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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

Registration date
06/02/2017

Last Edited
02/11/2021

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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

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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. 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) ≥ 1.5 x 109 [SI units 109/L]
9.2. Platelets ≥100 x109 [SI units 109/L] (without platelet transfusion)
9.3. Haemoglobin ≥9.0 g/dL [SI units gm/L] (with or without RBC transfusion)
9.4. Serum creatinine ≤1.5 x upper limit of normal (ULN)
9.5. Bilirubin ≤1.5 x ULN
9.6. AST/ALT ≤2.5 x ULN
10. Proteinuria ≤ 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 > = 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
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Sponsor type
University/education

ROR
https://ror.org/024mrxd33

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