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Phase 1 study of NG-350A plus pembrolizumab in metastatic or advanced epithelial tumours

Submission date
09/02/2022

Recruitment status
No longer recruiting

Registration date
17/06/2022

Overall study status
Ongoing

Last Edited
04/07/2022

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
This study will evaluate the safety (side effects), how the body processes the treatment (pharmacokinetics), and what the treatment does to the body (pharmacodynamic effects) of the drugs NG-350A plus pembrolizumab in patients with cancer.
Worldwide, almost 10 million deaths in 2020 were estimated to be due to cancer. Despite the introduction of multiple new therapies, the overall burden of cancer incidence and mortality is growing worldwide and there remains a critical need for new and effective treatments.
NG-350A is an experimental gene therapy medicinal product.
The other drug used in this study, pembrolizumab, works by changing the action of the immune system, directing it to attack cancer cells. Pembrolizumab belongs to a class of drugs known as monoclonal antibodies. Pembrolizumab is approved for use in the UK.

Who can participate?
Patients over 18 years, with one of the types of cancer being investigated.

What does the study involve?
The study will be conducted with participants in 2 phases. Phase 1a will investigate NG-350A administration by intravenous (IV) infusion in combination with fixed-dose pembrolizumab in a range of tumour types. Phase 1b will further investigate the efficacy and safety of the selected dose regimen in up to three of the tumour types evaluated in phase 1a.

What are the possible benefits and risks of participating?
Benefits:
There will be no direct medical benefit, we hope the information learned from this study will benefit other participants with cancer in the future.
Risks:
It is not possible to predict all side-effects but based on prior studies/literature. Kidney damage, breathing problems, intestinal blockages, abnormal blood clotting tests (not associated with bleeding/clotting) and cytokine release syndrome (see ICF) are considered important risks in this study. Successful mitigation strategies have been established to reduce the risk of these side-effects (eg not enrolling patients most at risk, extra monitoring & modifying dosing schedules). Pembrolizumab is approved for treating the cancer types in this study; further unknown risks

may occur when it is combined with NG-350A. Prior studies with related viral vectors + pembrolizumab have not identified new risks. A complete list of potential risks and side-effects are provided in the ICF. Patients will be closely monitored during the study and if the patient's condition worsens or disease progression occurs, study treatment will be discontinued. As relatively frequent visits are required, visit windows are in place to allow patients to attend at the most convenient times for them; some visits may be by phone. Patients need to have routine blood draws (max 122 mL drawn per visit), CT or MRI scans and biopsies. These are all common procedures which would likely be carried out as part of the patient's routine care. All procedures will be carried out by trained professionals. Biopsies can cause pain and so the area to be biopsied is numbed with a local anaesthetic and painkillers may be prescribed. The effect of NG-350A on babies before they are born, or on breastfeeding children is not known. Patients who are pregnant, planning pregnancy or are breastfeeding, will not be included in the study. A number or requirements are in place to prevent pregnancy.

Where is the study run from?
PsiOxus Therapeutics Ltd. (UK)

When is the study starting and how long is it expected to run for?
February 2022 to June 2026

Who is funding the study?
PsiOxus Therapeutics Ltd (UK)

Who is the main contact?
Pia Donaldson, IRASprojectdeputy@psioxus.com

Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-000335-22

Integrated Research Application System (IRAS)
1005052

ClinicalTrials.gov (NCT)
NCT05165433

Protocol serial number
NG-350A-02, IRAS 1005052, CPMS 52187

Study information

Scientific Title
A multicentre, open-label, non-randomized, phase 1a/1b study of NG-350A, a tumour-selective anti-CD40-expressing adenoviral vector in combination with pembrolizumab in patients with metastatic or advanced epithelial tumours

Study objectives

1. To characterise the safety and determine the recommended dose of NG-350A in combination with pembrolizumab in patients with advanced cancers
2. Explore the efficacy, distribution and immune response of NG-350A in combination with pembrolizumab in patients with advanced cancers

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, London - West London & GTAC (London), ref: 22/LO/0161

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Advanced cancer

Interventions
This is a phase 1a/1b, multicentre, open-label, non-randomized study of NG-350A in combination with pembrolizumab in patients with metastatic or advanced epithelial tumours. Phase 1a will investigate NG-350A administration by intravenous (IV) infusion in combination with fixed-dose pembrolizumab in a range of tumour types. Phase 1b will further investigate the efficacy and safety of the selected dose regimen in up to three of the tumour types evaluated in phase 1a. The estimated duration of the study from enrolment to follow-up is 112 weeks.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
NG-350A, pembrolizumab

Primary outcome(s)
1. Incidence of: adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation of study treatment or study discontinuation and AEs resulting in death measured continuously, up to 100 days after last dose of study
2. Incidence of abnormalities in vital signs or other clinical safety assessments measured continuously, up to 100 days after last dose of study treatment
3. Incidence of AEs meeting protocol defined dose-limiting toxicity (DLT) criteria measured continuously during DLT period

Key secondary outcome(s))

Measured at 26 and 52 weeks, and at study end (other timepoints may be utilized):
1. ORR, DCR and DoR according to Investigator (phase 1a) and IRRC (phase 1b) assessment, and using RECIST v1.1 and immune iRECIST measured using the number and percentage of patients who achieve either a CR or PR according to Investigator or IRRC (phase 1b only) assessments from the date of first dose of study treatment to the end of the study.
2. Median PFS and PFS rates according to Investigator (phase 1a) and IRRC assessments (phase 1b) measured using median PFS and PFS rates measured according to Investigator (phase 1a) and IRRC assessments (phase 1b) at weeks 26 and 52
3. OS rate defined as the interval between the day of the first dose of study treatment until the date of death due to any cause.
4. Measurements of NG-350A pharmacokinetics/blood concentrations of NG-350A measured using blood samples taken immediately after the end of infusion.
5. Measurements of NG-350A immunogenicity/anti-NG-350A antibody titres measured using blood samples taken at the timepoints defined in the schedule of assessments.

Completion date
01/06/2026

Eligibility

Key inclusion criteria
1. Provide written informed consent to participate
2. Aged 18 years or over on day of signing informed consent
3. Patients must have one of eleven histologically or cytologically confirmed metastatic /advanced carcinomas or adenocarcinomas that has progressed after at least one line of systemic therapy and are incurable by local therapy
4. At least one measurable site of disease according to RECIST v1.1 criteria; this lesion must be either (i) outside a previously irradiated area or (ii) progressive if it is in a previously irradiated area
5. Prior treatment with a PD-1/PD-L1 inhibitor (prior PD-1/PD-L1 may have been given as monotherapy or combination therapy)
6. Tumour accessible for biopsy, biopsy deemed safe by the Investigator, and patient willing to consent to tumour biopsies
7. Ability to comply with study procedures in the Investigator’s opinion
8. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Prior or planned allogeneic or autologous bone marrow or tissue/organ transplantation
2. Splenectomy
3. Active infections requiring systemic anti-infective treatment, physician monitoring/hospital admission or recurrent fevers (>38.0˚C) associated with a clinical diagnosis of active infection within 20 days of the anticipated first dose of study drug. Patients who have had an active infection requiring systemic therapy, but not hospital admission, which has resolved at least 10 days before the anticipated first dose of study drug are eligible
4. Treatment with the antiviral agents: ribavirin, adefovir, lamivudine or cidofovir within 10 days prior to the first dose of study treatment; or pegylated interferon in the 4 weeks before the first dose of study treatment
5. Known history of hepatitis B (defined as HBsAg reactive) or known active hepatitis C virus (defined as HCV RNA [qualitative] is detected) infection. Known history of HIV infection (no testing for HIV, hepatitis B or hepatitis C is required unless mandated by local health authority)
6. Patients who have active autoimmune disease that has required systemic therapy in the past 2 years, are immunocompromised in the opinion of the Investigator, or are receiving chronic systemic immunosuppressive treatment (including steroid therapy in doses exceeding 10 mg daily of prednisone equivalent)
7. Treatment with any live, live-attenuated or COVID-19 vaccine in the 30 days before first dose of study drug

Date of first enrolment
01/04/2022

Date of final enrolment
01/06/2025

Locations

Countries of recruitment
United Kingdom

England

United States of America

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

Study participating centre

Clatterbridge Cancer Centre
Clatterbridge Hospital
Clatterbridge Road
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CH63 4JY

Study participating centre
University of California, Los Angeles (UCLA) - Medical Center
2020 Santa Monica Blvd
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United States of America
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Study participating centre
MD Anderson Cancer Center
Division of Cancer Medicine, Unit 455
515 Holcombe Blvd
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Sponsor information

Organisation
PsiOxus Therapeutics Ltd.

Funder(s)

Funder type
Industry

Funder Name
PsiOxus Therapeutics Ltd

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No