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A Phase III placebo-controlled efficacy and safety study of mocravimod as an adjunctive and maintenance treatment in acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation

Submission date
21/04/2022

Recruitment status
No longer recruiting

Registration date
29/06/2023

Overall study status
Ongoing

Last Edited
19/07/2024

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Priothera S.A.S., the study sponsor, is looking at the effects of a new medicine called mocravimod. Transplantation is a standard treatment for acute myeloid leukaemia (AML) but it is not always successful and the disease often returns. Donor T cells from a healthy donor can prevent the return of AML by attacking the patient's cancer cells. Stem cell transplantation can cause complications. One major complication is graft-versus-host-disease (GvHD). This is where the donated cells attack the patient's healthy cells and can cause damage to the patient's body. When given together with other standard-of-care drugs, mocravimod may help to block the migration of donated lymphocytes (a type of white blood cells that can attack other cells) to other parts of the body. This may retain the donated lymphocytes in the lymphoid tissues, such as bone marrow, to attack the remaining cancer cells to prevent the patient's AML from returning.
The aim of this study is to assess the efficacy and safety of mocravimod compared to a placebo in adult participants with AML undergoing blood cell transplantation (HCT). These patients are at risk of developing complications linked with HCT namely graft-versus-host disease (GvHD), which occurs when the donated cells attack healthy cells. GvHD is currently prevented with a combination of drugs, yet this still remains a major potential complication of HCT.
In this study, mocravimod will be used in addition to the standard-of-care GvHD preventative drugs as it may block the movement of the donated cells, preventing them from attacking other parts of the body, thereby reducing GvHD. These donated cells then remain in the bone marrow tissue and may also attack the remaining cancer cells, thus preventing the AML from returning.

Who can participate?
Patients aged between 18 and 75 years with AML undergoing allogeneic HCT

What does the study involve?
Two thirds of participants will receive study drug and one third will receive placebo. Some of the study visits will take place whilst participants are hospitalised to undergo the transplantation. Participants will receive mocravimod or placebo daily, starting before the transplantation, up to 1 year after. The status of the AML disease will be periodically assessed by bone marrow aspirate and/or biopsy throughout the study. An independent committee will review the safety of all participants on a regular basis and may decide to discontinue participation if they observe any safety findings. The effects on relapse-free survival, overall survival, the occurrence of GvHD and quality of life will also be assessed.
Participants will only receive mocravimod/placebo during the treatment phase of the trial. Each participant ideally should complete the relapse-free survival and/or overall survival follow-up phase. The data support a clinical study to assess the efficacy and safety of mocravimod as an adjunctive and maintenance therapy for allogeneic HCT for a longer duration of treatment up to 1 year, which will be provided. The study drug will not be available for the treatment of patients in the study after the study treatment has ended. When the treatment period ends, the participants will receive the best available treatment that the study doctor considers most appropriate for their disease.

What are the possible benefits and risks of participating?
Mocravimod is a new drug that is still under investigation to be used as an add-on and maintenance treatment to reduce the risk of the disease coming back while reducing the risk of GvHD. There may or may not be a medical benefit to participants. The study medication may help AML or it may not. The participant's AML might not get better while they are in this study. Information from this study will add to what is known about the disease. This new knowledge might help researchers come up with new tests or medications to help others in the future. Mild to serious side effects of the study drug may be experienced but these are likely to be outweighed by the potential benefits. Participants will be given medicines to help lessen the main side effects. Women of childbearing potential will be informed of the risks associated with pregnancy and will be offered options to avoid pregnancy. Breach of confidentiality may be a concern therefore a participant will only be identified by means of a participant identification number and their identity will never be disclosed.
1. Blood sampling may cause distress, mild pain, redness, or bruising – good practices will minimise the discomfort
2. Bone marrow/tissue biopsy sampling may cause pain and discomfort – pain medication will be provided
3. Eye examination: Dilation of the eyes can cause blurry vision and light sensitivity - participants can wear sunglasses and have someone drive them home afterwards
4. Administration of fluorescent dye may cause a yellow tint to the skin and urine will be yellow-orange
5. A MUGA scan with a small amount of radioactive material will be injected - with a small dose of radioactivity the potential health risks from radiation exposure are low compared with the potential benefit
6. A CT scan. The small amount of radiation a person receives that poses a risk to their health is considered justified by the potential benefits. Women must test negative for pregnancy before the scan.

Where is the study run from?
Hammersmith Hospital, Catherine Lewis Centre (UK)

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

Who is funding the study?
Priothera S.A.S. (France)

Who is the main contact?
Malika Souquieres, malika.souquieres@priothera.com

Plain English summary under review with external organisation

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Additional identifiers

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IRAS number
1004810

ClinicalTrials.gov number
NCT05429632

Secondary identifying numbers
PKRPC001, IRAS 1004810, CPMS 49498

Study information

Scientific Title
A prospective randomized, double-blind, placebo-controlled, multi-center Phase III study to evaluate the efficacy and safety of mocravimod as an adjunctive and maintenance treatment in adult acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation

Acronym
MO-TRANS

Study objectives
1. To compare the efficacy of mocravimod to that of placebo
2. To compare mocravimod's effect on overall survival (OS) to that of placebo

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 17/06/2022, London - Brighton & Sussex Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford , London , E20 1JQ, United Kingdom; +44 (0)207 104 8202, +44 (0)2071048258, +44 (0)2071048189; brightonandsussex.rec@hra.nhs.uk), ref: 22/LO/0345

Study design
Randomized placebo-controlled double-blind parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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
Acute myeloid leukemia

Interventions
All eligible participants will be centrally assigned to randomised IMP using an IxRS -Interactive Voice Response System (IVRS) or Interactive Web Response System (IWRS).

1. 3 mg of mocravimod orally once per day for 12 months
2. 1 mg of mocravimod orally once per day for 12 months
3. Placebo orally once per day for 12 months

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Mocravimod

Primary outcome measure
Relapse-free survival (RFS) measured using patients' medical records at 12 months

Secondary outcome measures
Overall survival (OS) measured using patients' medical records at 24 months

Overall study start date
13/04/2022

Completion date
30/05/2027

Eligibility

Key inclusion criteria
Current inclusion criteria:
1. Subjects with a diagnosis of AML (excluding acute promyelocytic leukemia) according to the World Health Organization (WHO) 2022 classification of AML and related precursor neoplasms, including AML with myelodysplasia-related gene mutations.
2. Subjects with European LeukemiaNet (ELN) high-risk or intermediate-risk AML in CR1, intermediate-risk AML in CR1, or AML of any risk in CR2. (Complete remission with incomplete

count recovery [CRi] is also allowable).
3. Subjects planned to undergo allogeneic HCT
4. Life expectancy ≥6 months at screening
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
6. Male or female, age ≥18 years and ≤75 years

Previous inclusion criteria:
1. Subjects with a diagnosis of AML (excluding acute promyelocytic leukemia) according to the World Health Organization (WHO) 2016 classification of AML and related precursor neoplasms, including secondary AML after an antecedent hematological disease (e.g. myelodysplastic syndrome) and therapy-related AML
2. Subjects with European LeukemiaNet (ELN) high risk AML in CR1, intermediate-risk AML in CR1 if MRDpos, or AML of any risk in CR2. Complete remission is defined as: <5% marrow blasts by morphologic examination and no circulating peripheral blasts and blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count ≥1.0 x 10e9/L (1000/µl); platelet count ≥100 x 10e9/L (100 000/µl)
3. Subjects planned to undergo allogeneic HSCT
4. Life expectancy ≥6 months at screening
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
6. Male or female, age ≥18 years and ≤75 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
249

Key exclusion criteria
Current exclusion criteria as of 19/07/2024:
1. Planned use of anti-thymocyte globulin (ATG), alemtuzumab, abatacept for GvHD prophylaxis
2. Planned use of serotherapy during conditioning, including ATG and alemtuzumab
3. Planned ex vivo major graft manipulation, including T-cell depletion or CD34+ selection
4. Subjects having received prior allogeneic HCT or recipients of a solid organ transplant
5. Immunosuppressive drugs for concomitant disease. Subjects must be able to be off prednisone (> 10 mg/day) or other immunosuppressive medications for at least 3 days prior to the start of treatment of the study. Physiologic replacement dosing of hydrocortisone is permissible.
6. Require treatments for cardiac dysfunction
7. Subjects with acute promyelocytic leukemia

8. Blast crisis of chronic myeloid leukemia
9. Cardiac dysfunction
10. Pulmonary dysfunction
11. Significant liver disease or liver injury or known history of alcohol abuse, chronic liver or biliary disease. Hepatic dysfunction as defined by aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) >2.5 x upper limit of normal (ULN); or total bilirubin >1.5 x ULN
12. Renal dysfunction with creatinine clearance <45 ml/min by the Cockcroft-Gault formula
13. History of stroke or intracranial hemorrhage within 1 year prior to screening
14. Active clinically significant infection (viral, bacterial, or fungal) that requires ongoing antimicrobial therapy and in the judgment of the investigator represents a risk to proceeding with HCT

Previous exclusion criteria:
1. Planned use of anti-thymocyte globulin (ATG), post-transplantation cyclophosphamide, sirolimus, mycophenolate mofetil, abatacept, or any approved or non-approved medication other than MTX plus CsA or MTX plus TAC for GVHD prophylaxis
2. Planned use of serotherapy during conditioning, including ATG and alemtuzumab
3. Planned ex vivo major graft manipulation, including T-cell depletion or CD34+ selection
4. Subjects having received prior allogeneic HSCT or recipients of a solid organ transplant
5. Immunosuppressive drugs for concomitant disease. Subjects must be able to be off prednisone (>10 mg/day) or other immunosuppressive medications for at least 3 days prior to the start of treatment of the study. Physiologic replacement dosing of hydrocortisone is permissible.
6. Require treatments for cardiac dysfunction
7. Subjects with acute promyelocytic leukemia
8. Blast crisis of chronic myeloid leukemia
9. Cardiac dysfunction
10. Pulmonary dysfunction
11. Significant liver disease or liver injury or known history of alcohol abuse, chronic liver or biliary disease. Hepatic dysfunction as defined by aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) >2.5 x upper limit of normal (ULN); or total bilirubin >1.5 x ULN
12. Renal dysfunction with creatinine clearance <60 ml/min by the Cockcroft-Gault formula
13. History of stroke or intracranial hemorrhage within 1 year prior to screening
14. Active clinically significant infection (viral, bacterial, or fungal) that requires ongoing antimicrobial therapy and in the judgment of the investigator represents a risk to proceeding with HSCT

Date of first enrolment
30/06/2022

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
Argentina

Brazil

France

Germany

Israel

Italy

Japan

Poland

Romania

Spain

Switzerland

Taiwan

United Kingdom

United States of America

Study participating centre
-
United Kingdom
-

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Priothera S.A.S.

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Submission to regulatory authorities
4. Other

The sites and the investigators may publish/present the data after the publication of the multi-center data. All study information is reported in a clinical study report, which will be published and submitted to the MHRA ensuring identity protection.

Intention to publish date
01/07/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No