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Whole Brain Radiotherapy following local treatment of melanoma

Submission date 28/07/2011	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 28/07/2011	**Overall study status** Completed	[X] Statistical analysis plan [X] Results
Last Edited 07/11/2022	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-radiotherapy-melanoma-that-has-spread-brain

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01503827

Protocol serial number
9841

Study information

Scientific Title
Whole Brain Radiotherapy following local treatment of intracranial metastases of melanoma a randomised phase III trial

Acronym
WBRT

Study objectives
Brain metastases are a common cause of death in patients with melanoma. The use of whole brain radiotherapy (WBRT) after excision and/or stereotactic irradiation for melanoma brain metastases is variable and controversial because there is no high quality evidence to guide practice.

This study looks at whether the addition of WBRT following excision/steriotactic irradiation will improve intracranial control and survival, without significant impairment of quality of life or neurocognitive function.
Participants are randomly assigned to have WBRT or not after treatment of their brain metastases. Randomisation should occur within 6 weeks of completion of local treatment.
If allocated, WBRT treatment is given as 30 Gy in 10 fractions and should start within 8 weeks of local treatment.

On 10/04/2014 the following changes were made to the trial record:
1. The anticipated end date was changed from 30/04/2014 to 30/04/2018
2. The target number of participants UK sample size was changed from 40 to 20

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire Research Ethics Committee C, 14 March 2011, ref: 11/H0606/1

Study design
Randomised, interventional, treatment

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
1. Patients will be randomised 1:1 using an Interactive Voice Randomisation System (IVRS)
2. Randomisation will be stratified by centre, gender, number of CNS metastases, extracranial metastases and planned radiotherapy.
3. WBRT, 30 Gy in 10 fractions

Intervention Type
Other

Phase
Phase III

Primary outcome(s)
The proportion of patients with distant intracranial failure at 12 months after follow-up

Key secondary outcome(s))
1. Deterioration in neurocognitive function (NCF)
2. The main neurocognitive function endpoint will be defined as the proportion of patients who have deterioration
3. Overall survival - will be assessed from date of randomisation to date of death from any cause
4. Time to deterioration in health related Quality of Life parameters - the primary QOL endpoint will be time to deterioration in role function from randomisation, with deterioration
5. Time to deterioration in performance status as measured by ECOG - defined as the time that elapses between randomisation and the first recorded worsening (including time to distant intracranial failure) measured by the time difference between the randomisation MRI and Intracranial Failure
6. Time to local intracranial failure measured by the time difference between the pre-randomisation MRI and Intracranial Fail
7. Time to overall (distant + local) intracranial failure, determined through MRI and is defined as the time to the first recurrence of disease anywhere

Added 10/04/2014:
8. Incremental cost-effectiveness ratio (ICER). A within-trial economic evaluation of WBRT compared to observation

Completion date
30/04/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 10/04/2014:
1. One to three intracranial metastases on MRI from melanoma, locally treated with either surgical excision and/or stereotactic irradiation. It will be assumed that the metastases are melanoma if the patient has documented histological or radiological concurrent extracranial disease that has already made the patient stage IV. If the cerebral lesion(s) is/are the first presentation of stage IV disease, then one metastasis must be histologically proven to be melanoma for the patient to be included in the study
2. Life expectancy of at least 6 months
3. Aged 18 years or older
4. WBRT must begin within 8 weeks of completion of localised treatment and within 4 weeks of randomisation
5. Able to have an MRI brain scan with contrast. Estimated Glomerular Filtration Rate (eGFR) is adequate at the discretion of the radiologist and capable of having gadolinium-containing contrast medium for MRI (as per practice guidelines).
6. Localised treatment of all these metastases no more than 6 weeks prior to randomisation
7. An ECOG performance status between 0 and 2 at randomisation
8. CT or PET scan of chest, abdomen and pelvis as a minimum prior to randomisation. Scans must be within 12 weeks of randomisation

9. Serum Lactate Dehydrogenase (LDH) must be = 2 x upper limit of normal
10. Able to provide written informed consent
11. Male or female participants

Previous inclusion criteria:
1. One to three intracranial metastases on MRI from melanoma, locally treated with either surgical excision and/or stereotactic irradiation. It will be assumed that the metastases are melanoma if the patient has documented histological or radiological concurrent extracranial disease that has already made the patient stage IV. If the cerebral lesion(s) is/are the first presentation of stage IV disease, then one metastasis must be histologically proven to be melanoma for the patient to be included in the study
2. Life expectancy of at least 6 months
3. Aged 18 years or older
4. WBRT must begin within 8 weeks of completion of localised treatment and within 4 weeks of randomisation
5. Able to have an MRI brain scan with contrast. Estimated Glomerular Filtration Rate (eGFR) is adequate at the discretion of the radiologist and capable of having gadolinium-containing contrast medium for MRI (as per practice guidelines).
6. Localised treatment of all these metastases no more than 6 weeks prior to randomisation
7. An ECOG performance status between 0 and 2 at randomisation
8. CT scan of chest, abdomen and pelvis as a minimum prior to randomisation. Scans must be within 12 weeks of randomisation
9. Serum Lactate Dehydrogenase (LDH) must be = 2 x upper limit of normal
10. Able to provide written informed consent
11. Male or female participants

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any untreated intracranial disease
2. Any previous intracranial treatment (surgical excision and/or stereotactic irradiation treatment and/or WBRT) prior to this diagnosis of intracranial melanoma
3. Evidence of leptomeningeal disease on pre-local treatment MRI scan
4. Patients with prior cancers, except:
4.1. Those diagnosed more than five years ago with no evidence of disease recurrence within this time
4.2. Successfully treated basal cell and squamous cell skin carcinoma
4.3. Carcinoma in-situ of the cervix

5. A medical or psychiatric condition that compromises ability to give informed consent or complete the protocol
6. Positive urine pregnancy test for women of childbearing potential (+/-7 days of registration onto the trial)

Date of first enrolment
01/05/2011

Date of final enrolment
30/04/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Oncology
Oxford
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OX3 7DQ

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

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
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/11/2019	07/11/2022	Yes	No
Protocol article	protocol	17/04/2011	04/09/2019	Yes	No
Other publications	interim analysis	08/05/2015	04/09/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan	statistical analysis plan	05/08/2019	04/09/2019	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes