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A Phase I/IIa trial of NVG-222 in participants with solid tumours

Submission date	Recruitment status	[X] Prospectively registered
16/10/2025	Not yet recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
24/04/2026	Ongoing	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
24/04/2026	Cancer	[X] Record updated in last year

Plain English summary of protocol
Background and study aims
This clinical trial is testing a new cancer drug called NVG-222, which is designed to help the body's immune system find and kill cancer cells. NVG-222 is a type of drug called a bispecific T-cell engager. Bispecific T-cell engagers work by recognising and attaching to two different types of cells at the same time: cancer cells and immune cells in the body called T cells. NVG-222 has been designed to work by attaching to a protein called ROR1, which is found in high levels on certain types of cancer cells, and to CD3, a protein found on T cells. By connecting the cancer cells to the T cells, NVG-222 should help the immune system to target and kill the cancer cells more effectively. NVG-222 also contains an 'off switch' designed to reduce the risk of serious side effects by turning the drug off if early signs of side effects appear.
The main aims of the clinical trial are to find out:
1. The best dose of NVG-222 that can be given safely to participants in the trial.
2. What the side effects of NVG-222 are.
3. What happens to NVG-222 inside the body.
4. Whether NVG-222 can shrink or control cancer.

Who can participate?
Patients aged 18 years and over with certain types of advanced solid tumours that are expected to have ROR1 proteins on their cancer cells. Patients must have cancer that is no longer responding to standard treatment (refractory). Patients can also participate if the Investigator doesn't think any standard treatment is right for them, or if the patient decides not to have the treatment that has been offered to them.

What does the study involve?
This clinical trial is split into two phases.
Phase I is the 'dose escalation' phase and is split into two parts. In Part I, one participant at a time will receive NVG-222, starting with a low dose. If there are no serious side effects, the next participant will receive a higher dose, and so on. Part II will start after Part I has finished. In Part II, small groups of participants will receive NVG-222 at different dose levels, starting with a low dose. After reviewing the results from each group, it will be decided if the dose of NVG-222 can be increased for the next group of participants. This phase of the trial aims to find out the best dose of NVG-222 that does not cause too many side effects.

Phase II is the ‘dose expansion’ phase. This will start when the dose escalation phase has worked out the best dose of NVG-222 to give participants in the trial. In the dose expansion phase, this dose will be given to a larger number of participants who have specific types of solid tumours. This phase of the trial aims to find out more about how NVG-222 works against cancer. This phase of the trial may include testing NVG-222 in combination with other cancer treatments.

What are the possible benefits and risks of participating?
NVG-222 is a new drug. Possible risks and benefits are based on laboratory tests and experience with similar drugs. Participants in the trial will be monitored closely to find out the effects of NVG-222, and the study has been carefully designed to keep participants safe.

Where is the study run from?
Cancer Research UK

When is the study starting and how long is it expected to run for?
January 2027 to January 2032

Who is funding the study?
1. Cancer Research UK
2. NovalGen Ltd

Who is the main contact?
Prof. James Spicer, james.spicer@kcl.ac.uk

Plain English summary under review with external organisation

Contact information

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Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1012743

Protocol serial number
CRUKD/25/003

Study information

Scientific Title
A Cancer Research UK Phase I/IIa, dose escalation and expansion trial of NVG-222, an autoregulating, half-life extended bispecific ROR1-directed CD3 T-cell engager, given in participants with solid tumours

Study objectives
Primary objectives:
1. To propose a therapeutic dose range and/or optimal dose schedule for NVG-222 that can be given to participants with solid tumours.
2. To make an assessment of how safe and tolerable NVG-222 is in participants with solid tumours.

Secondary objectives:
1. To monitor levels of NVG-222 in the blood.
2. To make a preliminary assessment of the anti-tumour activity of NVG-222 in participants with solid tumours.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 19/01/2026, London - Chelsea Research Ethics Committee (Research Ethics Committee (REC) London Centre, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048 088; chelsea.rec@hra.nhs.uk), ref: 25/LO/0829

Study design
Multi-centre non-randomized Phase I/IIa open-label dose escalation and dose expansion adaptive design trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Solid tumours

Interventions
The dose escalation phase (Phase I) will consist of two parts. In Part I, NVG-222 will be administered in single participant cohorts. These participants will follow accelerated dose escalation, with intra-participant dose escalation permitted. In Part II, NVG-222 will be administered in multiple participant cohorts consisting of 3 to 6 participants each. Participants will receive NVG-222 as an intravenous infusion once every 2 weeks. The starting dose will be 6 µg.
In the dose expansion phase (Part III; Phase IIa), participants will receive NVG-222 as an intravenous infusion at a dose and schedule that will be determined based on data from the dose escalation phase.
All participants may receive NVG-222 for up to 12 cycles. If a participant is benefiting from treatment with NVG-222, a maximum of 12 further cycles may be given. Participants will be followed up for up to 100 days after the last administration of NVG-222.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
NVG-222

Primary outcome(s)
1. Nature and frequency of dose-limiting toxicities (DLTs). DLTs are defined and assessed according to specific criteria in the trial protocol. Evaluation of this endpoint will occur when sufficient participants have completed the DLT assessment period (first 28 days of administration) and all relevant data have been collected.
2. Determination of the maximum tolerated dose (MTD) and/or optimal biological dose (OBD) and/or therapeutic dose range and/or optimal dose schedule for NVG-222. The Bayesian optimal interval model will recommend the NVG-222 dose with an estimated DLT rate within the target

range of 20% to 33%. In the absence of DLT, the single agent recommended Phase II dose or OBD and schedule will be determined based upon the maximum administered dose and all available safety, pharmacokinetic (PK) and pharmacodynamic data. Evaluation of this endpoint will occur when sufficient participants have completed the DLT assessment period (first 28 days of administration) and all clinically relevant data have been reviewed by the Sponsor, Chief Investigator and Principal Investigators.
3. Frequency of adverse events (AEs) considered at least possibly related to NVG-222 and number of Grade 3, 4 and 5 AEs considered at least possibly related to NVG-222. AEs, including relatedness, seriousness and severity (graded according to National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] Version 5.0 with the exception of cytokine release syndrome [CRS] and neurotoxicity [ICANS], which will be graded according to American Society for Transplantation and Cellular Therapy [ASTCT] consensus grading) will be assessed by the Investigator.

Key secondary outcome(s))

1. PK parameters of NVG-222, including minimum concentration (Cmin), maximum concentration (Cmax), area under the curve (AUC), clearance (CL), volume of distribution (Vd) and terminal elimination half-life (t1/2), in blood (serum) for intravenous administration, measured using a standard ligand binding assay. Additional PK parameters may be determined as appropriate. Samples for PK analysis will be taken at up to 30 timepoints for each participant over the duration of the trial.
2. Objective response rate, defined as the proportion of participants who achieve complete response (CR) or partial response (PR) as the best overall response according to RECIST V1.1. This endpoint will be evaluated at end of trial (EoT).
3. Disease control rate, defined as the percentage of participants who achieve CR, PR or a minimum of stable disease for 12 weeks based on Response Evaluation Criteria in Solid Tumours (RECIST) V1.1. This endpoint will be evaluated at EoT.
4. Duration of response, defined as the time from the initial occurrence of a documented PR or CR until documented disease progression or death due to any cause, whichever occurs first, according to RECIST V1.1. This endpoint will be evaluated at EoT.
5. Progression-free survival, defined as the time from the date of administration of the first dose of NVG-222 on this trial to disease progression or death from any cause or the date of censoring at the last time the participant was known to be progression free. Participants who start a new anti-cancer treatment will not be censored. This endpoint will be evaluated at EoT.
6. Overall survival, defined as the time from the date of administration of the first dose of NVG-222 on this trial to the date of death due to any cause, or to the date of censoring at the last time the participant was known to be alive. Participants who are lost to follow-up will be censored at the time of last contact; participants who start a new anti-cancer treatment will not be censored. This endpoint will be evaluated at EoT.

Completion date

31/01/2032

Eligibility

Key inclusion criteria

1. Written (signed and dated) informed consent and capable of co-operating with investigational medicinal product (IMP) administration and follow-up.
2. Histologically or cytologically proven advanced solid tumours (including non-small cell lung cancer, triple-negative breast cancer, malignant melanoma, ovarian cancer, and other solid tumour types where there is supportive ROR1 expression data), refractory to conventional

treatment, or for which no conventional therapy is considered appropriate by the Investigator or is declined by the patient.
3. Objectively evaluable or measurable disease, according to RECIST V1.1.
4. Consent to access and analyse suitable archival sample or consent for fresh tumour biopsy at baseline (if no suitable archival sample is available).
5. Life expectancy of at least 12 weeks.
6. Eastern Cooperative Oncology Group performance status of 0–1.
7. Haematological and biochemical indices within prescribed ranges. These measurements should be performed to confirm the patient's eligibility to participate in the trial.
8. 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
1. Radiotherapy (except for palliative reasons), endocrine therapy, chemotherapy or other investigational medicinal products (IMPs) during the previous 28 days before the first dose of IMP (or last dose of an immunotherapy during the previous 12 weeks).
2. Therapeutic antibodies (for any indication), within 28 days prior to first NVG-222 administration.
3. Ongoing toxic manifestations of previous treatments greater than Common Terminology Criteria for Adverse Events (CTCAE) Grade 1 (other than alopecia of any grade or Grade 2 peripheral neuropathy) with certain exceptions permitted as per protocol.
4. Any central nervous system metastases (unless patients had local therapy and are asymptomatic AND radiologically stable AND have been off steroids for the last 28 days prior to screening).
5. History or presence of dementia or psychosis. Patients with a previous history of epilepsy may participate if it is controlled with medication. Patients who have made a good recovery from a stroke, and who have no residual cognitive impairment and minimal or no motor or sensory loss, may participate if the neurological insult occurred >1 year prior to screening with no further recurrence.
6. Women who are pregnant or breastfeeding (or planning to breastfeed).
7. Women of childbearing potential. However, those patients who are not already pregnant or

breastfeeding (or planning to breastfeed) are eligible, provided they have a negative highly sensitive serum pregnancy test within 7 days before enrolment and agree to follow the trial's contraceptive requirements.
8. Male patients with partners of childbearing potential. However, those patients who agree to follow the trial's contraceptive guidance are eligible.
9. Major surgery from which the patient has not yet recovered.
10. Concomitant steroids. The use of corticosteroids at a dose ≤10 mg/day prednisone or equivalent is permitted; however, there must be documentation that the patient was on a stable dose of at least 7 days duration prior to trial enrolment. Inhaled and topical steroids are permitted.
11. At high medical risk because of non-malignant systemic disease, including active, uncontrolled infection.
12. Known to be serologically positive for hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV).
12.1. Active hepatitis B infection. Patients with negative serologic or PCR test results for acute or chronic HBV infection are eligible.
12.2. Active hepatitis C infection. Patients who test positive for hepatitis C antibody with a detectable HCV load are not eligible.
12.3. Patients with known HIV are excluded unless viral load is undetectable and CD4 count is above 350 cells/mm3 on stable Highly Active Antiretroviral Therapy.
13. Known or suspected hypersensitivity reaction to previous biological therapy or any of the NVG-222 excipients that, in the opinion of the Investigator, is a contraindication for participation in this study.
14. Patient is unable to receive at least 1 of the following prophylactic medications for tumour lysis syndrome: allopurinol, febuxostat or rasburicase.
15. Significant cardiovascular disease, as defined within the protocol.
16. Clinically significant lung disease, as defined within the protocol.
17. Participating in or plans to participate in another interventional clinical trial whilst taking part in this Phase I/IIa trial of NVG-222. Certain exceptions are permitted as per protocol.
18. Current or prior malignancy that could affect safety or efficacy assessment of the IMP or compliance with the protocol or interpretation of results. Certain exceptions are permitted as per protocol.
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. Certain exceptions are permitted as per protocol.
20. Live vaccine or live-attenuated vaccine within 28 days of trial enrolment.
21. Any other condition that, in the Investigator's opinion, would mean that the trial is not in the best interests of the patient.

Date of first enrolment
31/01/2027

Date of final enrolment
31/01/2031

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy's Hospital
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SE1 9RT

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

Funder Name
NovalGen Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current trial will be available upon request

IPD sharing plan summary
Available on request