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First-in-human study evaluating the effect of various doses of ODM-212 in subjects with selected advanced solid tumours

Submission date 05/07/2023	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 16/02/2024	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 04/03/2024	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
ODM-212 is a new study medication that possibly inhibits biological processes which promote tumour cell growth. The primary purpose of this study is to look at the safety of ODM-212 when given to participants who have locally advanced primary or recurrent cancer, or metastatic solid tumours. This is a first-in-human study (the study medication has not been given to humans before).

Who can participate?
Patients aged 18 years and over with locally advanced primary or recurrent cancer, or metastatic solid tumours

What does the study involve?
There are two parts to this study. In Part 1, participants will receive increasing doses of ODM-212 in groups. As long as the previous dose was tolerated well the next group of participants will receive a higher dose until a maximum, tolerated dose is reached (this is the dose that does not produce serious side effects). In Part 2, a larger group of participants will receive the dose established in Part 1 to further study the safety of and the effect ODM-212 has on cancer. Participants enrolled in either part of the study will be on the study for approximately 14 months (up to 1 year on treatment), with the possibility of extension for an additional 1 year on treatment if deemed beneficial for them by the study doctor (the total duration of study approximately 26 months).

What are the possible benefits and risks of participating?
As ODM-212 is given to humans for the first time, it is unknown whether participants will benefit from taking ODM-212. This means that ODM-212 has not been approved for sale in any country. Please see the following sections of the Main Participant Information Sheet and Informed Consent Form for a full list of potential risks and burdens.

Where is the study run from?
Orion Corporation (Finland)

When is the study starting and how long is it expected to run for?
June 2023 to May 2027

Who is funding the study?
Orion Corporation (Finland)

Who is the main contact?

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2022-503061-29-00

IRAS number
1008447

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
3134001, IRAS 1008447, CPMS 56737

Study information

Scientific Title
Two-part, first-in-human study on ODM-212 in subjects with selected advanced solid tumours

Acronym
TEADES

Study objectives
Primary objectives:
Part 1:
1. To evaluate the safety and tolerability profile of ODM-212 as a single agent administered orally in subjects with selected advanced solid tumours

Part 2:
2. To further evaluate the safety and tolerability of ODM-212

Secondary objectives:
Part 1:
1. To define the maximum tolerated dose (MTD) and dose-limiting toxicities (DLTs) of ODM-212, if possible
2. To define the recommended dose (RP2D) of ODM-212 for Part 2
3. To evaluate the pharmacokinetic (PK) profiles of ODM-212 after single and repeated administration, and to evaluate the dosing schedule of ODM-212
4. To evaluate the preliminary antitumour activity of ODM-212, to the extent possible
5. To evaluate overall survival (OS) in subjects treated with ODM-212

Part 2:
1. To evaluate the objective response rate (ORR) in subjects treated with ODM-212
2. To evaluate the clinical benefit rate (CBR) in subjects treated with ODM-212
3. To evaluate progression-free survival (PFS) in subjects treated with ODM-212
4. To evaluate overall survival (OS) in subjects treated with ODM-212
5. To further evaluate the preliminary antitumour activity of ODM-212 in subjects treated with ODM-212

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 06/09/2023, London Central REC (Health Research Authority, HRA RES Centre Manchester, Floor 3, 3 Piccadilly Place, London Road , Manchester , M1 3BN, United Kingdom; +44 (0)207 104 8225, +44 (0)207 104 8077, +44 (0)207 104 8258; londoncentral.rec@hra.nhs.uk), ref: 23/LO/0644

Study design
Non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

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
Neoplasms, benign, malignant and unspecified (including cysts and polyps)

Interventions
This is an open-label study with ODM-212.

Part 1 is a dose escalation part. The anticipated maximum duration of the study for an individual subject is approximately 14 months including 1 year (365 days) on treatment, with the possibility of extension for an additional 1 year on treatment (total duration of study approximately 26 months), if deemed beneficial for an individual subject by the investigator. A survival sweep will be performed 1 year after the end of the study.

Part 2 is a dose expansion part. The dose(s) and the dosing schedule in Part 2 of the study will be decided based on the data collected in Part 1. The dose selected will not exceed the highest dose administered in Part 1. The anticipated maximum duration of the study for an individual subject is approximately 14 months including 1 year (365 days) on treatment, with the possibility of extension for an additional 1 year on treatment (total duration of study approximately 26 months), if deemed beneficial for an individual subject by the investigator. A survival sweep will be performed 1 year after the end of the study.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
ODM-212

Primary outcome measure
Part 1 and 2:
1. Incidence, frequency, and severity of treatment-emergent adverse events (TEAEs): adverse

events will be recorded from the start of treatment administration until 28 days
2. Other general safety assessments: laboratory tests, physical examination findings, body temperature, systolic and diastolic blood pressure, 12-lead ECGs including heart rate will be assessed per protocol schedule

Secondary outcome measures

Part 1:
1. MTD defined using DLTs evaluated during the first 21 days of treatment of each patient in Part 1. According to Bayesian Optimal Interval (BOIN) this is the dose for which the estimated toxicity rate (the rate of DLTs) is closest to the target toxicity rate of 25%. A DLT is defined as an event related to ODM-212 as judged by the investigator and/or the SMB, occurring during the DLT period and leading to treatment discontinuation at the current dose level
2. Dose selection based on MTD, DLT, TEAEs, clinical and laboratory assessments. The dose will be selected at the end of Part 1 before starting Part 2. Data will be evaluated after each cohort.
3. ODM-212 concentrations and PK variables evaluated using plasma samples are collected at multiple timepoints during Day 1 and Day 15 and prior to dosing on all at other visit days in accordance with the protocol schedule (Day 1: AUCt, AUC0-12, AUC0-24, AUC∞, 1z, Vz/F, Cl /F, t1 /2, Cmax, Tmax; Day 15: AUCt, AUC0-12, AUC∞, 1z, t1/2, Cmax, Cav, Tmax, Rac,obs).

Part 1 of the CT:
Antitumour activity assessed using CT or MRI images taken every 8 weeks for the first 52 24 weeks and every 12 weeks thereafter. The images are evaluated according to the RECIST criteria to assess the antitumour activity based on: clinical benefit rate (CBR) at week 8, as best response of either complete response (CR), partial response (PR), or stable disease (SD) at week 8. CBR, as best response of either CR, PR, or at least 8 weeks of SD. Objective response rate (ORR) as response of either CR or PR. Both defined clinical benefit rates and ORR will be assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) v.1.1 (modified RECIST for MPM, as assessed by the investigator. In addition, the investigator will assess the Eastern Cooperative Oncology Group (ECOG) performance status at every visit to assess the antitumour activity based on change from baseline.

Part 2:
1. PFS will be assessed by the investigator according to RECIST v.1.1 (modified RECIST for MPM). Imaging is performed once every 8 weeks until week 24 and thereafter every 12 weeks.
2. ECOG performance status, CBR, duration of objective response, clinical disease progression. ECOG performance status is assessed at every visit. CBR is measured via RECIST at all imaging visits - see above.

Part 1 and 2:
1. OS will be assessed throughout the study and a survival sweep will be performed 1 year after Last Subject Last Visit (LSLV)
2. ORR i.e. the rate of CR and/or PR by the investigator according to RECIST v. 1.1 (modified RECIST for MPM). Imaging is performed once every 8 weeks until week 24 and thereafter every 12 weeks.
3. The rate of clinical benefit defined as: as best response of CR and/or PR and/or SD at week 8; as best response of CR and/or PR and/or at least 8 weeks of SD by RECIST v. 1.1 (modified RECIST for MPM).

Overall study start date

30/06/2023

Completion date
01/05/2027

Eligibility

Key inclusion criteria
1. Male or female subjects ≥18 years old
2. Subjects must have histological diagnosis of local advanced or metastatic solid tumour with available local data for loss-of-function genetic alterations in NF2/LATS1/LATS2, or YAP/TAZ fusions
Part 2 of the CT: Any solid tumour type potentially harbouring a Hippo pathway alteration and, therefore, potentially responsive to TEAD inhibition based on data from Part 1 or other existing or emerging scientific data
3. Subjects must be in need of systemic treatment for their cancer and to either be refractory to or have progressed on, are intolerant to, or are not otherwise a candidate, in the opinion of the investigator, for any of the currently available established therapies
4. Part 2 of the CT only: Subjects must have measurable disease by response evaluation criteria in solid tumours (RECIST v. 1.1 or modified RECIST for MPM)
5. Part 2 of the CT only: A fresh or recent (taken up to 1 year ago) primary tumour tissue sample from a diagnostic biopsy/surgery or a tumour biopsy taken from a metastasis must be available; exemptions possible by the sponsor’s decision
6. Performance status 0-1 on the Eastern Cooperative Oncology Group (ECOG) Performance Scale
7. Life expectancy of >12 weeks
8. Willing and able to comply with all aspects of the protocol
9. Provide written informed consent (or witness consent) prior to any study-specific screening procedures

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
213

Key exclusion criteria
1. Other malignancy active within the previous 2 years except for basal cell or squamous cell skin cancer, superficial bladder cancer, or carcinoma in situ of the cervix or breast, for which the subject has completed curative therapy.
2. Prior chemotherapy, immunotherapy (tumour vaccine, cytokine or growth factor given to control the cancer) or other anti-cancer therapy within less than 2 weeks before study drug administration, or any persistent unresolved toxicity from such previous therapy that, according

to the judgement of the investigator, may pose a risk for the subject if taking part in the study.
3. Prior definitive radiation therapy within less than 4 weeks and prior palliative radiotherapy within less than 2 weeks before study drug administration. Radiopharmaceuticals (strontium, samarium) within less than 8 weeks before study drug administration.
4. Subjects with brain or subdural metastases are not eligible unless the metastases are asymptomatic and do not require treatment or have been adequately treated with local therapy. Confirmation of radiographic stability must be done by comparing the brain scan (CT or MRI) performed during the screening period to a brain scan performed at least 4 weeks earlier (and following local therapy where applicable) using the same imaging modality as during the screening period. It is not the intention of this protocol to treat subjects with active brain metastasis.
5. Known human immunodeficiency virus (HIV) infection
6. Active infection requiring therapy, including known positive tests for Hepatitis B surface antigen and hepatitis C virus (HCV) RNA. Pre-study testing for these pathogens is not required.
7. Major surgery within 4 weeks before the first dose of the study drug or minor surgery within 1 week (subject must also have recovered from any surgery-related toxicities to less than CTCAE Grade 2).
8. Immunosuppressive doses of systemic medications, such as steroids or absorbed topical steroids (doses >10 mg/day prednisone or equivalent) within 2 weeks before study drug administration.
9. Inability to take oral medication, or malabsorption syndrome or any other uncontrolled gastrointestinal condition (e.g. nausea, diarrhoea, or vomiting) that might impair the bioavailability of ODM-212.
10. Use of other IMPs within 2 weeks or at least 5 half-lives (whichever is longer) before stud drug administration, or any persistent unresolved toxicity from such treatment that, according to the judgement of the investigator, may pose a health risk for the subject, if taking part in the study. For drugs such as investigational monoclonal antibodies with half-lives >10 days, at least 8 weeks is required. In addition, all visits (apart from survival follow-up) related to the use of another IMP must be completed before dosing with ODM-212 may commence
11. Use of any live or live-attenuated vaccines (e.g., intranasal influenza, measles, mumps, rubella, oral polio, BCG, yellow fever, varicella, and TY21a typhoid vaccines) within 28 days prior to the first dose of study drug.)
12. Any clinically important abnormalities in rhythm, conduction, or morphology of resting ECG, e.g., complete left bundle branch block, third-degree heart block, second-degree heart block, PR interval >250 ms, a prolonged QTcF/B interval (QTc >470 ms) as demonstrated by repeated ECG at screening, performed according to local practice. A history of risk factors for torsade de pointes (e.g. heart failure, hypokalaemia, family history of long QT Syndrome) or the use of concomitant medications that prolong the QTc interval.
13. Significant cardiovascular impairment: history of congestive heart failure of New York Heart Association (NYHA) Class III-IV, uncontrolled arterial hypertension, unstable angina, myocardial infarction, or stroke, left ventricular ejection fraction (LVEF) <50% cardiac arrhythmia requiring medical treatment (including oral anticoagulation) within 6 months prior to the first dose of study drug.
14. Female subjects who are breastfeeding or pregnant at screening or baseline (as documented by a positive beta-human chorionic gonadotropin [β-hCG] test with a minimum sensitivity of 25 IU /L or equivalent units of β-hCG).
15. A separate baseline assessment for pregnancy is required if a negative screening pregnancy test was obtained more than 72 hours before the first dose of the study drug.

Date of first enrolment
26/10/2023

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
England

Finland

France

Spain

Switzerland

United Kingdom

Study participating centre
The Royal Marsden NHS Foundation Trust
Downs Rd
Sutton
United Kingdom
SM2 5PT

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Weston Park Cancer Centre
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Sponsor type
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Funder(s)

Funder type
Industry

Funder Name
Orion Corporation

Results and Publications

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Other publication
6. Submission to regulatory authorities
7. Other
8. Coded study data will be shared via secure Sponsor systems. Data sharing will be in accordance with current data privacy legislation and restricted to authorised parties with the necessary confidentiality agreements in place.

Intention to publish date
01/05/2028

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