

ReoGlio: REOLYSIN® plus GM-CSF in combination with standard of care chemotherapy and radiotherapy for patients with glioblastoma multiforme (GBM)

Submission date 06/02/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 06/02/2017	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 02/11/2021	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-reolysin-and-gm-csf-for-glioblastoma-multiforme-reoglio>

Study website

https://medhealth.leeds.ac.uk/homepage/642/early_phase

Contact information

Type(s)

Public

Contact name

Miss Amber Reid

Contact details

Leeds Institute of Clinical Trials Research
University of Leeds
Leeds
United Kingdom
LS2 9JT
+44 113 3438391
CTRU-reoglio@leeds.ac.uk

Type(s)

Public

Contact name

Mr George Picard

Contact details

Clinical Trials Research Unit
Level 10, Worsley Building
Clarendon Way
University of Leeds
Leeds
United Kingdom
LS2 9LU
+44 (0)113 343 9077
G.Picard@leeds.ac.uk

Additional identifiers**EudraCT/CTIS number**

2016-001632-35

IRAS number**ClinicalTrials.gov number****Secondary identifying numbers**

31893

Study information**Scientific Title**

A dose-finding study of the safety and tolerability of intravenous reovirus (REOLYSIN®) (pelareorep) plus granulocyte-macrophage colony-stimulating factor (GM-CSF) in combination with standard of care chemoradiotherapy (CTRT) /adjuvant chemotherapy for Glioblastoma Multiforme (GBM)

Study objectives

The aim of the dose escalation phase of the trial is to determine the Maximum Tolerated Dose (MTD) of REOLYSIN® and GM-CSF in combination with standard of care chemoradiotherapy (CTRT) in adult participants with glioblastoma multiforme (GBM), to determine a recommended dose to take forward to the expansion phase. The dose expansion phase will assess the longer-term toxicity and safety of REOLYSIN® and GM-CSF in combination with standard of care CTRT in adult participants with GBM.

Ethics approval required

Old ethics approval format

Ethics approval(s)

East of England – Cambridge East Research Ethics Committee, 22/12/2016, ref: 16/EE/0494

Study design

Non-randomised; Both; Design type: Treatment, Drug, Radiotherapy, Cohort study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Specialty: Cancer, Primary sub-specialty: Brain Cancer; UKCRC code/ Disease: Cancer/ Malignant neoplasms of eye, brain and other parts of central nervous system

Interventions

Where possible trial treatment should start within 31 days of biopsy/debulking surgery. However trial treatment must start within a maximum of 42 days (6 weeks) after biopsy/surgery. Participants will receive:

Chemoradiotherapy

1. Focal brain external beam radiotherapy consisting of 60Gy in 30 2Gy fractions over 42 days (6 weeks, from Monday to Friday) as per standard treatment. Up to a 7 day delay in radiotherapy is permitted; maximum duration of delivery will be 49 days (7 weeks).
2. Concurrent temozolomide 75mg/m²/day po given daily from the first to the last day of radiotherapy as per standard treatment for a maximum of 49 days
3. Trial treatment (Weeks 1 and 4): GM-CSF 50µg/day sc on days 1-3 plus REOLYSIN® iv on days 4-5.
5. If delays in radiotherapy and/or temozolomide occur without a trial treatment-related DLT, GM-CSF and REOLYSIN® should be delivered on schedule

Adjuvant treatment

Adjuvant treatment should start within 28 to 31 days after the final dose of radiotherapy, and must start within 42 days. If adjuvant treatment cannot start within 42 days of the final dose of radiotherapy due to toxicity, the participant will come off trial treatment.

Adjuvant treatment will comprise up to six 28-day cycles of

2. Temozolomide 150mg/m² po on days 1-5 of the first cycle; increased to 200mg/m² po on days 1-5 of cycles 2 to 6 if cycle 1 tolerated with acceptable toxicity, as per standard treatment
2. Trial treatment (each cycle): GM-CSF 50µg/day sc on days 1-3 plus REOLYSIN® iv on days 4-5

At the escalation phase, the dose of REOLYSIN® used will depend on which cohort the participant is in. Dose escalation will start at dose level 1 (1x10¹⁰TCID₅₀) and proceed to either dose level -1 (5x10⁹ TCID₅₀) or dose level 2 (3x10¹⁰TCID₅₀) depending on the number of DLTs experienced by participants in the original cohort.

The total duration of follow-up for all participants

Follow-up assessments will take place every 84 days until disease progression or the initiation of a new systemic anticancer treatment. The duration of protocol treatment for individual participants will vary. The median progression free survival of patients with GBM is approximately 8-9 months from diagnosis.

Intervention Type

Mixed

Primary outcome measure

Dose escalation phase

Dose limiting toxicities' (DLTs) will be assessed between day 1 of chemoradiotherapy treatment and up to (but not including) day 1 of planned adjuvant chemotherapy, and will be reviewed in patient notes.

Dose expansion phase

Adverse events and serious adverse events will be assessed from the time of consent until 30 days post treatment. SARs and SUSARs will be assessed from the time of consent until the end of the trial.

Secondary outcome measures

1. Safety will be reported based on the occurrence of SAEs, SARs and SUSARs. Toxicity will be reported based on adverse events as graded by CTCAE V4.0. SAEs and AEs will be reported up to 30 days post treatment and SUSARs, SARs and ARs will be reported until the end of trial.
2. Progression free survival will be calculated from the date of registration to first documented evidence of disease progression or death whichever is sooner and will be reviewed in patient notes.
3. For participants with measurable disease, response is assessed using RANO criteria and is defined as the proportion of participants achieving each response category at the time of each follow-up MRI (every 84 days). This will be reviewed in patient notes.
4. Overall survival (OS) will be calculated from the date of registration to death and will be reviewed in patient notes.
5. Treatment compliance will include details of any dose reductions, delays, omissions and withdrawals. and will be reviewed in patient notes.

Overall study start date

29/03/2015

Completion date

25/02/2020

Eligibility

Key inclusion criteria

1. Male or female subjects with a histologically confirmed diagnosis of Glioblastoma Multiforme (WHO Grade IV, including variants).
2. Previous biopsy or debulking surgery.
3. Trial treatment must start within a maximum of 42 days (6 weeks) after biopsy/surgery.
4. Eligible for first line standard treatment with Stupp regimen (radiotherapy concomitant with temozolomide followed by adjuvant temozolomide)

5. If the participant is receiving dexamethasone (or equivalent) this must be a maximum of 8mg dexamethasone daily (or equivalent)
6. Aged over 16
7. ECOG performance status 0-1 (see appendix 2)
8. Life expectancy ≥ 4 months
9. Required laboratory values within 7 days prior to registration
 - 9.1. Absolute neutrophil count (ANC) $\geq 1.5 \times 10^9$ [SI units $10^9/L$]
 - 9.2. Platelets $\geq 100 \times 10^9$ [SI units $10^9/L$] (without platelet transfusion)
 - 9.3. Haemoglobin ≥ 9.0 g/dL [SI units gm/L] (with or without RBC transfusion)
 - 9.4. Serum creatinine $\leq 1.5 \times$ upper limit of normal (ULN)
 - 9.5. Bilirubin $\leq 1.5 \times$ ULN
 - 9.6. AST/ALT $\leq 2.5 \times$ ULN
10. Proteinuria \leq Grade 1 or Urinary protein < 1 g/24hr
11. Ability to provide written informed consent prior to participating in the trial and any trial-related procedures being performed.
12. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests and any other trial procedures.
13. Female participants of child-bearing potential must agree to use dual methods of contraception for the duration of the trial . Male participants must agree to use dual methods of contraception for the duration of the trial and for 6 months after the last dose of trial treatment is received if sexually active with a female of child-bearing potential.

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

Planned Sample Size: 24; UK Sample Size: 24

Key exclusion criteria

1. Pregnant (positive pregnancy test, serum or urine acceptable) or breast feeding
2. Previous treatment for GBM other than debulking surgery
3. Concurrent or previous malignancies (< 12 months post end of treatment) at other sites, with the exception of appropriately treated localised epithelial skin or cervical cancer. Participants with histories (≥ 12 months) of other tumours may be entered
4. Patients seropositive for HIV, Hepatitis B or C infection
5. Immunosuppressive therapy other than steroids (maximum of 8mg daily dexamethasone or equivalent)
6. Any history of hypersensitivity to any of the trial medications or excipients
7. Participants with active uncontrolled infections
8. Participants with peripheral neuropathy \geq CTC grade 3
9. Poorly controlled or serious medical or psychiatric illness that, in the Investigator's opinion, is likely to interfere with participation and/or compliance in this clinical trial
10. Patients with the following significant cardiovascular diseases within 1 year of consent; history of arrhythmia, myocardial infarction, symptomatic heart failure, uncontrolled hypertension, or history of QTc abnormalities

11. Participants must not have received G-CSF since confirmed diagnosis of Glioblastoma Multiforme

Date of first enrolment

19/09/2017

Date of final enrolment

01/09/2018

Locations

Countries of recruitment

England

Scotland

United Kingdom

Study participating centre

Beatson West of Scotland Cancer Centre

1053 Great Western Road

Glasgow

United Kingdom

G12 0YN

Study participating centre

St James' University Hospital

Beckett Street

Leeds

United Kingdom

LS9 7JT

Study participating centre

Christie NHS Foundation Trust

550 Wilmslow Road

Manchester

United Kingdom

M20 4BX

Sponsor information

Organisation

University of Leeds

Sponsor details

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Leeds

England

United Kingdom

LS2 9JT

+44 113 3431477

CTRU-reoglio@leeds.ac.uk

Sponsor type

University/education

ROR

<https://ror.org/024mrx33>

Funder(s)**Funder type**

Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Funder Name

Oncolytics Biotech

Alternative Name(s)

Oncolytics Biotech, Inc., Oncolytics

Funding Body Type

Private sector organisation

Funding Body Subtype

For-profit companies (industry)

Location

Canada

Funder Name

Brain Tumour Charity

Alternative Name(s)

The Brain Tumour Charity

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal

Intention to publish date

17/12/2021

Individual participant data (IPD) sharing plan

The current 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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1	24/02/2021	24/02/2021	No	No
Basic results	version 2	02/11/2021	02/11/2021	No	No
HRA research summary			26/07/2023	No	No