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A Phase II trial of ginisortamab in participants with metastatic pancreatic ductal adenocarcinoma

Submission date
04/11/2023

Recruitment status
Recruiting

Registration date
04/03/2024

Overall study status
Ongoing

Last Edited
26/04/2024

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
In this study the researchers are testing a drug called ginisortamab that blocks a protein called gremlin-1. Gremlin-1 is mainly found outside cancer cells and it stops the function of other proteins called bone morphogenetic proteins (BMPs). BMP proteins work by suppressing cancer cells as they occur but in cancer this mechanism has often been switched off. Blocking gremlin-1 with ginisortamab is expected to allow BMP protein function, and we hope this will change the way the cancer cells develop, making them more sensitive to other targeted treatments and/or chemotherapy.
The researchers are testing ginisortamab in two different settings (modules), in people with pancreatic ductal adenocarcinoma (PDAC) that has spread (metastatic). Module 1 will involve participants about to start first-line therapy of ginisortamab with standard-of-care chemotherapy, nab-paclitaxel and gemcitabine. Module 2 will involve participants whose tumours have either shrunk or not grown significantly with a first-line standard of care regimen (FOLFIRINOX [folinic acid, fluorouracil, irinotecan hydrochloride, and oxaliplatin], or nab-paclitaxel plus gemcitabine) after ≥16 weeks of treatment who will then be randomised to either i) maintenance therapy of ginisortamab in combination with another treatment called a MEK inhibitor (which can help stop cancer cells from growing and may kill them by blocking two proteins called MEK1 and MEK2) or ii) observation only.
The four main aims of this clinical trial are to find out:
1. The best dose of ginisortamab to be given to participants along with nab-paclitaxel and gemcitabine (Module 1) or a MEK inhibitor (Module 2).
2. More about potential side effects of ginisortamab when given with nab-paclitaxel and gemcitabine (Module 1) or a MEK inhibitor (Module 2) and how they can be managed.
3. To see if adding ginisortamab to treatment improves the effectiveness of treatment.
4. What happens to ginisortamab inside the body and what effect it has on tumour samples.

Who can participate?
Patients aged 18 years and over with metastatic PDAC

What does the study involve?
Both modules will start with a safety run-in, which aims to find the dose of ginisortamab that is best to give along with other treatments (nab-paclitaxel and gemcitabine, or the MEK inhibitor). The dose of ginisortamab could be lowered from the starting dose in this part of the trial, if needed. After each safety run-in is completed, an expansion cohort will open using the best dose of ginisortamab from the safety run-in. We aim to recruit between 6 and 36 participants in each safety run-in and then up to 60 participants in each expansion cohort. Module 2 participants in the expansion cohort will be randomised (randomly allocated) to either i) maintenance therapy of ginisortamab in combination with a MEK inhibitor or ii) observation only, where no medications are given as part of the trial.

What are the possible benefits and risks of participating?
Ginisortamab is a new drug that has not been tested in very many people. Possible risks and benefits are based on laboratory tests and experience with similar drugs. We do not yet have much information about the effects of ginisortamab in humans. Participants in the trial will be monitored closely to find out the effects of ginisortamab.

Where is the study run from?
Cancer Research UK

When is the study starting and how long is it expected to run for?
November 2023 to June 2029

Who is funding the study?
Cancer Research UK

Who is the main contact?
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https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-ginisortamab-for-pancreatic-cancer-that-has-spread#undefined

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007925

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CRUKD/24/002, IRAS 1007925

Study information

Scientific Title
A Cancer Research UK Phase II open label trial in participants with metastatic pancreatic ductal adenocarcinoma of ginisortamab given intravenously i) with first-line standard of care nab-paclitaxel and gemcitabine, or ii) in combination with MEK inhibitor maintenance therapy

Study objectives

Primary objectives:
Module 1:
1. To assess the safety and toxicity profile of ginisortamab when given with standard of care (SoC) nab-paclitaxel and gemcitabine first-line therapy.
2. To identify a recommended dose of ginisortamab when given with SoC nab-paclitaxel and gemcitabine first-line therapy.
3. To document anti-tumour activity of ginisortamab when given with SoC nab-paclitaxel and gemcitabine first-line therapy.

Module 2:
1. To assess the safety and toxicity profile of ginisortamab when given in combination with a MEK inhibitor as maintenance therapy.
2. To identify a recommended dose of ginisortamab when given in combination with a MEK inhibitor as maintenance therapy.
3. To document possible anti-tumour activity of ginisortamab when given in combination with a MEK inhibitor as maintenance therapy in participants with ongoing response or disease stabilisation after ≥16 weeks of a SoC regimen.

Secondary objectives:
Module 1:
1. To further describe anti-tumour activity of ginisortamab when given with SoC nab-paclitaxel and gemcitabine first-line therapy.
2. To investigate pharmacokinetic (PK) parameters of ginisortamab in participants when given with SoC nab-paclitaxel and gemcitabine first-line therapy.

Module 2:
1. To further describe anti-tumour activity of ginisortamab when given in combination with a MEK inhibitor as maintenance therapy in participants with ongoing response or disease stabilisation after ≥16 weeks of a SoC regimen.
2. To investigate PK parameters of ginisortamab in participants when given in combination with a MEK inhibitor as maintenance therapy (Arm A).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 04/01/2024, London - West London & GTAC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8098; westlondon.rec@hra.nhs.uk), ref: 23/LO/0662

Study design
Multi-centre, open-label, Phase II non-randomized (Module 1) and randomized (Module 2) trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Metastatic pancreatic ductal adenocarcinoma

Interventions
Module 1: Participants will receive ginisortamab (investigational medicinal product [IMP]) administered by 30 (±10)-minute intravenous (IV) infusion once every 2 weeks. Participants will also receive standard of care (SoC) treatment of nab-paclitaxel and gemcitabine (non-IMPs). The starting dose of ginisortamab administered will be 2000 mg, which may be de-escalated to 1000 or 500 mg, and SoC treatment will be given in accordance with the recommended dose and schedule. Participants may receive up to twelve 28-day cycles and be followed for up to 6 months after their last dose. Participants deemed to be benefitting from ginisortamab may be considered for treatment beyond 12 cycles.

Module 2 Arm A: participants randomised to this arm will receive ginisortamab (IMP) by 30 (±10)-minute IV infusion once every 2 weeks, in combination with a MEK inhibitor (IMP). The starting dose of ginisortamab administered will be 2000 mg, which may be de-escalated to 1000 or 500 mg, and the MEK inhibitor dose and schedule will be based on the choice of agent. Further details will be provided once the MEK inhibitor is confirmed.

Module 2 Arm B: Participants randomised to this arm will be under observation only, with no IMP administered.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Module 1:
1. Frequency of adverse events (AEs) considered at least possibly related to ginisortamab, and the number of Grade 3, 4 and 5 AEs at least possibly related to ginisortamab for up to an initial maximum of 12 cycles (~1 year) and no more than 24 cycles (~2 years). AEs, including relatedness, seriousness and severity according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0, will be assessed by the Investigator. Evaluation of this endpoint will occur once the last participant enrolled to Module 1 has received up to 24 cycles (~2 years) of ginisortamab.
2. Recommended dose of ginisortamab for use with standard of care (SoC) nab-paclitaxel and ginisortamab following the review of all available clinically relevant data, including but not limited to toxicity, efficacy and PK data by the Sponsor and Investigators. Evaluation of this endpoint will occur once all participants in the module have completed the safety run-in period (28 days) and all relevant data have been collected.
3. Progression-free survival (PFS), defined as the time from the date of starting ginisortamab plus SoC nab-paclitaxel and gemcitabine to the date of disease progression or date of death, whichever occurs first. Response will be assessed at baseline, at the end of every 8 weeks and at end of treatment. Participants who withdraw from the trial due to reasons other than progression will be followed up for survival for up to 12 months after the date upon which the last participant enrolled to Module 1 receives their first dose of ginisortamab.
4. Disease control rate (DCR), defined as the proportion of participants who achieve a best

response of complete response (CR), partial response (PR), or SD of duration ≥16 weeks, evaluated according to Response Evaluation Criteria in Solid Tumours (RECIST) Version 1.1. Response will be assessed at baseline, at the end of every 8 weeks and at end of treatment.

Module 2:
5. Frequency of AEs considered at least possibly related to IMP(s), and the number of Grade 3, 4 and 5 AEs at least possibly related to IMP(s). AEs, including relatedness, seriousness and severity according to NCI CTCAE Version 5.0, will be assessed by the Investigator. Further details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
6. Recommended dose of ginisortamab for use in combination with a MEK inhibitor, following the review of all available clinically relevant data, including but not limited to toxicity, efficacy and PK data by the Sponsor and Investigators. Evaluation of this endpoint will occur once all participants in the module have completed the safety run-in period (28 days) and all relevant data have been collected.
7. PFS 1, defined as the time from date of randomisation to date of disease progression or date of death, whichever occurs first. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.

Key secondary outcome(s))

Module 1:
1. Overall survival (OS), calculated from the date of starting ginisortamab plus SoC nab-paclitaxel and gemcitabine to the date of death. Participant status will be reviewed throughout the trial and for up to 12 months after the date upon which the last participant enrolled to Module 1 receives their first dose of ginisortamab.
2. Overall response rate (ORR), defined as the proportion of participants who achieve a best response of CR or PR according to RECIST Version 1.1. Response will be assessed at baseline, at the end of every 8 weeks and at end of treatment.
3. Duration of response (DoR), defined as the time from the date of the first confirmed CR or PR according to RECIST Version 1.1 to the date of disease progression. Response will be assessed at baseline, at the end of every 8 weeks and at end of treatment. Participants who withdraw from the trial due to reasons other than progression will be followed up for survival for up to 12 months after the date upon which the last participant enrolled to Module 1 receives their first dose of ginisortamab.
4. Time to next therapy, defined as the time from the date of starting ginisortamab plus SoC nab-paclitaxel and gemcitabine to the date of starting the next treatment regimen following discontinuation of trial treatment in this trial. Participant status will be reviewed throughout the trial and for up to 12 months after the date upon which the last participant enrolled to Module 1 receives their first dose of ginisortamab.
5. PK parameters for ginisortamab when given with SoC nab-paclitaxel and gemcitabine, including maximum observed plasma concentration (Cmax), area under the concentration-time curve (AUC), terminal elimination half-life (T1/2), volume of distribution at steady state (Vss), clearance (CL) and trough concentration (Ctrough) for the safety run-in, and Cmax and Ctrough for the dose expansion. Samples for PK analysis will be taken at up to 17 timepoints across Cycles 1 and 2 and up to 9 timepoints thereafter.

Module 2:
6. PFS 2: defined as the time from the date of starting a first-line SoC regimen to the date of disease progression or date of death, whichever occurs first. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
7. OS, calculated from the date of starting a first-line SoC regimen to the date of death. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been

finalised.
8. ORR, defined as the proportion of participants who achieve a best response of CR or PR according to RECIST Version 1.1. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
9. DCR, defined as the best response of CR, PR or SD according to RECIST Version 1.1 at 3, 6, 9 and 12 months after randomisation. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
10. DoR 1, defined as the time from the date of the first confirmed CR or PR according to RECIST Version 1.1 to the date of disease progression. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
11. DoR 2: defined as the time from the date of randomisation to the date of disease progression, measured in participants who had CR/PR at randomisation. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
12. Time to next therapy, defined as the time from the date of randomisation to the date of starting the next treatment regimen. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.
13. PK parameters for ginisortamab when given in combination with a MEK inhibitor, including Cmax, AUC, T1/2, Vss, CL and Ctrough for the safety run-in, and Cmax and Ctrough for the expansion. Details of the evaluation of this endpoint will be provided once the study design for Module 2 has been finalised.

Completion date
01/06/2029

Eligibility

Key inclusion criteria
Module 1:
1. Written (signed and dated) informed consent, and capable of co-operating with IMP (and SoC) administration and follow-up.
2. Histologically or cytologically confirmed diagnosis of PDAC with metastatic disease.
3. Consent for pre- and on-treatment tumour biopsy samples for assessment of molecular markers, including but not limited to, SMAD4 and gremlin-1. Pre- and on-treatment tumour samples are mandatory in the first instance. These tumour samples may become optional as considered appropriate by the Sponsor and Investigators based on a review of emerging data during the trial. Participants must have disease amenable to biopsy as deemed safe by the Investigator.
4. Measurable disease according to RECIST Version 1.1.
5. Eastern Cooperative Oncology Group performance status of ≤1.
6. Haematological and biochemical indices within defined ranges. These measurements should be performed to confirm the patient's eligibility to participate in the trial.
7. Aged 18 years or over at the time consent is given.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Module 1 exclusion criteria:
1. Previous radiotherapy (except palliative) within 6 months prior, chemotherapy, investigational therapy for metastatic PDAC, other anti-cancer therapy within 28 days or 5 half-lives (whichever is shorter) before the first dose of IMP.
2. Live vaccinations will not be permitted within 28 days before trial enrolment.
3. Neuroendocrine (carcinoid, islet cell) or acinar pancreatic carcinoma.
4. Prior neo-adjuvant, peri-operative, or adjuvant chemotherapy for non-metastatic pancreatic adenocarcinoma with curative intent unless recurrent (i.e. metastatic) disease is documented more than 6 months since the last dose of systemic therapy.
5. Clinically significant/symptomatic third space fluid accumulation (e.g. ascites or pleural effusion).
6. Ongoing toxic manifestations of previous treatments considered by the Investigator to make the patient unsuitable for the trial.
7. Brain or leptomeningeal metastases.
8. Clinically significant ongoing pulmonary disease, including but not limited to interstitial lung disease, idiopathic pulmonary fibrosis or pulmonary hypersensitivity pneumonitis.
9. History of pulmonary embolism or deep vein thrombosis unless continuing anticoagulant treatment as clinically indicated.
10. Female patients of childbearing potential. However, those patients of childbearing potential who are not already pregnant or breastfeeding, or who agree to discontinue breastfeeding, or who meet the following points are considered eligible:
11. Have a negative highly sensitive serum pregnancy test within 7 days before Day 1 and either:
11.1. Agree to one form of highly effective contraception
11.2. Or agree to sexual abstinence
Effective from the date of the negative pregnancy test, throughout the trial and for 6 months after the last administration of IMP or SoC chemotherapy agents (whichever component is administered last).
11.3. Male patients with partners of childbearing potential or who are pregnant or breastfeeding. However, those patients who meet the following points are considered eligible:
11.3.1. Agree to take measures not to father children by using a barrier method of contraception (condom) or sexual abstinence effective from the date of the first administration of IMP and SoC chemotherapy agents, throughout the trial and for 6 months after the last administration of IMP or SoC chemotherapy agents (whichever component is administered last).
11.3.2. Non-vasectomised male patients must also be willing to ensure that any partner who is of childbearing potential uses a highly effective method of contraception or agrees to sexual abstinence for the same duration.
11.3.3. Male patients with pregnant or breastfeeding partners must be advised to use barrier method contraception (male condom) to prevent exposure of the foetus or neonate.
12. Major thoracic or abdominal surgery from which the patient has not yet recovered.
13. At high medical risk because of non-malignant systemic disease, including active uncontrolled infection.
14. Known hypersensitivity to any of the ingredients/excipients in the IMP to be administered.

Date of first enrolment
18/03/2024

Date of final enrolment
31/12/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
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Study participating centre
UCLH
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Study participating centre
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Sponsor information

Organisation
Cancer Research UK

ROR
https://ror.org/054225q67

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request. Data from this trial and the final clinical study protocol will be submitted to a public registry and will be available immediately following publication, with no end date. Individual deidentified participant data that underlie the results reported will be shared with researchers whose proposed use of the data is approved by a review committee of the Sponsor. All requests made within 5 years from end of trial will be considered; requests made subsequently will be considered where possible. Requests should be submitted to drugdev@cancer.org.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes