

Neoadjuvant intravitreal ranibizumab treatment in high-risk ocular melanoma patients

Submission date 16/03/2012	Recruitment status Stopped	☒ Prospectively registered ☐ Protocol
Registration date 16/03/2012	Overall study status Stopped	☐ Statistical analysis plan ☒ Results
Last Edited 25/10/2022	Condition category Cancer	☐ Individual participant data ☐ Record updated in last year

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-ranibizumab-eye-cancer-nitro>

Contact information

Type(s)

Scientific

Contact name

Prof Heinrich Heimann

Contact details

Liverpool University
Liverpool
United Kingdom

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hheimann@liverpool.ac.uk

Type(s)

Public

Contact name

Mr Tony Coffey

Contact details

North West Surgical Trials Centre
Cancer Research UK Liverpool Clinical Trials Unit
Block C
Waterhouse Building
1-3 Brownlow Street

Liverpool
United Kingdom
L69 3GL
+44 151 794 8929
tony.coffey@liverpool.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2011-000961-10

Protocol serial number
11316

Study information

Scientific Title

Neoadjuvant IntraviTreal Ranibizumab treatment in high-risk Ocular melanoma patients: a two-stage single-centre phase II single arm study (NITRO trial)

Acronym

NITRO

Study objectives

NITRO is a two stage phase II non-randomised single centre trial. The trial will recruit patients who require radical treatment (e-nucleation) due to tumour size. Participants will receive 0.5mg in 0.05ml ranibizumab as an intravitreal injection on day 1 of treatment. Tumour assessment will follow 28 days later and one of the following three decisions will be made.

1. If the tumour shows an increase in size, the patient will stop trial treatment and eye removal will be planned.
2. If the assessment shows a reduction in tumour size that may allow for eye sparing treatment (such as endoresection or radiotherapy), the patient will stop trial treatment and appropriate eye sparing treatment will be planned.
3. If a small response or the tumour size has remained stable, the patient may have a further dose of Ranibizumab. Up to 6 doses of trial treatment may be given.

All patients will be followed at 6 weeks, 3 months and 6 months following surgery/radiotherapy. Translational samples will be taken at first treatment (day 1) (blood sample, intravitreal fluid sample and tumour biopsy). A second tumour biopsy and intravitreal fluid sample will be taken at final surgery. A second translational blood sample will be taken at the 6 month follow-up.

The primary outcome of the trial is to determine the response rate of intravitreal Ranibizumab in high risk Ocular melanoma patients. The secondary outcomes are to explore relationships between ultrasonographic response, serum and intravitreal VEGF levels.

Ethics approval required

Old ethics approval format

Ethics approval(s)

11/NW/0656; First MREC approval date 07/12/2011

Primary study design

Interventional

Study design

Non-randomised; Interventional; Design type: Treatment

Study type(s)

Treatment

Health condition(s) or problem(s) studied

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

Interventions

Ranibizumab, Intravitreal injection of 0.5mg in 0.05ml Ranibizumab; Follow Up Length: 6 month(s); Study Entry: Registration only

14 patients will be recruited in the first stage of the trial. The trial will be paused after recruitment and treatment of patient 14. A further 11 patients will be recruited if there are any responders to treatment identified in the first stage.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

ranibizumab

Primary outcome(s)

Response Rate; Timepoint(s): Response will be measured per patient every 28 days after treatment. Maximum of 6 treatments.

Key secondary outcome(s)

To explore relationships between ultrasonographic response, serum and intravitreal VEGF levels

Completion date

01/08/2013

Reason abandoned (if study stopped)

Participant recruitment issue

Eligibility

Key inclusion criteria

1. Confirmed diagnosis of uveal melanoma requiring enucleation
2. Must have ultrasonographically documented measurable disease within 4 weeks of treatment according to the WHO criteria
3. Prior treatments with chemotherapeutic or antiangiogenic agents for other malignancies are

allowed after 6 months of discontinuation

4. Age ≥ 18 years
5. Eastern Cooperative Oncology Group (ECOG) Performance Status ≤ 2
6. Platelets $\geq 100,000/\text{mm}^3$
7. White cell count (WCC) $\geq 3.0 \times 10^9/\text{L}$
8. Absolute neutrophil count (ANC) $\geq 1.0 \times 10^9/\text{L}$
9. Bilirubin $<$ twice normal, Alkaline Phosphatase $< 5 \times$ normal
10. International Normalized Ratio (INR) < 2
11. Cr ≤ 1.5 ULN
12. Normal blood pressure or controlled hypertension
13. No recent major surgical procedures (laparotomy or thoracotomy) within 4 weeks
14. No thromboembolic event within 6 months
15. No known coagulopathy disorder
16. Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and followup schedule; those conditions should be discussed with the patient before registration in the trial
17. Before patient registration, written informed consent must be given according to ICH/GCP, and national regulations
18. Previous or present vascular intraocular diseases not requiring use of antiangiogenic agents will be allowed
19. Hb $\geq 10\text{g/dl}$

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Total final enrolment

7

Key exclusion criteria

1. Serious underlying medical condition according to the judgement of the Principal Investigator
2. Pregnant or nursing patients
3. Inability to provide adequate informed consent
4. Hypersensitivity to the active substance or to any of the excipients
5. Active or suspected ocular or periocular infections
6. Active severe intraocular inflammation

Date of first enrolment

02/04/2012

Date of final enrolment

01/08/2013

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Liverpool CR-UK Centre - Waterhouse Building

Liverpool

United Kingdom

L69 3GL

Sponsor information

Organisation

Royal Liverpool and Broadgreen University Hospitals NHS Trust (UK)

ROR

<https://ror.org/009sa0g06>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK (CRUK) (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	results	01/02/2020	07/11/2019	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			07/11/2019	No	Yes