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An early safety study testing a drug combination given before possible surgery for people with pancreatic cancer that can’t be easily removed yet or hasn’t spread far

Submission date 12/11/2025	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 12/01/2026	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 12/01/2026	**Condition category** Cancer	[ ] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
This study is for people with a type of pancreatic cancer that has not spread far away, but cannot be easily removed with surgery right now. We want to find out if a new drug combination can make surgery more successful and help control the cancer. This is an early-phase (Phase I) study. That means the main aim is to check safety: what side effects people get and how severe they are. We will also look for early signs that the treatment is helping.

Who can participate?
Patients aged 18 years and over with borderline resectable or locally advanced pancreatic cancer

What does the study involve?
Everyone in the study will receive standard chemotherapy for pancreatic cancer (gemcitabine and nab-paclitaxel). You will also receive three new study medicines that help the immune system attack cancer: nogapendekin alfa inbakicept (NAI), sotevtamab, and zabadinostat. These medicines are still experimental and are not yet approved.
You will get these medicines before surgery. This part is called neoadjuvant treatment, which means treatment given before surgery to try to shrink or control the tumour. You may get between 2 and 6 treatment blocks (cycles), which usually takes about 2 to 6 months in total. How long you stay on treatment before surgery depends on how your cancer responds and how you are feeling.
If your cancer can then be removed, you will have surgery. After surgery, you may continue on one of the study medicines (NAI) every 2 weeks. This is sometimes called maintenance treatment. You can keep getting it unless the cancer gets worse or the side effects are too strong.
We will check the size of your tumour with scans, and we will take blood and tissue samples to see how the treatment is working in your body.

What are the possible benefits and risks of participating?
The information collected during this study may help the sponsor, study doctors, and researchers learn more about your cancer and the study treatment that may benefit you and other participants. However, there is no guarantee that this will happen.
Participants may experience side effects from the investigational treatments and the standard chemotherapy. Common expected side effects include fever, chills, flu-like symptoms, fatigue, itching, nausea, vomiting, diarrhea, and low blood cell counts. Infusion reactions can occur with the antibody treatment (sotevtamab) – e.g. rash, fever, breathing difficulty, or low blood pressure during the IV infusion. Injection-site reactions (redness, pain, rash at the SC injection site) can occur with NAI. Chemotherapy (gemcitabine/nab-paclitaxel) is known to cause bone marrow suppression (leading to low red blood cells, white cells, or platelets), neuropathy (nerve pain/numbness), infections, and other organ toxicities in some patients. There is also a risk of serious allergic/hypersensitivity reactions to any of the drugs. Because this is a combination of five agents, there is a possibility of compounded toxicities, and some side effects may be unpredictable (since the combination's full profile in pancreatic cancer is not yet known).
In addition to drug-related risks, participants face procedural risks. Blood sample collection can cause pain, bruising, or rarely fainting. CT scans involve exposure to ionising radiation. Surgery (tumor resection) carries significant risk as a major operation – including bleeding, infection, surgical complications, or delayed recovery.
The trial is designed with several safety measures. Medical monitoring is rigorous: participants have regular lab tests and evaluations at each visit to detect side effects early. The trial uses standard pre-medications (e.g. acetaminophen and antihistamines) before sotevtamab infusions to reduce infusion reactions. If severe side effects occur, dose adjustments or treatment delays are built into the protocol (the Safety Review Committee will halt or modify dosing if needed for safety). Participants are required to meet strict inclusion criteria (e.g. good performance status, adequate organ function) so that frail participants are not exposed to undue risk. Contraception requirements are enforced (two reliable methods of birth control) to prevent pregnancy due to unknown fetal risks. If a participant does become pregnant, the trial has a plan to follow and monitor outcomes, and the drug will be stopped.

Where is the study run from?
Serum Life Science Europe GmbH (Germany)

When is the study starting and how long is it expected to run for?
January 2026 to June 2028

Who is funding the study?
ImmunityBio, Inc. (USA)

Who is the main contact?
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Contact information

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Additional identifiers

Integrated Research Application System (IRAS)
1013114

Protocol serial number
ResQ108B-PANC

Study information

Scientific Title
Open-label, Phase I clinical trial of neoadjuvant nogapendekin alfa inbakicept, sotevtamab, and zabadinostat in combination with gemcitabine and nab-paclitaxel for participants with borderline resectable or locally advanced pancreatic cancer

Study objectives
Primary objective:
Evaluate safety of experimental treatment

Secondary objective:
Evaluate efficacy of experimental treatment using recurrence-free survival (RFS) as measured by Response Evaluation Criteria in Solid Tumors (RECIST v1.1)

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Treatment

Study type(s)
Efficacy, Safety, Not Specified

Health condition(s) or problem(s) studied
Borderline resectable or locally advanced pancreatic ductal adenocarcinoma (PDAC)

Interventions
Sotevtamab (800 mg IV infusion), gemcitabine (1,000 mg/m2 IV infusion), nab-paclitaxel (125 mg /m2 IV infusion), NAI (1.2 mg SC injection), and zabadinostat (10 mg BID PO for 5 days) will be the interventions used in this study. This study is conducted using 4-week (28-day) repeating cycles. For up to the first six cycles, the treatment regimen will be as follows: Day 1 treatments include sotevtamab, gemcitabine, nab-paclitaxel, NAI, and zabadinostat. Day 8 treatments include sotevtamab, gemcitabine, and nab-paclitaxel. Day 15 treatments include sotevtamab, gemcitabine, nab-paclitaxel, NAI, and zabadinostat. At this point, if eligible, the patients will undergo resection of their tumor. After resection, patients will continue treatment of only NAI every other week until discontinuation from the study for any reason. Once discontinued for any reason, participants will be followed up every 12 weeks after the last dose of study drug, for 2 years or until death.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
N-803 (nogapendekin alfa inbakicept [NAI]) , sotevtamab, zabadinostat, gemcitabine, nab-paclitaxel

Primary outcome(s)
1. Adverse events (AEs) and serious AEs (SAEs) graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Safety is assessed from first

study treatment through the End-of-Treatment (EOT) visit at 30 (+7) days post-last dose. AEs /SAEs are collected at every visit during neoadjuvant and adjuvant treatment. Non-serious AEs are followed for 30 days post-last dose; SAEs are followed until resolution/stabilisation.
2. Clinically significant changes in laboratory tests and vital signs. Vitals at every visit; labs per schedule; ECG at screening, baseline and Day 1 of each neoadjuvant cycle.

Key secondary outcome(s))
Key Efficacy:
RFS defined as time from surgical resection to disease recurrence or death from any cause, whichever occurs first, by RECIST v1.1.

Additional Efficacy:
1. R0 resection rate, defined as the percentage of cases having a pathologically complete resection with a negative resection margin
2. ORR by RECIST v1.1
3. DOR by RECIST v1.1
4. iRFS, iORR, and iDOR by iRECIST
5. OS, defined as time from start of study treatment to death resulting from any cause
6. Major pathologic response, defined as College of American Pathologists Tumor Regression Grading (CAP TRG) of 0 or 1 at time of surgical resection
7. Biochemical response, defined as >50% decrease in CA 19-9 from baseline

Imaging-based endpoints (ORR/DOR; iORR/iDOR; progression by iRECIST) measured every 8 weeks (±1) from first dose until last dose or iCPD. R0 rate, CAP-TRG and major pathologic response measured at surgical resection (≤8 months from first dose). Biochemical response (CA19-9) at baseline and Day 1 each cycle. RFS measured from resection to recurrence/death; OS from first dose to death; survival/post-treatment therapies captured every 12 weeks (±2) during follow-up to 104 weeks post-last dose.

Completion date
30/06/2028

Eligibility

Key inclusion criteria
1. Age ≥18 years old.
2. Able to understand and provide a signed informed consent that fulfills the relevant Institutional Review Board (IRB) or Independent Ethics Committee (IEC) guidelines.
3. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1.
4. Histologically or cytologically confirmed PDAC that is confined to the pancreas.
5. Borderline resectable (surgical resection possible but challenging) or locally advanced (surgical resection not possible) PDAC, as determined by the local investigator based on local institutional guidelines.
6. Measurable tumor lesions according to RECIST v1.1 (within 90 days prior to first dose of study treatment).
7. Have not received prior anticancer therapy for pancreatic cancer.
8. Ability to attend required study visits and return for adequate follow-up, as required by this protocol.
9. Agreement to practice effective contraception for female participants of child-bearing potential and non-sterile males. Female participants of child-bearing potential must agree to use effective contraception for up to 7 months after completion of therapy, and nonsterile male

participants must agree to use a condom for up to 7 months after treatment. Effective contraception includes surgical sterilization (eg, vasectomy, tubal ligation), orals, injectables, two forms of barrier methods (e.g., condom, diaphragm) used with spermicide, intrauterine devices (IUDs), and hormonal therapy.

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
1. Resectable PDAC, meeting the following criteria upon CT/MRI:
1.1. No superior mesenteric vein (SMV) or portal vein (PV) distortion; and
1.2. Clear fat planes around superior mesenteric artery (SMA), celiac artery (CA), and common hepatic artery (CHA).
2. Participants for whom an operation is not considered in the participant's best interest (eg, due to comorbidity).
3. Histologically or cytologically confirmed pancreatic tumor that is not adenocarcinoma.
4. CA19-9 > 1,000 U/mL.
5. QTc interval using Fridericia's formula (QTcF) > 470 ms.
6. If participants have had major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment.
7. Have received a live vaccine within 30 days prior to the first dose of study drug. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella /zoster (chicken pox), yellow fever, rabies, BCG, and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines are live attenuated vaccines and are not allowed.
8. Have known active central nervous system (CNS) metastases and/or carcinomatous meningitis.
9. Inadequate hematologic and end organ function, defined by the following laboratory results obtained within 14 days prior to baseline:
9.1. Absolute neutrophil count (ANC) < 1,500 cells/μL without granulocyte colonystimulating factor support
9.2. Lymphocyte count < 500/μL
9.3. Platelet count < 100,000/μL without transfusion
9.4. Hemoglobin < 8.0 g/dL
Note: Participants may be transfused to meet this criterion.
9.5. International Normalized Ratio (INR) or aPTT activated partial thromboplastin time (aPTT) < 1.5 × upper limit of normal (ULN)

Note: This applies only to participants who are not receiving therapeutic anticoagulation; participants receiving therapeutic anticoagulation should be on a stable dose.
9.6. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase > 2.5 × ULN, with the following exception:
Participants with documented liver metastases: AST and/or ALT > 5 × ULN.
9.7. Serum bilirubin ≤ 3 × ULN
9.8. Creatinine clearance ≤ 60 mL/min (calculated using the Cockcroft-Gault formula).
9.9. Serum albumin ≤ 3.0 g/dL.
9.10. Urine dipstick for proteinuria > 2+ (within 7 days prior to initiation of study treatment). Participants with ≥ 2+ proteinuria on dipstick urinalysis at baseline should undergo a 24-hour urine collection and must demonstrate < 1 g of protein in 24 hours.
10. Significant cardiovascular disease (such as New York Heart Association cardiac disease class II or greater), myocardial infarction within 3 months prior to baseline, unstable arrhythmias, or unstable angina.
11. Severe infections at the time of enrollment, including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia.
12. Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment. Participants receiving prophylactic antibiotics (eg, to prevent a urinary tract infection or chronic obstructive pulmonary disease exacerbation) are eligible for the study.
13. Prior allogeneic bone marrow transplantation or solid organ transplant.
14. Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the participant at high risk for treatment complications.
15. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.
16. Treatment with systemic immunosuppressive medications (including, but not limited to prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti–tumor necrosis factor [anti-TNF] agents) within 2 weeks prior to initiation of study treatment, or anticipation of the need for systemic immunosuppressive medication during study treatment, with the following exceptions:
16.1. Participants who have received acute, low-dose, systemic immunosuppressant medications (eg, a one-time dose of dexamethasone for nausea) may be enrolled in the study after discussion with and approval by the Medical Monitor.
16.2. The use of inhaled corticosteroids for chronic obstructive pulmonary disease, mineralocorticoids (eg, fludrocortisone) for participants with orthostatic hypotension, and low-dose supplemental corticosteroids for adrenocortical insufficiency are allowed.
17. Participation in an investigational drug study or history of receiving any investigational treatment within 30 days prior to the start of treatment on this study.
18. Assessed by the Investigator to be unable or unwilling to comply with the requirements of the protocol.
19. Pregnant and nursing women.

Date of first enrolment
01/01/2026

Date of final enrolment
01/04/2027

Locations

Countries of recruitment
United Kingdom

England

United States of America

Study participating centre
NIHR/Wellcome Trust Clinical Research Facility
First Floor, Heritage Building
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
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Study participating centre
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Sponsor information

Organisation
Serum Life Science Europe GmbH

Funder(s)

Funder type

Funder Name
ImmunityBio, Inc.

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary

Published as a supplement to the results publication