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

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
17/08/2011		Protocol		
Registration date 17/08/2011	Overall study status Completed	Statistical analysis plan		
		[X] Results		
<b>Last Edited</b> 24/03/2022	Condition category	[] 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

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# 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, AZ

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