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The evaluation of safety and biological effects of cancer-killing virus vaccine given to patients with advanced brain tumours

Submission date 13/02/2021	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 28/06/2021	**Overall study status** Ongoing	
Last Edited 09/09/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-vcn-01-to-treat-brain-tumours

Background and study aims
Patients with recurrent high-grade primary brain tumours or tumours that have spread to the brain from elsewhere have poor outcomes, most of them will die from their illness within a year from diagnosis. The benefits from currently available treatments are very limited, so new effective therapies need to be found.

A common respiratory virus (human adenovirus serotype 5) has been found to be useful in developing treatments for cancer. These viruses can be genetically modified so that they can infect and kill cancer cells and do not affect non-cancer cells.VCN-01 is a genetically modified strain of adenovirus serotype 5 which has been previously tested in several clinical trials either on its own or in combination with other treatments. The results of these studies showed that VCN-01 acts against cancer by stimulating the immune system to attack the cancer cells, and has few side effects.

The purpose of this study is to investigate the effects of VCN-01 when given via the vein to brain cancer patients. Often treatments are unable to enter the brain from the bloodstream due to the selective blood-brain barrier that protects the brain from toxins and infections. However, tumours can cause changes to the blood vessels surrounding them in order to help them grow, and this may allow treatments such as VCN-01 to reach the tumour. This study hopes to find whether VCN-01 can reach brain tumours when given via the vein rather than as an injection into the tumour during a surgical procedure, as this would be a better-tolerated way to provide this treatment. The trial will also determine treatment safety and immune response to viral therapy. The findings will be taken forward to develop VCN-01 for the treatment of patients with brain tumours both on its own and in combination with other treatments.

Who can participate?
Adults aged over 16 years with recurrent high-grade glioma or brain metastases and with planned surgical resection of their tumour.

What does the study involve?
Each patient will have to provide informed consent and undergo screening investigations before beginning the trial treatment. Participants will be invited to a visit on the day of VCN-01 being given (day 1) and the next two days (day 2 and day 3). Participants will also attend visits on the day of/day before the scheduled surgery and at 1 and 3 months follow-up. At each visit, the patients will have their vital signs measured, undergo a physical exam and have blood samples taken for analysis.

What are the possible benefits and risks of participating?
The likelihood of the patient deriving benefit from the study is minimal. There should be benefits to the treatment for future cancer patients.

The main risk of this treatment involves possible side effects related to VCN-01 therapy. The adverse events reported in previous VCN-01 trials include fever, weakness or lack of energy, infections and infestations, gastrointestinal (digestive) disorders, decreased level of platelets, white blood cells and lymphocytes. The observations were consistent with the adverse events previously seen in other trials involving adenoviruses targeting cancer. The adverse effects will be monitored closely and managed carefully to ensure patient safety.

It is important that patients of childbearing potential, and the partners of childbearing potential of patients, do not become pregnant whilst on this clinical trial as it is not known whether treatment with VCN-01 poses a risk to an unborn child.

Where is the study run from?
The University of Leeds (UK)

When is the study starting and how long is it expected to run for?
From July 2020 to July 2028

Who is funding the study?
Cancer Research UK (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2020-003405-59

Integrated Research Application System (IRAS)
283902

Protocol serial number
CO20/134663, IRAS 283902

Study information

Scientific Title
A clinical study to evaluate the biological effects of preoperative intravenous administration of VCN-01 in patients prior to surgical resection of high-grade brain tumours

Acronym
VCN-01 BRAIN

Study objectives
1. VCN-01 is able to cross the blood-brain barrier
2. Intravenous virus administration is safe in patients with recurrent high-grade glioma or brain metastases

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/04/2021, North East – York Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ; +44 (0)207 1048091; york.rec@hra.nhs.uk), ref: 21/NE/0061

Study design
Open-label single-centre Phase 1b non-randomized study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Malignant neoplasm of brain, high-grade brain tumour

Interventions
All patients will be recruited in one cohort, to receive a single dose of intravenous VCN-01 at a concentration of 1x10e13 virus particles prior to planned surgery for recurrent high-grade primary or metastatic brain tumours. Participants will be invited to attend visits on day 1 (VCN-01 infusion), day 2, day 3, day of/day before the scheduled surgery, 1-month post-infusion of VCN-01 and 3 months post-infusion of VCN-01. At each visit, the patients will have their vital signs measured, undergo a physical exam, and have blood samples taken for analysis.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
VCN-01, genetically modified oncolytic adenovirus

Primary outcome(s)
1. Presence of VCN-01 within the resected surgical specimen measured using identification of VCN-01 DNA (qPCR technique) and VCN-01 proteins (IHC technique) at a single timepoint after surgical sample of tumour tissue collected
2. Safety of intravenous VCN-01 in patients with recurrent high-grade glioma or brain metastases, ahead of planned surgical resection measured using the incidence of Adverse Events (serious and non-serious) and their duration between VCN-01 administration and 3 months

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
01/07/2028

Eligibility

Key inclusion criteria
1. Histologically confirmed recurrent grade 3 or 4 glioma, histologically confirmed recurrent grade 2 glioma with clinical/radiological evidence for high-grade transformation, or metastatic brain secondaries with previous histological confirmation of a non-central nervous system (non-CNS) primary solid malignancy
2. Be planned for surgical resection as per standard clinical care
3. Have no continuing acute toxic effects of any prior radiotherapy, chemotherapy, or surgical procedures. All such effects must have resolved to Common Terminology Criteria for Adverse Events (CTCAE, Version 5.0) Grade ≤1. Radiotherapy, chemotherapy, or surgery (except biopsies) must have occurred at least 28 days prior to study enrolment.
4. Aged ≥16 years
5. Have completed any previous systemic therapy at least five half-lives of the given agent before entry into the study

6. Have an Eastern Cooperative Oncology Group (ECOG) Performance Score of ≤1
7. Have a life expectancy of ≥1 month
8. Have screening laboratory results as follows:
8.1. Absolute neutrophil count (ANC) ≥1.5 x 10^9/l
8.2. Platelets ≥100 x10^9/l (without platelet transfusion)
8.3. Haemoglobin ≥9.0 g/dl (with or without RBC transfusion)
8.4. Serum creatinine ≤1.5 x upper limit of normal (ULN)
8.5. Bilirubin ≤2.5 x ULN, unless diagnosed with Gilbert's syndrome, in which case bilirubin ≤5 x ULN
8.6. Aspartate transaminase (AST)/alanine transaminase (ALT) ratio ≤2.5 x ULN
9. Negative serum pregnancy test for participants of childbearing potential. Women of childbearing potential are defined as those who are not surgically sterile (bilateral tubal ligation, bilateral oophorectomy, or complete hysterectomy) or postmenopausal. Women aged <50 years would be considered postmenopausal if they have been amenorrheic for ≥12 months following cessation of exogenous hormonal treatments and if they have luteinizing hormone and follicle stimulating hormone levels in the post-menopausal range for the institution. Women aged ≥50 years would be considered postmenopausal if they have been amenorrheic for ≥12 months following cessation of all exogenous hormonal treatments, had radiation-induced oophorectomy with last menses >1 year ago, had chemotherapy-induced menopause with >1 year interval since last menses, or underwent surgical sterilization (bilateral oophorectomy or hysterectomy).
10. Participants of reproductive potential must agree to use effective contraception. Participants of childbearing potential must agree to use effective contraception and their partners must also use male condom plus spermicide throughout this period. Non-sterilized male subjects must use male condom plus spermicide with partners of childbearing potential. Appropriate contraception must be used for up to 60 days following VCN-01 infusion. Effective methods of contraception are defined as:
10.1. Barrier/Intrauterine Device Methods (copper T intrauterine device or levonorgestrel-releasing intrauterine system)
10.2. Hormonal Methods (implants, hormone shot or injection, combined pill, minipill, patch)
10.3. Other (sexual abstinence, bilateral tubal occlusion, vasectomised partner)
11. Able to provide written informed consent prior to performing any protocol-related procedures, including study-specific screening procedures
12. Willing and able to comply with scheduled visits, the treatment plan, laboratory tests, and additional precautions to prevent the spread of the virus

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
All

Key exclusion criteria

1. Receive concurrent therapy with any other standard or investigational anticancer agent while on study or within 5 half-lives of the agent prior to VCN-01 infusion
2. Immunosuppressive therapy other than steroids, or a positive test for HIV infection or Hepatitis B or C
3. Positive COVID-19 Coronavirus RNA test performed according to the up-to-date LTHT SOP ("COVID-19 testing for adult patients before surgery/treatment/attendance and whilst IP at LTHT")
4. Pregnant or breast-feeding
5. Dementia or altered mental status that would prohibit informed consent
6. Any other severe, acute, or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration or may interfere with the interpretation of study results and, in the judgment of the Principal Investigator, would make the patient inappropriate for this study
7. Active infection or another serious illness or serious autoimmune disease
8. Treatment with live attenuated or mRNA vaccines within three weeks before planned VCN-01 treatment and within 2 weeks after planned VCN-01 treatment
9. Known chronic liver disease (such as liver cirrhosis, chronic hepatitis)
10. Treatment with another investigational agent within its five half-lives prior to VCN-01 infusion
11. Viral syndrome diagnosed during the two weeks before inclusion
12. In close contact with immunosuppressed patients (such as patients with chronic immunosuppressive therapy including high dose of corticosteroids, AIDS, and other chronic immune system diseases)
13. Li Fraumeni syndrome or previously known retinoblastoma protein (pRb) pathway deficiency
14. Receiving full-dose anticoagulant/antiplatelet therapy or in whom these therapies cannot be withdrawn within two days prior to the VCN-01 injection
15. Significant alcohol history (>70 units per week for 5 or more years)

Date of first enrolment
01/06/2021

Date of final enrolment
30/09/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St James's University Hospital
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LS9 7TF

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

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 and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

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