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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
17/11/2026

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] 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). BMPs 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 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 alongside standard-of-care chemotherapy with 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 cobimetinib (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 cobimetinib (Module 2).
2. More about potential side effects of ginisortamab when given with nab-paclitaxel and gemcitabine (Module 1) or cobimetinib (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.

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 [Module 1], or cobimetinib [Module 2]). 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 cobimetinib 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, experience with similar drugs and the limited experience with ginisortamab in people to date. 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?
April 2024 to October 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

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Scientific, Public

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Protocol serial number
CRUKD/24/002

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 cobimetinib as maintenance therapy.
2. To identify a recommended dose of ginisortamab when given in combination with cobimetinib as maintenance therapy.
3. To document possible anti-tumour activity of ginisortamab when given in combination with cobimetinib 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 cobimetinib 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 cobimetinib 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

Primary study design
Interventional

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

Study type(s)
Efficacy, Safety

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

Interventions
Current interventions as of 13/07/2026:
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 12 months after Cycle 1 Day 1 of the last participant to enroll in this module. Participants deemed to be benefiting from ginisortamab, who are not experiencing any severe adverse reactions, 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 cobimetinib (IMP). The starting dose of ginisortamab administered will be 2000 mg, which may be de-escalated to 1000 or 500 mg, and cobimetinib will be administered orally as 60 mg once daily in 28-day cycles. Cobimetinib should be taken for 21 consecutive days, followed by a 7-day break. Participants are planned to receive IMP for up to twelve 28-day cycles; however, those participants deemed to be benefiting from ginisortamab in combination with cobimetinib, who are not experiencing any severe adverse reactions, may be considered for treatment beyond 12 cycles.

Module 2 Arm B: Participants randomised to this arm will be under observation only, for up to twelve 28-day cycles of trial visits, i.e. 48 weeks.

Previous interventions as of 07/04/2026:
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, who are not experiencing any severe adverse reactions, 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 cobimetinib (IMP). The starting dose of ginisortamab administered will be 2000 mg, which may be de-escalated to 1000 or 500 mg, and cobimetinib will be administered orally as 60 mg once daily in 28-day cycles. Cobimetinib should be taken for 21 consecutive days, followed by a 7-day break. Participants deemed benefiting from ginisortamab in combination with cobimetinib, who are not experiencing any severe adverse reactions, may be considered for treatment beyond 12 cycles.

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

Original 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)
Current primary outcomes as of 13/07/2026:
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 stable disease (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) for up to an initial maximum 12 cycles (~1 year) and no more than 24 cycles (~2 years). AEs, including relatedness, seriousness and severity according to NCI CTCAE Version 5.0, will be assessed by the Investigator. Evaluation of this endpoint will occur once the last participant enrolled to Module 2 has received up to 24 cycles (~2 years) of

ginisortamab (Arm A), or 12 cycles of study visits (Arm B).
6. Recommended dose of ginisortamab for use in combination with cobimetinib, 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. Response in Arm A 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 2 has their Cycle 1 Day 1 visit.

Previous primary outcomes:
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 cobimetinib, 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)

Current secondary outcomes as of 13/07/2026:
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 (TTNT), 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. 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 disease progression will be followed up for survival for up to 12 months after the date upon which the last participant enrolled to Module 2 has their Cycle 1 Day 1 visit.
7. OS, calculated from the date of starting a first-line SoC regimen 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 2 has their Cycle 1 Day 1 visit.
8. 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.
9. DCR, defined as the proportion of participants with best response of CR, PR or SD according to RECIST Version 1.1 at 3, 6, 9 and 12 months after randomisation. Response will be assessed at baseline, at the end of every 8 weeks and at end of treatment.
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. 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 disease progression will be followed up for survival for up to 12 months after the date upon which the last participant enrolled to Module 2 has their Cycle 1 Day 1 visit.
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. 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 disease progression will be followed up for survival for up to 12 months after the date upon which the last participant enrolled to Module 2 has their Cycle 1 Day 1 visit.
12. TTNT, defined as the time from the date of randomisation to the date of starting the next treatment regimen. 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 2 has their Cycle 1 Day 1 visit.
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. Samples for PK analysis will be taken from participants in Arm A at up to 17 timepoints across Cycles 1 and 2 and up to 9 timepoints thereafter.

Previous secondary outcomes:
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 (TTNT), 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 cobimetinib, 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
31/10/2029

Eligibility

Key inclusion criteria
Current inclusion criteria as of 13/07/2026:
Applicable to All Trial Participants:
1. Written (signed and dated) informed consent, and capable of co-operating with IMP/s (and SoC [auxiliary medicinal products], as applicable) 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.

Module 2 – Additional Inclusion Criteria:
1. Investigator determination that the clinical interests of the participant are best served by stopping SoC induction therapy (FOLFIRINOX, or nab-paclitaxel plus gemcitabine) after attainment of a best response of ≥ SD.
2. At least ongoing SD or response (CR/PR) after ≥16 weeks of treatment with a SoC first-line induction regimen (FOLFIRINOX, or nab-paclitaxel plus gemcitabine).
- Ongoing SD or response must be confirmed on the trial baseline scan.
3. Not a candidate for PARP inhibitor maintenance therapy.

Previous inclusion criteria as of 07/04/2026:
Applicable to All Trial Participants:
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.

Module 2 – Additional Inclusion Criteria:
1. Investigator determination that the clinical interests of the participant are best served by stopping SoC induction therapy (FOLFIRINOX, or nab-paclitaxel plus gemcitabine) after attainment of a best response of ≥ SD.
2. At least ongoing SD or response (CR/PR) after ≥16 weeks of treatment with a SoC first-line induction regimen (FOLFIRINOX, or nab-paclitaxel plus gemcitabine).
- Ongoing SD or response must be confirmed on the trial baseline scan.
3. Not a candidate for PARP inhibitor maintenance therapy.

Original 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
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 13/07/2026:
Applicable to All Trial Participants:
1. Prior radiotherapy to the only measurable index lesion unless radiological progression has occurred following completion of radiotherapy.
2. Radiotherapy (for non-metastatic disease) within the last 6 months prior to Cycle 1 Day 1 with the exception of palliative treatment (≤10 Gy single fraction or 25 Gy fractionated total) that has been completed at least 7 days prior to Cycle 1 Day 1.
3. Previous investigational therapy for the treatment of metastatic PDAC.
4. Previous concurrent anti-cancer treatment within 28 days or 5 half-lives (whichever is shorter) prior to Cycle 1 Day 1 (e.g. cytoreductive therapy, immunotherapy, biologic therapy, or cytokine therapy [with the exception of erythropoietin]).
5. Live vaccinations will not be permitted within 28 days before trial enrolment or randomisation.
6. Neuroendocrine (carcinoid, islet cell) or acinar pancreatic carcinoma.
7. 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. Exception applies.
8. Clinically significant/symptomatic third space fluid accumulation (e.g. ascites or pleural effusion).
9. Ongoing toxic manifestations of previous treatments considered by the Investigator to make the patient unsuitable for the trial.
10. Brain or leptomeningeal metastases.
11. Clinically significant ongoing pulmonary disease, including but not limited to interstitial lung disease, idiopathic pulmonary fibrosis or pulmonary hypersensitivity pneumonitis.
12. History of pulmonary embolism or deep vein thrombosis unless continuing anticoagulant treatment as clinically indicated.
13. Major thoracic or abdominal surgery from which the patient has not yet recovered.
14. At high medical risk because of non-malignant systemic disease, including active uncontrolled infection. Patients with previous hepatitis C virus (HCV) exposure but no current infection are eligible to participate. Any uncontrolled active systemic infection requiring systemic IV treatment that was completed ≤7 days before Cycle 1 Day 1.
15. Known to be serologically positive for hepatitis B virus (HBV), HCV or HIV. Patients who are positive for hepatitis B core antibody, hepatitis B surface antigen, or hepatitis C antibody must have an undetectable HCV RNA by polymerase chain reaction (PCR) or HBV DNA (by PCR) that is <500 IU/mL before enrolment. Patients who are HBV core antibody positive should receive SoC antiviral therapy during trial treatment.
16. Known hypersensitivity to any of the ingredients/excipients in the IMP/s to be administered.
17. Significant cardiovascular disease as defined in the trial protocol.
18. Baseline corrected QTcF >450 ms measured on triplicate ECG (if an average QTcF of >450 ms then the patient is ineligible).
19. Is a participant or plans to participate in another interventional clinical trial, whilst taking part in this Phase II trial of ginisortamab. Participation in an observational trial or interventional

clinical trial that does not involve administration of an IMP, and that would not place an unacceptable burden on the patient, in the opinion of the Investigator, would be acceptable.
20. Current or prior malignancy that could affect safety or efficacy assessment of the IMP or compliance with the protocol or interpretation of results. Patients with curatively treated nonmelanoma skin cancer, non-muscle-invasive bladder cancer, or carcinomas-in-situ are generally eligible. Patients with asymptomatic prostate cancer without known metastatic disease and with no requirement for therapy, or who require only hormonal therapy and have had normal prostate-specific antigen for >1 year prior to the start of therapy, are eligible for participation in the trial.
21. Patients with any congenital or acquired immunodeficiency syndrome or who are receiving immunosuppressive therapy (including any dose of systemic corticosteroids), or who are immunosuppressed post-organ transplant. Exceptions apply.
22. Any other condition that, in the Investigator's opinion, would mean that the trial is not in the best interests of the patient.

Module 1 – Additional Exclusion Criteria:
1. Prior chemotherapy for unresectable disease

2. 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:
2.1. Have a negative highly sensitive serum pregnancy test within 7 days before Cycle 1 Day 1 and either:
2.1.1. Agree to one form of highly effective contraception;
2.1.2. 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.

Module 2 – Additional Exclusion Criteria:
1. More than one systemic chemotherapy regimen given in the metastatic setting.
2. Clinically significant ophthalmoscopic findings at the time of screening or history of ophthalmological findings, such as retinal detachment, severe visual impairment, central serous chorioretinopathy, neovascular retinopathy, or retinopathy of prematurity.
3. History of retinal vein occlusion.
4. Any strong inhibitors or inducers of CYP3A (including supplements) within 7 days prior to initiation of Cycle 1 Day 1, and during study treatment for participants in the safety run-in and expansion Arm A.
5. LVEF <40%. This measurement should be performed to confirm the participant's eligibility to participate in the trial.
6. Participant is unable to swallow cobimetinib intact, without chewing or crushing the tablets (as per the dosing schedule) or is known to have dysphagia, short-gut syndrome, gastroparesis, or other condition that limits the ingestion or gastrointestinal absorption of drugs administered orally.

7. 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:
7.1. Have a negative highly sensitive serum pregnancy test within 7 days before Cycle 1 Day 1 and either:
7.1.1. Agree to a highly effective contraception method plus a barrier method (condom or other barrier method with spermicide, if available);

7.1.2. Or agree to sexual abstinence.
Effective from the date of the negative pregnancy test, throughout the trial and for 4 months after the last administration of IMPs (whichever component is administered last). Participants randomised to Module 2 expansion Arm B do not need to adhere to the on-trial or post-trial contraception requirements.

Applicable to Participants in Module 1 and Module 2:
1. Male patients with partners of childbearing potential or who are pregnant or breastfeeding. However, those patients who meet the following points are considered eligible:
1.1. Non-vasectomised males must 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/s and /or SoC chemotherapy agents as applicable, throughout the trial and for 6 months (Module 1) or for 2 weeks (Module 2) after the last administration of IMP/s or SoC chemotherapy agents as applicable (whichever component is administered last).
1.2. 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 6 months (Module 1) or 4 months (Module 2) after the last administration of IMP/s or SoC chemotherapy agents (whichever component is administered last for both modules).
1.3. 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 for 6 months (Module 1) or 2 weeks (Module 2) after the last administration of IMP/s and/or SoC chemotherapy agents as applicable (whichever component is administered last for both modules).
1.3.1. All male patients must refrain from donating sperm throughout the trial and for 6 months (Module 1) or 2 weeks (Module 2) after the last administration of IMP/s and/or SoC chemotherapy agents as applicable. Participants randomised to Module 2 expansion Arm B do not need to adhere to the on-trial or post-trial contraception requirements.

Previous exclusion criteria as of 07/04/2026:
Applicable to All Trial Participants:
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. Major thoracic or abdominal surgery from which the patient has not yet recovered.
11. At high medical risk because of non-malignant systemic disease, including active uncontrolled infection. Patients with previous HCV exposure but no current infection are eligible to participate. Any uncontrolled active systemic infection requiring systemic IV treatment that

was completed ≤7 days before Cycle 1 Day 1.
12. Known to be serologically positive for HBV, HCV or HIV. Patients who are positive for hepatitis B core antibody, hepatitis B surface antigen, or hepatitis C antibody must have an undetectable HCV RNA by PCR or HBV DNA (by PCR) that is <500 IU/mL before enrolment. Patients who are HBV core antibody positive should receive SoC anti-viral therapy during trial treatment.
13. Known hypersensitivity to any of the ingredients/excipients in the IMP to be administered.
14. Significant cardiovascular disease, defined as:
14.1. History of congestive heart failure requiring therapy (New York Heart Association III or IV) or LVEF <40% (moderate or severe);
14.2 History of unstable angina pectoris or myocardial infarction within 6 months prior to trial entry, or current poorly controlled angina (symptoms weekly or more);
14.3 Presence of symptomatic or severe valvular heart disease (severe by local echocardiographic criteria or American Heart Association/American College of Cardiology Stage C or D);
14.4 History of a clinically significant cardiac arrhythmia within 6 months prior to trial entry (asymptomatic atrial fibrillation or asymptomatic first-degree heart block is permitted).
15. Baseline corrected QTcF >450 ms measured on triplicate ECG (if an average QTcF of >450 ms then the patient is ineligible).
16. Is a participant or plans to participate in another interventional clinical trial, whilst taking part in this Phase II trial of ginisortamab. Participation in an observational trial or interventional clinical trial that does not involve administration of an IMP and that would not place an unacceptable burden on the patient, in the opinion of the Investigator, would be acceptable.
17. Current or prior malignancy that could affect safety or efficacy assessment of the IMP or compliance with the protocol or interpretation of results. Patients with curatively treated non-melanoma skin cancer, non-muscle-invasive bladder cancer, or carcinomas-in-situ are generally eligible.
18. Patients with asymptomatic prostate cancer without known metastatic disease and with no requirement for therapy, or who require only hormonal therapy and have had normal prostate-specific antigen for >1 year prior to the start of therapy, are eligible for participation in the trial.
19. Patients with any congenital or acquired immunodeficiency syndrome or who are receiving immunosuppressive therapy (including any dose of systemic corticosteroids), or who are immunosuppressed post-organ transplant. However, patients receiving inhaled corticosteroids and patients with a history of allergy (other than anaphylaxis) are eligible, as are patients with a history of autoimmune disease.
20. Any other condition that, in the Investigator’s opinion, would mean that the trial is not in the best interests of the patient.

Module 1 – Additional Exclusion Criteria:
1. Prior chemotherapy for unresectable disease

Module 2 – Additional Exclusion Criteria:
1. More than one systemic chemotherapy regimen given in the metastatic setting.
2. Clinically significant ophthalmoscopic findings at the time of screening or history of ophthalmological findings, such as retinal detachment, severe visual impairment, central serous chorioretinopathy, neovascular retinopathy, or retinopathy of prematurity.
3. History of retinal vein occlusion.
4. Any strong inhibitors or inducers of CYP3A (including supplements) within 7 days prior to initiation of Cycle 1 Day 1, and during study treatment for participants in the safety run-in and expansion Arm A.
5. LVEF <40%. This measurement should be performed to confirm the participant’s eligibility to participate in the trial.

6. Participant is unable to swallow cobimetinib intact, without chewing or crushing the tablets (as per the dosing schedule) or is known to have dysphagia, short-gut syndrome, gastroparesis, or other condition that limits the ingestion or GI absorption of drugs administered orally.

Applicable to Participants in Module 1 and Module 2:
1. 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:
1.1. Have a negative highly sensitive serum pregnancy test within 7 days before Day 1 and either:
1.1.1. Agree to one form of highly effective contraception;
1.1.2. Or agree to sexual abstinence.
1.2. 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).
1.3. Participants randomised to Module 2 expansion Arm B do not need to adhere to the on-trial or post-trial contraception requirements.
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:
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 (Module 1) or for 2 weeks (Module 2) after the last administration of IMPs (whichever component is administered last for both Modules).
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 after the last administration of IMPs (whichever component is administered last for both Modules).
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 (for 2 weeks for Module 2) after the last administration of IMPs (whichever component is administered last for both Modules).
3.3.1. All male patients must refrain from donating sperm throughout the trial and for 6 months (Module 1) or 2 weeks (Module 2) after the last administration of IMPs (whichever component is administered last).
3.3.2. Participants randomised to Module 2 expansion Arm B do not need to adhere to the on-trial or post-trial contraception requirements.

Previous 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
25/06/2024

Date of final enrolment
31/10/2028

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Germany

Norway

Spain

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
Scotland
G12 0YN

Study participating centre
UCLH
250 Euston Road
London
England
NW1 2PQ

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
Scotland
EH4 2XU

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
Scotland
AB25 2ZN

Study participating centre
Guys Hospital
Guys Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre

Ninewells Hospital
Ninewells Avenue
Dundee
Scotland
DD1 9SY

Study participating centre
St James's University Hospital
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
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OX3 7LE

Study participating centre
Royal Free Hospital
Pond Street
London
England
NW3 2QG

Study participating centre
Clatterbridge Cancer Centre
65 Pembroke Place
Liverpool
England
L7 8YA

Study participating centre
Northern Ireland Cancer Centre
Belfast City Hospital
Lisburn Road

Belfast
Northern Ireland
BT9 7AB

Study participating centre
Velindre Cancer Centre
Velindre Road
Cardiff
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CF14 2TL

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Hospital Universitario Fundación Jimenéz Díaz
Avenida Reyes Católicos, 2
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Passeig Vall d'Hebron, 119-129
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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?
HRA research summary			17/11/2026	No	No