ISRCTN20253034 https://doi.org/10.1186/ISRCTN20253034

A randomised double blind phase 2 trial of whole brain radiotherapy with or without vandetanib in metastatic melanoma with brain metastases

Submission date
17/08/2011

Recruitment status
No longer recruiting

Registration date
17/08/2011

Overall study status
Completed

Last Edited
24/03/2022

Condition category
Cancer

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

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

Contact information

Type(s)
Scientific

Contact name
Ms Linda Collins

Contact details
Old Road Campus
Roosevelt Drive Headington
Oxford
United Kingdom
OX3 7DQ
-
Linda.Collins@oncology.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
2011-000661-12

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
10620

Study information

Scientific Title
A randomised double blind phase 2 trial of whole brain radiotherapy with or without vandetanib in metastatic melanoma with brain metastases

Acronym
RADVAN - XRT +/vandetanib in CNS melanoma

Study objectives
This is a randomised, double-blind, placebo-controlled, multi-centre phase 2 trial. Eighty patients (forty in each of two arms) will be randomised 1:1 between radiotherapy with placebo or radiotherapy with vandetanib, with stratification for recursive partitioning analysis (RPA) score (2 levels, RPA 1 and RPA 2). Patients will receive three weeks of either vandetanib 100mg once daily or placebo, starting 4 days (+/- 1 day) before whole brain radiotherapy (30 Gy in 10 fractions). The main study will be preceded by a safety run in phase (involving 6 patients) to confirm the tolerability of vandetanib 100mg with radiotherapy at 30 Gy in 10 fractions in this patient group. Tolerability will be defined as no study treatment related toxicity of grade 3 or more (CTCAE version 4.0) in at least 5 out of the 6 patients in the safety run in phase at 30 days post end of study treatment. Patients will continue to be reviewed on study until progression of brain metastases (by RECIST version 1.1) or 12 months post randomisation into study, whichever comes first, and thereafter will be followed up for survival alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
11/SC/0282

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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
Topic: National Cancer Research Network; Subtopic: Melanoma; Disease: Melanoma

Interventions
Eighty patients (forty in each of two arms) will be randomised 1:1 between radiotherapy with placebo or radiotherapy with vandetanib, with stratification for RPA score (2 levels, RPA 1 and RPA 2). The main study will be preceded by a safety run in phase involving 6 patients on radiotherapy with vandetanib.

Radiotherapy will be administered via parallel opposed lateral beams dosed to the midpoint as 30 Gy in 10 fractions over 2 weeks (i.e. over 10-14 days, to allow for weekends), starting 4 days (+/- 1 day) after commencing study drug.

Vandetanib/Placebo: Patients in the safety run-in phase will all receive vandetanib 100 mg OD, starting 4 days (+/- 1 day) before whole brain radiotherapy (WBRT) and continuing for 21 days in total. Patients in the randomisation phase will receive vandetanib/placebo, starting 4 days (+/- 1 day) before WBRT and continuing for 21 days in total. No study treatment is to be given beyond day 21, even if any doses are missed during this period.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Vandetanib

Primary outcome measure
Efficacy of vandetanib in combination with radiotherapy, compared with radiotherapy; Timepoint(s): Progression free survival in brain (as assessed by MRI scan)

Secondary outcome measures
1. Safety and tolerability of vandetanib in combination with radiotherapy; Timepoint(s): Adverse events using National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0
2. Vital signs and weight
3. Biochemistry, haematology
4. Efficacy of vandetanib in combination with radiotherapy, compared with radiotherapy; Timepoint(s): Maintenance of cognitive function (as assessed by Wide Range Achievement Test)

Overall study start date
08/12/2011

Completion date
28/11/2014

Eligibility

Key inclusion criteria
1. More than or equal to 18 years of age, written informed consent
2. Histological confirmation of malignant melanoma
3. Unresectable Stage III or IV metastatic melanoma with brain metastases
4. Karnofsky Performance Score > 70%
5. Radiation Therapy Oncology Group recursive partitioning analysis (RTOG RPA) score 1 or 2
6. Measurable disease as defined by RECIST version 1.1
7. Adequate haematological, hepatic and renal function
8. Adequate cardiac function New York Heart Association (NHYA) 0-1
9. QTc < 480msec
Target Gender: Male & Female ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 86; UK Sample Size: 86

Key exclusion criteria
1. Radiotherapy or systemic melanoma therapy within 28 days prior to starting treatment
2. Prior whole brain irradiation
3. Central nervous system (CNS) melanoma where all detectable disease has been treated by neurosurgery or stereotactic irradiation
4. Presence of leptomeningeal disease
5. More than 3 extra-cranial organ sites involved with melanoma
6. Pregnancy or breastfeeding women
7. Significant cardiovascular disease
8. Uncontrolled hypertension
9. Serum calcium, magnesium or potassium below the normal range despite supplementation
10. Requirement for medication that increases QTc and/or the risk of torsades de point
11. Requirement for medication that is a potent inducer of CYP3A4 function
12. Ocular malignant melanoma
13. Another active malignancy within the past five years
14. Clinically significant and uncontrolled major medical condition(s)
15. Any condition that would preclude adequate absorption of vandetanib

Date of first enrolment
08/12/2011

Date of final enrolment
28/11/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Old Road Campus
Oxford
United Kingdom
OX3 7DQ

Sponsor information

Organisation
Oxford University (UK)

Sponsor details
Wellcome Trust Centre for Human Genetics
Oxford
England
United Kingdom
OX3 7BN

Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2016		Yes	No
Plain English results			24/03/2022	No	Yes
HRA research summary			28/06/2023	No	No