or equivalent) ≤20 mg QD during the study. For participants who achieve an improvement in Hgb, the protocol contains a recommended corticosteroid tapering schedule to potentially alleviate any risks associated with chronic steroid use. The risks to an unborn or nursing child are unknown, measures to avoid pregnancy are detailed. The Sponsor will review AEs at regular meetings. An external Data Safety Monitoring Committee (DSMB) will review the safety.

Where is the study run from?
Incyte Corporation (USA)

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

Who is funding the study?
Incyte Corporation (USA)

Who is the main contact?
Dr Catherine Bagot, catherine.bagot@ggc.scot.nhs.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05073458

Clinical Trials Information System (CTIS)
2021-002844-66

Integrated Research Application System (IRAS)
1004495

Central Portfolio Management System (CPMS)

49579

Protocol serial number
INCB50465-309

Study information

Scientific Title
A phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of parsaclisib in participants with primary warm autoimmune hemolytic anemia (PATHWAY)

Acronym
PATHWAY

Study objectives
Primary objective:
To evaluate the efficacy of parsaclisib in the treatment of participants with wAIHA.

Key secondary objective:
To further evaluate the efficacy of parsaclisib in the treatment of participants with wAIHA.

Other secondary objectives:
1. To further evaluate the efficacy of parsaclisib in the treatment of participants with wAIHA.
2. To evaluate the safety and tolerability of parsaclisib in participants with wAIHA.

Exploratory objectives:
1. To further evaluate the efficacy of parsaclisib.
2. To evaluate the participant's quality of life and other PROs.
3. To characterize serum biomarkers and/or leukocyte profiles in participants with wAIHA treated with parsaclisib.
4. To evaluate PK of parsaclisib in participants with wAIHA.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, ref: 22/NW/0383

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Primary Warm Autoimmune Hemolytic Anemia

Interventions
Group A: Parsaclisib
Participants will receive parsaclisib for 24 weeks (double-blind period). Parsaclisib will be administered QD orally.
A participant who completed the double-blind period and tolerates the study treatment in the investigator's opinion will continue into open-label period for an additional 24 weeks.
Participants may then continue to receive parsaclisib for a long-term extension period.

Group B: Placebo followed by Parsaclisib
Participants will receive placebo for 24 weeks (double-blind period). Placebo will be administered QD orally
Participants who completed the double-blind period will receive parsaclisib in the 24 week open-label period. Participants may then continue to receive parsaclisib for a long-term extension period.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Parsaclisib, INCB050465

Primary outcome(s)
Proportion of participants attaining a durable hemoglobin response, defined as hemoglobin ≥ 10 g/dL with an increase from baseline of ≥ 2 g/dL not attributed to rescue therapy at ≥ 3 of the 4 available visits at Week 12 and/or later during the 24-week double-blind treatment period.

Key secondary outcome(s))
1. Proportion of participants with a ≥ 3-point increase in FACIT-F score Up to Week 24. Increase is measured by Functional Assessment of Chronic Illness Therapy - Fatigue questionnaire. The FACIT-F is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days.
2. Proportion of participants with a 50 m increase in a 6MWT. Up to Week 24. Defined as an increase of 50 m using the Six-minute walk test, a self-paced measurement of the distance that a participant can quickly walk on a flat, hard surface in a period of 6 minutes.
3. Change in FACIT-F score. Up to 3 years. Change will be measured by Functional Assessment of Chronic Illness Therapy - Fatigue questionnaire. The FACIT-F is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days.
4. Percent Change in FACIT-F. Up to 3 years. Will be measured by Functional Assessment of Chronic Illness Therapy - Fatigue questionnaire. The FACIT-F is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function over the past 7 days.
5. Change in haemoglobin. Up to 3 years. Changes will be measured and compared in the hematology panel.
6. Percentage change in haemoglobin. Up to 3 years. Percentage change will be measured and compared in the hematology panel.
7. Proportion of participants who received transfusions. Up to 48 weeks
8. Change in corticosteroid dose from baseline. Up to Week 24
9. Percentage change from baseline in daily corticosteroid dose. Up to Week 24
10. Proportion of participants who required rescue therapy at any visit. Up to 48 weeks. Rescue

therapy will include new/increased dose of corticosteroids, transfusions, intravenous immunoglobulin (IVIG), and Erythropoietin.
11. Number of Participants with Treatment Emergent Adverse Events (TEAE). Up to 3 years. Defined as any adverse event either reported for the first time or worsening of a pre-existing event after first dose of study drug.

Completion date
22/04/2027

Eligibility

Key inclusion criteria
1. Ability to comprehend and willingness to sign a written ICF for the study.
2. Men or women, age ≥18 years at the time of signing the ICF.
3. Diagnosis of primary wAIHA based on the presence of hemolytic anemia and serological evidence of anti-erythrocyte antibodies,
detectable by a DAT positive for IgG only or IgG plus C3d.
Note: A DAT performed at screening is preferred; however, prior documentation of DAT results within 3 months of randomisation is permitted.
4. Participants who were inadequately controlled with, were intolerant to, or have a contraindication to other therapies. There is no limit to the number of prior treatment regimens.
5. Hemoglobin ≥6.5 to <10 g/dL with symptoms of anemia as assessed by the investigator at screening (Hgb as determined by local laboratory).
6. FACIT-F score ≤43 at screening.
7. Willingness to avoid pregnancy or fathering children based on the criteria below.
7.1. Male participants with reproductive potential must agree to take appropriate precautions to avoid fathering children (with 99% certainty) from screening through 90 days after the last dose of study drug and must refrain from donating sperm during this period. Permitted methods in that are at least 99% effective preventing pregnancy should be communicated to the participants and their understanding confirmed.
7.2. Female participants who are WOCBP must have a negative serum pregnancy test at screening and a negative urine pregnancy test before randomisation and must agree to take appropriate precautions to avoid pregnancy (with 99% certainty) from screening through 90 days after the last dose of study drug and must refrain from donating oocytes during this period. Permitted methods in that are at least 99% effective preventing pregnancy should be communicated to the participants and their understanding confirmed.
7.3. A female participant not considered to be of childbearing potential is eligible.
Note: This criterion does not apply to women of nonchildbearing potential (i.e., surgically sterile with a hysterectomy and/or bilateral oophorectomy OR postmenopausal, defined as amenorrhea at least 12 months before screening, confirmed by FSH levels at screening).
8. Willingness to receive PJP prophylaxis during the study period from Day 1 through at least 2 to 6 months after the last dose of study drug.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Women currently pregnant or breastfeeding or participants expecting to conceive or father children within the projected duration of the study, starting with the screening visit through 90 days from the date of last dose of study drug.
2. A diagnosis of other types of AIHA; CAD, cold agglutinin syndrome, mixed-type AIHA or paroxysmal cold hemoglobinuria.
3. Warm AIHA suspected to be secondary to a lymphoproliferative malignancy or secondary to an autoimmune disease (eg, systemic lupus
erythematosus, Castleman's disease, Sjögren's syndrome, or other autoimmune diseases) or diagnosis of Evans syndrome
4. A splenectomy less than 3 months before randomization.
5. Concurrent conditions or history of other diseases:
5.1. History or clinical manifestations of significant unstable metabolic, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal, urological, neurological, or psychiatric disorders.
5.2. Current or previous malignancy within 5 years of study entry, except basal or squamous cell skin cancer with removal considered to be
curative, superficial bladder cancer, prostate intraepithelial neoplasm, carcinoma in situ of the cervix, or other noninvasive or indolent
malignancy without sponsor approval.
5.3. Clinically significant cardiac disease, including unstable angina, acute myocardial infarction, and/or cardiac conduction issues within 6 months of randomisation.
5.4. Current New York Heart Association Class II to IV congestive heart failure or uncontrolled arrhythmia.
6. Known diagnosis of anti-phospholipid syndrome or history of persistent anti-phospholipid antibodies.
7. Hepatitis B (HBV) or hepatitis C (HCV) infection: Participants who are positive for the hepatitis B surface antibody or hepatitis B core antibody will be eligible if they are negative for HBV-DNA; these participants should be considered for prophylactic antiviral therapy. Participants who are positive for the anti-HCV antibody will be eligible if they are negative for HCV-RNA.
8. Known HIV infection or positivity on immunoassay.
9. History or presence of an abnormal ECG that, in the investigator's opinion, is clinically meaningful. Participants with screening QTc interval > 470 milliseconds for males and > 480 milliseconds for females (corrected by Fridericia) are excluded. In the event that a single QTcF is > 470 milliseconds for males or > 480 milliseconds for females, the participant may enroll if the average QTcF for triplicate ECGs is < 470 milliseconds for males or < 480 milliseconds for females.
10. Use of the following medications:
10.1. Treatment with rituximab within 6 weeks of randomisation
10.2. Use of immunosuppressive therapy within 28 days of randomisation.
10.3. Use of IVIG or erythropoietin within 2 weeks of randomisation.
10.4. Chronic or current active infectious disease requiring systemic antibiotics, antifungal, or antiviral treatment or exposure to a live vaccine within 30 days of randomisation.
10.5. Use or expected use during the study of any prohibited medications, including potent

CYP3A4 inhibitors or moderate or potent CYP3A4 inducers, within 14 days or 5 halflives (whichever is longer) before randomisation.
11. Current treatment or treatment within 30 days or 5 half-lives (whichever is longer) before randomisation with another investigational medication, or current enrollment in another investigational drug and/or device protocol.
12. Known hypersensitivity or severe reaction to parsaclisib or its excipients.
13. Unable to swallow oral medication, malabsorption syndrome, disease significantly affecting gastrointestinal function, total resection of the stomach or small bowel, ulcerative colitis, symptomatic inflammatory bowel disease, or partial or complete bowel obstruction.
14. Current alcohol or drug use that, in the opinion of the investigator, will interfere with the participant's ability to comply with the dose regimen and study evaluations.
15. Participants who, in the opinion of the investigator, are unable or unlikely to comply with the dose regimen and study evaluations.
16. Any condition that would, in the investigator's judgment, interfere with full participation in the study, including administration of study drug and attending required study visits; pose a significant risk to the participant; or interfere with interpretation of study data.
17. Prior treatment with parsaclisib or another PI3Kδ, or a pan-PI3K inhibitor for any indication.
18. Participants with exclusionary laboratory values at screening

Date of first enrolment
12/08/2021

Date of final enrolment
29/02/2024

Locations

Countries of recruitment
United Kingdom

Austria

Belgium

Canada

France

Germany

Israel

Italy

Japan

Netherlands

Poland

Spain

Ukraine

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Incyte Corporation

Funder(s)

Funder type
Industry

Funder Name
Incyte

Alternative Name(s)
Incyte Corporation, Incyte Corp

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Incyte shares data with qualified external researchers after a research proposal is submitted. These requests are reviewed and approved by a review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

The trial data availability is according to the criteria and process described on https://www.incyte.com/our-company/compliance-and-transparency

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