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Brain imaging to predict toxicity in elderly patients after radiotherapy

Submission date
18/04/2023

Recruitment status
No longer recruiting

Registration date
31/05/2023

Overall study status
Completed

Last Edited
08/03/2024

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The aim of this study is to produce a way of predicting who might be more or less likely to suffer side effects from radiotherapy prior to starting treatment for a glioblastoma, a type of brain tumour. This will enable doctors and patients to make more individual, tailored treatment plans, exploring other treatment options or recognising the need for extra support in certain cases.
Glioblastoma (GBM) is the commonest primary malignant brain tumour. The chances of developing a GBM peak in your 70s and 80s. Outcomes from this disease in older patients are poor. Part of the reason is the lack of good clinical trials for this age group. Treatment options are best supportive care where the focus is on maintaining a good quality of life for as long as possible.
Treatment of GBMs can involve chemotherapy and radiotherapy. Research has shown that there is a particular test oncologists can perform on the tumours which suggests whether that particular tumour is more or less sensitive to chemotherapy. This test is used to guide whether chemotherapy is offered. As yet there is no such test to guide radiotherapy treatment.
Radiotherapy to the brain is an effective treatment. However, it does often produce side effects. These can include fatigue, nausea, problems with memory and sometimes a worsening of the original symptoms that led to the discovery of the tumour. The degree of side effects which different patients experience can vary widely. Some of this due to the amount of radiotherapy given and how it's given but there is a lot that we don't understand as to why certain patients are much more affected than others. It has been thought that if the patient's underlying normal brain (i.e. not the part affected by the tumour) is fragile due to an underlying mild dementia or problems associated with high blood pressure or cholesterol then this might make them more vulnerable.
MRI scans can be used to assess whether there are changes in the normal brain from these background conditions. This study aims to use MRI scans to see whether we can predict those patients who might be more at risk of side effects caused by radiotherapy.

Who can participate?
Patients aged 65 or over who have been newly diagnosed with a GBM and are going to receive radiotherapy as part of their treatment.

What does the study involve?
Patients who agree to take part in the study will have already had an MRI scan as part of their normal diagnosis. They will undertake some questionnaires before starting their radiotherapy which will aim to assess their quality of life and their mental processes of perception, memory, judgment, and reasoning (called cognitive function).
They will then repeat these questionnaires 4 and 8 weeks after their treatment has finished when they come for their follow-up appointments. The results of these questionnaires will be compared to measurements made on their pre-treatment MRI scan. Occasionally the MRI scan the patients had as part of their diagnosis will not have quite enough information on it and some patients may need to have an extra scan before starting their radiotherapy treatment.

What are the possible benefits and risks of participating?
Participation in the study does not change the treatment the patient receives. There are no direct benefits to the participants in undergoing this study. The risk of significant harm to the participant is unlikely within this study.
Participants who require a further MRI scan may require the administration of gadolinium contrast. This is generally safe and well tolerated however the risk profile of this will be discussed with the patient prior to administration and local policies will be followed if the patient has a reaction to the contrast agent. MRI scans do not involve ionising radiation therefore do not carry with them any increased risk of cancer.
Participants will be attending clinic for their routine follow-up visits when they complete the assessments and therefore will not need any extra visits to the hospital. During their clinic visit, they may need to spend slightly more time than they would usually do in order to complete the questionnaires. In order to minimise this, we have allowed for carers/family/a member of the trial team to assist with the self-reported questionnaires or for the patient to take the questionnaire home with them to complete and post back to the trial team.
The participant's GP will be informed of their involvement in the study. If there are concerns from the answers to the questionnaires that the participants may be at risk of harm to themselves or to others then this will be discussed with the participant's GP or other teams. The participants will be aware of this. In the unlikely event that any psychological distress is caused to the participants by completing the questionnaires, we would address this within the clinic visit and if necessary refer to their GP or local psychiatric services for further support. Participants who require a further MRI scan may require the administration of gadolinium contrast. This is generally safe and well tolerated however the risk profile of this will be discussed with the patient prior to administration and local policies will be followed if the patient has a reaction to the contrast agent. MRI scans are in general well tolerated and do not involve ionising radiation therefore do not carry with them any increased risk of cancer.

Where is the study run from?
The study is run from University Hospitals Sussex NHS Trust as lead and sponsor but is open in a number of centres across the UK.

When is the study starting and how long is it expected to run for?
May 2018 to December 2022

Who is funding the study?
1. The Sussex Cancer Fund (UK)
2. BrainsTrust (UK)

Who is the main contact?
Dr Cressida Lorimer, cressida.lorimer@nhs.net

Contact information

Type(s)
Principal Investigator

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Dr Cressida Lorimer

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
216343

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 38723, IRAS 216343

Study information

Scientific Title
Brain Imaging to predict Toxicity in Elderly patients after Radiotherapy (BRITER): an observational cohort study

Acronym
BRITER

Study objectives
The BRITER study is being performed on patients aged 65 or over who have a new diagnosis of glioblastoma (GBM). It tests the hypothesis that there is a relationship between 5 scores of a

‘vulnerable’ brain seen on pre-treatment MRI and a clinically significant change in patient quality of life, as defined by a 10-point change in the EORTC QLQ questionnaire from baseline to 8 weeks post-treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/06/2018, London - Bloomsbury Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8285; bloomsbury.rec@hra.nhs.uk), ref: 18/LO/0997

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Glioblastoma

Interventions
All participants received an extra pre-treatment MRI scan and undertook a series of questionnaires at time points through their treatment. Study participants were eligible if they were receiving radiotherapy to their brain for a Glioblastoma. The type of radiotherapy or dose is at the discretion of the treating physician.
Data will be gathered on patient quality of life via toxicity assessments and completion of EORTC QoL questionnaires

Intervention Type
Other

Primary outcome measure
The proportion of patients with a 10-point change in the EORCT QLQ C30 quality of life questionnaire (with the BN-20 brain and ELD14 elderly patient subsets of questions added) from baseline to 8 weeks

Secondary outcome measures

The impact of side effects from cranial radiotherapy will also be assessed by:
1. MoCA cognitive screening questionnaire, scored as impaired (< 25) or unimpaired (>25), at baseline and at 8 weeks
2. Corticosteroid dose, recorded in milligrams at baseline and at 8 weeks
3. Treatment-associated toxicities of fatigue, headache, confusion, nausea, vomiting and seizures, measured using the Common Terminology Criteria for Adverse Events (CTCAE) at baseline and 8 weeks. Those scoring >3 will be recorded.
4. Overall survival, measured from the date of diagnosis (defined as the first imaging modality reviewed by a neuroradiology consultant within the multidisciplinary team meeting (MDM) setting which shows changes consistent with a GBM) until the date of death or censoring of the study
5. Progression-free survival, measured from the date of diagnosis (defined as the first imaging modality reviewed by a neuroradiology consultant within the MDM setting which shows changes consistent with a GBM) until the date of progression as confirmed by imaging reviewed by a neuroradiologist

Overall study start date
09/05/2018

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Patients aged >65 years with a new diagnosis of GBM. Diagnosis made via histological confirmation following biopsy or debulking surgery or radiologically during an MDM meeting confirmed by a consultant neuroradiologist. This lower age limit is due to previous clinical trials which have established gold-standard treatment regimes for patients under the age of 65 years. Patients aged 65 years or over have less clinical trial data available to them and treatment decisions are more nuanced with a greater emphasis on quality of life given the poorer prognosis of older patients.
2. Patients undergoing radiotherapy treatment to the brain for the treatment of their GBM
3. Patients able to undergo an MRI scan
4. Patients undergoing treatment at one of the study centres
5. Patients have the capacity to participate in the study
6. Patients with physical impairments that prevent them from filling in their questionnaires involved in the study may still participate if they are able to communicate their answers through a third party

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants

100

Total final enrolment
120

Key exclusion criteria
1. Patients not fit for radiotherapy treatment or having single-agent chemotherapy with no radiotherapy
2. Patients lacking capacity
3. Patients who do not have a sufficient grasp of the English language to be able to complete the questionnaires
4. Patients unable to communicate their responses to the questionnaires
5. Patients who are concurrently enrolled in a Clinical Trial of an Investigational Medicinal Product (CTIMP)

Date of first enrolment
05/11/2018

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Royal Sussex County Hospital
University Hospitals Sussex
Sussex Cancer Centre
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
Royal Marsden Hospital
Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre
Nottingham Hospital
Nottingham University Hospitals NHS Trust
City Campus
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Addenbrookes Hospital
Cambridge University Hospitals NHS Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Castle Hill Hospital
Hull University Teaching Hospitals NHS Trust
Queens Centre
Castle Road
Cottingham, Hull
United Kingdom
HU16 5JQ

Study participating centre
The Christie
The Christie NHS Foundation Trust
Wilmslow Road
Manchester
United Kingdom
M20 4BX

Study participating centre
Norfolk & Norwich University Hospital
Colney Lane
Norwich, Norfolk
United Kingdom
NR4 7UY

Study participating centre
Mount Vernon Hospital
Rickmansworth Road
North Middlesex
United Kingdom
HA6 2RN

Study participating centre
Maidstone Hospital
Kent Oncology Centre
Meritage Lane
Maidstone, Kent
United Kingdom
ME16 9QQ

Study participating centre
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
Oncology
Mindelsohn Way
Edgebaston
Birmingham
United Kingdom
B15 2WB

Study participating centre
Charing Cross Hospital
Imperial College Healthcare NHS Trust
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre

Western General Hospital
Edinburgh Cancer Centre
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

Sponsor information

Organisation
University Hospitals Sussex NHS Foundation Trust

Sponsor details
R&D Department
Clinical Research Facility
L2 Sussex House
Royal Sussex County Hospital
Abbey Road
Brighton
England
United Kingdom
BN2 5BE
+44 (0)1273 696955 x63522
scott.harfield@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.uhsussex.nhs.uk/

ROR
https://ror.org/03wvsyq85

Funder(s)

Funder type
Charity

Funder Name
Sussex Cancer Fund

Funder Name
BrainsTrust

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 19/01/2024:
Abstract presented as a POSTER to European Association of Neuro-Oncology April 2023 and the Society of Neuro-Oncology annual conference November 2023.

Currently accepted for publication by Neuro-Oncology Practice pending revisions

Previous publication and dissemination plan:
Abstract submitted to European Association of Neuro-Oncology April 2023

Intention to publish date
28/02/2024

Individual participant data (IPD) sharing plan
The datasets from this study are stored in a non-publicly available repository. The results will be published in peer-reviewed journals and presented at international conferences. The trial participants consented to their data being available only to members of the trial team in order to respect confidentiality. As this is an important repository of anonymised images and quality-of-life data, if requests are made for raw data to the BRITER study email address the researchers can assess these on an individual basis and seek advice from the HRA as to whether they can share anonymised datasets on a case-by-case basis.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 0.5	03/04/2019	28/04/2023	No	Yes
Protocol file	version 0.8	03/04/2019	28/04/2023	No	No
HRA research summary			28/06/2023	No	No
Poster results	Abstract submitted to European Association of Neuro-Oncology April 2023		19/01/2024	No	No