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Phase II study of roginolisib in uveal melanoma patients

Submission date 17/09/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol
Registration date 01/11/2024	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 01/11/2024	**Condition category** Eye Diseases	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Roginolisib is a new tablet that uses the body's immune system to attack cancer cells. Clinical studies and experiments show that it stops a specific type of cell (T-reg cells) lowering the body's immune response. The main purpose of the study is to see whether a patient with a type of eye cancer (uveal melanoma), that has spread to other parts of the body, has an improved survival when taking roginolisib as compared to a standard treatment that would normally be prescribed for this disease. The secondary objectives of the study are to provide more information on how well tolerated roginolisib is across 2 dose levels; the impact the treatment may have on overall well-being and the number of healthcare resources needed to give this treatment; the pharmacokinetics (how the body interacts with the treatment); and, to assess any changes in the tumour cells and immune cells that infiltrate cancer tissue and in the blood.

Who can participate?

Patients aged over 18 years old with advanced or metastatic uveal melanoma

What does the study involve?

In this study, patients will be divided into three groups based on a random schedule. The groups will be in a 2:1:1 ratio. Group 1 will receive 80 mg of Roginolisib daily (50 patients). Group 2 will receive a treatment chosen by the investigator (25 patients). Group 3 will receive 40 mg of Roginolisib daily (10 patients). Recruitment for Group 3 will stop once 10 patients are enrolled. The study duration for each patient depends on how long they are treated and they will be followed up for about 2 years from the start of their treatment. After 10 patients are enrolled in Group 3, new patients will be divided into Groups 1 and 2 in a 2:1 ratio. The treatment each patient receives will be decided by a computer-generated list.

What are the possible benefits and risks of participating?

Potential risks and burdens are explained to the participants in the Main PICD quoted: number of routine tests performed that could be uncomfortable or painful. Another disadvantage is that participants will have several hospital visits to schedule, which may disturb their daily life.

Females: should ensure that they use effective contraception as it is possible that if the study drug is given to a pregnant woman it may harm the unborn child. The following highly effective

methods are considered to be used:
•Birth control that uses both oestrogen and progesterone hormones to prevent ovulation, available as pills, vaginal rings, or skin patches.
•Birth control that uses only progesterone hormone to stop ovulation, available as pills, injections, or implants.
•Intrauterine device (IUD) (a small device placed inside the uterus to prevent pregnancy
•Intrauterine hormone-releasing system (IUS) (a small device placed inside the uterus that releases hormones to prevent pregnancy
•Bilateral tubal occlusion (blockage of both fallopian tubes. Fallopian tubes connect the ovaries to the uterus)
•Vasectomised partner (a partner who has had a vasectomy, a procedure to prevent them from being able to father children
•Sexual abstinence (not having sex)

Pregnant women must not therefore take part in this study. Women who can become pregnant will be asked to have a pregnancy test before and during taking part to exclude any possibility of pregnancy. If they or their partner can become pregnant, they must make sure to use a highly effective contraceptive method (including sexual abstinence) during the study and for a minimum of one month after the last study drug administration. Women who become pregnant while taking part in the study should immediately tell their study doctor to discuss appropriate measures to be followed. If they are lactating (breastfeeding), they cannot take part in the study because it is not known whether this drug is present in human breast milk. They should also not breastfeed for one month after the last study drug administration.

Males: Male patients must ensure that they use a barrier form of contraception such as a condom or abstain from sexual relations during the study and for one month after the last roginolisib administration. Males should refrain from donating sperm from the day of the first dose of the study drug, throughout the study and until 3 months after the last dose of the study drug. If your partner becomes pregnant whilst they are taking part in the study then she should talk to her doctor.

Blood samples: the risks that come with taking blood samples include mild pain where the needle enters the skin and later maybe bruises. In rare cases it may cause a blood clot or the injection place may be infected. In each study visit about 36 ml (2.5 tablespoons) of blood will be taken from you.

Genetic analysis: The leftover samples may be stored for up to 10 years in a secure biorepository, at which point they will be destroyed. The samples will not be sold to other people or companies.

Tumour assessment: Obtaining a Biopsy: Participants may feel some discomfort as the biopsy needle is inserted. Sometimes a further ultrasound, CT scan or chest X-ray may be taken to confirm that there are no subsequent problems, for example bleeding as a result of the biopsy. The problems associated with obtaining tissue from your tumour can include bleeding, infection and wound healing problems.

Electrocardiogram (ECG) (Heart Tracing): although the ECG test itself is painless, being connected to the ECG machine involves the preparation of the skin on the chest (such as shaving) to place the sensors. The sensors are sticky patches that are attached to the chest. Skin irritations are rare but could occur from the electrodes or gel that is used. The skin irritation usually disappears when the patches are removed. They may experience some pain when the patches are removed.

CT scan: Participants may be exposed to radiation if a CT scan is used. The dose from each CT scan of your body is about the same as they would receive from 4 to 8 years' natural background radiation. In this study, medical imaging for assessment of your tumour is in accordance with established standard practice for tumour assessments. A contrast agent may need to be taken by mouth and/or injected into your vein to make certain organs and disease sites visible on the scan. Oral contrast may cause side effects such as nausea, constipation, diarrhoea, and stomach bloating. Pain, bruising, redness, swelling, or into your vein. It is normal to experience a warm, flushing feeling when the contrast material is given. They may have an allergic reaction to the contrast material that may cause rash, hives, shortness of breath, wheezing, and itching, and rarely may cause your heart to stop beating ("cardiac arrest").

Where is the study run from?
iOnctura SA, Switzerland

When is the study starting and how long is it expected to run for?
September 2024 to June 2027

Who is funding the study?
iOnctura SA, Switzerland

Who is the main contact?
Dr Paul Nathan, p.nathan@nhs.net

Contact information

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Public, Scientific

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Additional identifiers

EudraCT/CTIS number
2024-514333-37

IRAS number
1010248

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IOA-244-201, IRAS 1010248

Study information

Scientific Title
A phase II, multi-centre, open-label, randomised study to evaluate the anti-tumour activity of roginolisib in patients with advanced/metastatic ocular/uveal melanoma

Acronym
OCULE-01

Study objectives
To evaluate clinical efficacy of roginolisib as single agent, against Investigator´s choice of therapy by assessment of overall survival (OS).

To evaluate clinical efficacy of roginolisib, as single agent, using Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 and also using survival probability.
To further evaluate the safety profile of roginolisib as a single agent.
To assess the pharmacokinetic (PK) concentrations of roginolisib as single agent.
To assess the Quality of Life (QoL) impact of roginolisib vs Investigator's choice via patient-reported outcome (PRO).
To further evaluate and compare the safety of roginolisib 40 vs 80 mg.
To assess the health care resource utilisation for patients receiving roginolisib vs Investigator's choice.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Pending approval; ref: 24/SW/0113

Study design
Phase II multi-centre open-label randomized controlled study

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, Medical and other records

Study type(s)
Safety, Efficacy

Participant information sheet

Health condition(s) or problem(s) studied
Medical condition: Advanced Metastatic Ocular/Uveal Melanoma
Medical condition in lay language: Eye cancer
Therapeutic areas: Diseases [C] - Eye Diseases [C11]

Interventions
Patients will be in two stages i.e., will be randomised into 3 groups, as follows, in the ratio 2:1:1 according to a randomisation schedule:
• Arm 1 (Active treatment arm): Roginolisib oral tablet 80 mg daily (n=50)
• Arm 2 (Control arm): Investigator's choice of therapy (n=25)
• Arm 3 (Active treatment arm): Roginolisib oral tablet 40 mg daily (n=10*)
*Note: Arm 3 recruitment will be closed once 10 patients have been randomised.
The total duration of the study for each patient depends on the duration of the study treatment. Patients will be followed up for approximately 2 years from the start of treatment.
At the second stage i.e., once 10 patients have been randomised in Arm 3, the patients will be randomised into Arms 1 and 2 in the ratio 2:1: according to a randomisation schedule.
The treatment assigned to each patient will be determined according to a computer-generated randomisation list.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response, Pharmacogenetic, Pharmacogenomic, Diagnosis, Therapy

Phase
Phase II

Drug/device/biological/vaccine name(s)
Roginolisib [hemi fumarate] [Roginolisib hemi fumarate]

Primary outcome measure
Overall survival (OS) measured using data collected in medical records to evaluate the clinical efficacy of roginolisib as a single agent, against Investigator’s choice of therapy in patients followed for 24 months from the last patient enrolled

Secondary outcome measures

1. Progression-free survival (PFS) measured from the date of the first dose of IMP until the earliest date of disease progression, as determined by radiographic/objective disease assessment per RECIST v1.1, every 8 weeks whilst on treatment
2. Objective response rate (ORR) defined as the percentage of patients with a Complete Response (CR) or Partial Response (PR), measured every 8 weeks whilst on treatment
3. Duration of response (DOR) defined as the time from the date of first documented response (CR, PR) by RECIST v1.1 until the date of documented progression or death in the absence of disease progression, measured every 8 weeks whilst on treatment
4. Time to response defined as the time from the date of the first dose of IMP until the date of the first documented objective response, measured every 8 weeks whilst on treatment
5. Disease control rate (DCR) defined as the proportion of patients with a Best Objective Response (BOR) of CR, PR, or Stable Disease (SD) recorded at ≥8 weeks (±1 week), measured every 8 weeks whilst on treatment
6. Clinical benefit rate (CBR) defined as the proportion of patients with a BOR of CR, PR, or SD recorded at Cycle 5 Day 1, measured at Cycle 5 - approximately 16 weeks from the start of dosing
7. Safety and tolerability assessed by AEs, laboratory parameters, vital signs, physical exam, ECG, and ECOG status, measured every 4 weeks whilst on treatment
8. Pharmacokinetics measured by the concentration of roginolisib at pre-dose and steady-state levels (including Area under the curve [AUC], population PK), every 4 weeks for 12 months from the start of treatment
9. Quality of Life measured by changes in PRO relative to baseline, every 4 weeks for 12 months from the start of treatment
10. Safety of 40 vs 80 mg of roginolisib assessed by AEs, laboratory parameters, vital signs, physical exam, ECG, and ECOG status, measured every 4 weeks whilst on treatment
11. Health care utilisation assessed by health resource use (e.g., hospitalisations, outpatient visits, emergency visits, preparation and time for IMP administration, etc.), measured every 4 weeks whilst on treatment
12. Circulating DNA measured to assess any treatment-related changes in tumour tissue and/or circulating DNA from blood, every 4 weeks for 12 months from the start of treatment

Overall study start date
13/09/2024

Completion date
05/06/2027

Eligibility

Key inclusion criteria
1. Male and female patients aged over 18 years with advanced or metastatic uveal melanoma (UM)
2. Patients must have progressed following at least 1 prior immunotherapy treatment
3. The disease must be measurable (at least 1 measurable lesion) as per RECIST v1.1 by CT scan or MRI
4. All melanoma arising from melanocytes of the eye, regardless of intraocular location, will be included in the study
5. Ocular melanoma and UM are used interchangeably in the Protocol

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
85

Key exclusion criteria
Must meet all of the inclusion criteria

Date of first enrolment
02/12/2024

Date of final enrolment
17/02/2026

Locations

Countries of recruitment
Italy

Spain

United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
iOnctura

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
iOnctura SA

Results and Publications

Publication and dissemination plan
1. Internal report
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities
6. To develop the study IMP, study data will be shared with relevant and authorised research groups and only external stakeholders collaborating with the study sponsor under strict confidentiality agreements.

Intention to publish date
05/06/2028

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publicly available repository

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