ISRCTN78231121 https://doi.org/10.1186/ISRCTN78231121

Testing 123I-ATT001, a new type of targeted radiotherapy, administered directly to the brain tumour of patients in whom the glioblastoma has returned after previous treatment

Submission date
04/01/2024

Recruitment status
Recruiting

Registration date
23/07/2024

Overall study status
Ongoing

Last Edited
28/01/2025

Condition category
Cancer

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

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-a-targeted-treatment-for-glioblastoma-citadel-123

Background and study aims
In this study, a type of therapy called targeted radionuclide therapy (TRT) will be used to treat patients with relapsed glioblastoma. The TRT in this study, 123I-ATT001, contains two parts. A radioactive part is a radioactive iodine isotope and a chemical part, which can bind to specific targets (proteins) inside cancer cells to kill them while having a much weaker effect on healthy cells. 123I-ATT001 is a new experimental treatment, meaning it has not been approved by any regulatory authorities, such as the UK's MHRA. This new treatment will only be available for those enrolled in this study.

Who can participate?
Patients aged 18 years old and over with relapsed glioblastoma multiforme

What does the study involve?
The study consists of two parts. Part 1 is a dose escalation study, where three doses of 123I-ATT001 will be tested, starting with the lowest dose. When the Data Monitoring Committee declare a recommended dose, an additional 8 patients will be recruited at that dose level in Part 1 of the study. In Part 2, one dose of 123I-ATT001 will be tested in a larger group of patients in combination with other therapies. Part 2 will begin after Part 1 has been completed.

123I-ATT001 will be given via an Ommaya reservoir. An Ommaya reservoir is a soft, plastic, dome-shaped device that is placed under the scalp. In Part 1 participants will receive a 123I-ATT001 dose, once per week, for four weeks. Each week is considered a treatment cycle.
Any participant who tolerates the 123I-ATT-001 treatments well and shows clinical benefit (e.g., tumour size reduction) may receive up to two additional treatments (one per week). This will be a joint decision between the doctor and the participant. The doctor may decide to reduce the

dose or extend the time between treatment cycles in response to any side effects. However, no further treatments will be given in case any unacceptable side effects are observed.

The specific details and combination therapies for Part 2 of the study will be added via a substantial amendment at a later date.

What are the possible benefits and risks of participating?
The study uses an unlicensed drug that also contains radiation. Only trained members of the research team will administer the drug. A radiation expert has reviewed the maximum dose of radiation that a patient could be exposed to and deemed this acceptable.

The study also uses ionising radiation in the form of SPECT-CT scans. A radiation expert has reviewed the proposed number of scans and found them to be acceptable.

Blood samples also carry risks in terms of possible bruising. Only those who have been appropriately trained in phlebotomy will take samples.

There are several visits for this study which may present a time burden to the patients. The sponsor has tried to minimise the number of visits to ensure the minimum burden to the patients.

The surgery and installation of the Ommaya reservoir carries the risk of infection and will also mean participants have small bumps on their heads. This procedure is usually carried out as part of the standard of care in this patient population.

No additional precautions are needed to be taken by patients after the radiation exposure except pregnancy prevention. Female patients who are pregnant or plan to become pregnant within 3 months following the end of the study, or are breast-feeding, are excluded from the study. Male patients should also not father a baby whilst taking part in the study and for 3 months after the last dose of the study drug. Patients of childbearing potential will have a pregnancy test at the beginning of the study and will be asked to use two highly effective and complementary forms of contraception.

Where is the study run from?
Theragnostics Limited

When is the study starting and how long is it expected to run for?
December 2023 to December 2026

Who is funding the study?
Theragnostics Limited

Who is the main contact?
citadel-123@ariceum-therapeutics.com

Contact information

Type(s)
Public, Scientific

Contact name

Dr Trial team -

Contact details
Holborn Gate, 330 High Holborn
London
United Kingdom
WC1V 7QH
+44 (0)203 6218436
admin_citadel-123@ariceum-therapeutics.com

Type(s)
Principal investigator

Contact name
Dr Paul Mulholland

Contact details
250 Euston Road
London
United Kingdom
NW1 2PQ
-
admin_citadel-123@ariceum-therapeutics.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1006521

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
PIL101, IRAS 1006521, CPMS 54319

Study information

Scientific Title
CITADEL-123: A Phase I clinical trial to assess the activity of I-123 Poly Adenosine Diphosphate Ribose Polymerase I inhibitor (123I-ATT001) directly administered in subjects with relapsed glioblastoma

Acronym
CITADEL-123

Study objectives

The primary objectives of the study are to understand:
- If it is safe and tolerable to give 123I-ATT001 to patients with Glioblastoma multiforme.
-The maximum tolerated dose of 123I-ATT001 that can be given to patients without having any unacceptable side effects.

The secondary objectives of the study are to understand:
Where 123I-ATT001 is distributed in the brain, how much is taken up by the tumour, and whether it reaches other parts
of the body.
Whether any changes in the tumour size occur.
Whether any change in the participants neurological function occur.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 04/03/2024, Health Research Authority (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None provided; approvals@hra.nhs.uk), ref: 24/SC/0034

Study design
Non-randomized phase I trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Relapsed glioblastoma

Interventions
Part 1 - Monotherapy of 123I-ATT001

Dose 1: 500 MBq of 123I-ATT001 administered intercranially via an Ommaya Reservoir once a week for four weeks.
Dose 2: 800 MBq of 123I-ATT001 administered intercranially via an Ommaya Reservoir once a week for four weeks.
Dose 3: 1200 MBq of 123I-ATT001 administered intercranially via an Ommaya Reservoir once a week for four weeks.

Each dose level will start as a single subject dose level. In the case of a Dose Limiting Toxicity, additional subjects on that same dose level as per the statistical plan.

Expansion at Recommended Dose: The recommended dose of 123I-ATT001 from the first three cohorts will be administered intercranially via an Ommaya Reservoir once a week for four weeks in 8 additional participants.

Within each cohort, there is the option for participants to receive two additional weekly treatments if tolerated and a clinical benefit is shown as determined by the treating physician /investigator.

Part 2 - Combination Therapies with 123I-ATT001

In Part 2 of the study, the maximum tolerated dose of 123IATT001 from Part 1 will be further investigated. An additional 4 cohorts of 8 to 12 participants each may be further explored using a combination of 123IATT001 with other anticancer therapies. Specifics will be decided at a later date and included via a protocol amendment.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
123I-ATT001 [123I-ATT001]

Primary outcome(s)
Part 1 only:
1. Safety and tolerability will be evaluated by monitoring of adverse events, vital signs, performance status, clinical laboratory assessments, electrocardiograms, review of concurrent illness, concomitant medication, weight and physical examination findings. This will be performed from screening to the end of the treatment visit (28 days after the last dose of 123I-ATT001).
2. To determine the recommended dose of 123I-ATT001 via intracavitary direct instillation in subjects with relapsed glioblastoma, both as monotherapy and in combination with other anticancer therapies. The incidence of dose-limiting toxicity (DLT) will be evaluated by monitoring adverse events from day 1 to day 15 of 123I-ATT001 administration (pre-third dose).

Key secondary outcome(s))
Part 1 only:
1. To determine the biodistribution and pharmacokinetics of 123I-ATT001, blood and urine samples will be collected from the first 6 patients in Part 1. Blood will be collected 1 hour, 4 hours and 24 hours post each dose and optionally at 48 hours post first dose. Urine will be collected only 24 hours post first dose.
2. To determine the radiation dosimetry of 123I-ATT001 (exposure of each organ to radiation):
2.1. Whole body and brain SPECT/CT imaging will be performed 1-hour post each dose
2.2. Whole body and brain SPECT at 4 hours post each dose
2.3. Brain only SPECT will be done 24 hours post-injection of the first dose
2.4. An optional brain SPECT image may be taken 48 hours post-injection of the first dose
2.5. Brain only SPECT will be done at 4 hours ±30min post-injection of the fourth dose
3. To obtain a preliminary assessment of the antitumour activity of 123I-ATT001 RANO response criteria using MRI Scans will be assessed at screening, day 14 post each dose, end of treatment visit, then a further 3 times every 8 weeks at follow up.
4. To evaluate the effect of 123I-ATT001 on neurological function according to NANO criteria at screening and then pre-dose on the day of the 1st, 3rd and 5th (if given) and at the end of the treatment visit. Additionally, patients will complete the MDASI-BT questionnaire at screening (after surgery) and then pre-dose on the day of the 1st, 3rd and 5th (if given) and at the end of the treatment visit.

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Ability to give written informed consent as evidenced by signature on the subject consent form, to communicate well with the Investigator, and to comply with the expectations of the study
2. Men and women over 18 years of age
3. Histologically confirmed recurrent glioblastoma (grade IV) as per WHO criteria 2021 (IDH- wild type only) where the subjects have an Ommaya reservoir in an intralesional cavity of at least 5 mL volume
4. Documented recurrent disease (radiological, based on RANO v.1.0) within 3 months before first study drug administration
5. Eastern Cooperative Oncology Group Performance status of 0 or 1
6. Adequate organ function:
6.1. Serum creatinine <1.5x upper limit of normal (ULN)
6.2. Liver function tests: serum bilirubin <1.5xULN (except subjects with known Gilbert's syndrome: serum total bilirubin must be <3×ULN in these subjects); transaminases <3xULN and <5 in case of liver metastases
6.3. Absolute neutrophil count (ANC) ≥1000/mL; Platelets ≥100,000/mL; haemoglobin ≥9 g/dL or ≥5.6mmol/L
6.4. International normalisation ratio or prothrombin time ≤1.5x ULN, unless the subject is receiving anticoagulant therapy
7. Women of childbearing potential must use two forms of reliable contraception before starting 123I-ATT001 treatment, during therapy and for 6 months after receiving the last dose of 123I-ATT001. Two highly effective and complementary forms such as hormonal birth control, and intrauterine devices with supplementary barrier methods are recommended. Male subjects and their female partners of childbearing potential should use reliable contraception such as hormonal birth control, and intrauterine devices with supplementary barrier method (male condom) during therapy and for 6 months after receiving the last dose of 123I-ATT001. All male subjects must agree to not donate sperm during the study and for 6 months after the last dose of the study drug.
8. Be able to understand and comply with the requirements of the study, as judged by the Investigator

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. Is currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks of the first dose of treatment
2. Diagnosis of immunodeficiency or receiving systemic steroid therapy of up to 4 mg/ day dexamethasone or equivalent or any other form of immunosuppressive therapy within 7 days before the first dose of study treatment
3. Prior anticancer treatments within the following periods:
3.1. Chemotherapy within 4 weeks of enrolment or 5 half-lives, whichever is shorter
3.2. Targeted small molecule therapy within 4 weeks of enrolment or 5 half-lives, whichever is shorter
3.3. Immunotherapy (including monoclonal antibody therapy) or radiation therapy within 4 weeks before study day 1
4. Unresolved NCI-CTCAE grade 2 or higher toxicity (except stable neurological toxicities/deficits related to disease process, alopecia)
5. Patients with a known allergy to Olaparib or Iodine
6. Known additional malignancy that is progressing or requires active treatment except for basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy, or in situ cervical cancer
7. Any condition that precludes the proper performance of SPECT and/or MRI scan:
7.1. Subjects who are not able to tolerate the contrast agent
7.2. Subjects with metal implants or arthroplasty, or any other objects that might interfere with the MRI analysis
7.3. Subjects unable to raise arms for prolonged imaging purposes
7.4. Subjects unable to lie still for the entire imaging time
7.5. Subjects weighing greater than 130 kg (287 lb)
8. Any clinically significant abnormalities in resting ECG at the time of screening including prolonged QTcF (>450 ms for males; >470 ms for females) and cardiac arrhythmias, as judged by the Investigator or designee
9. Unstable systemic disease (including but not limited to active infection, uncontrolled hypertension, unstable angina, congestive heart failure, myocardial infarction within the previous year, serious cardiac arrhythmia requiring medication, hepatic, renal, or metabolic disease)
10. Psychiatric, substance misuse or functional disorders that prevent subjects from providing informed consent, following protocol instructions or cooperating with the requirements of the study
11. Active infection requiring systemic therapy
12. Pregnant, breastfeeding, or expecting to conceive or father children within the projected duration of the study, starting with the pre-screening or screening visit through 3 months after the last dose of study treatment
13. Subject that has a condition or is in a situation, which in the investigator's opinion may put the subject at significant risk, may confound the study results, or may interfere significantly with the subject’s participation in the study
14. History of non-infectious pneumonitis within the last 3 years

Date of first enrolment
09/07/2024

Date of final enrolment
31/10/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
University College Hospital
1st Floor Central, 250 Euston Road
London
United Kingdom
NW1 2PQ

Sponsor information

Organisation
Theragnostics Limited

Funder(s)

Funder type
Industry

Funder Name
Theragnostics Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date