

# Neoadjuvant intravitreal ranibizumab treatment in high-risk ocular melanoma patients

<b>Submission date</b> 16/03/2012	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/03/2012	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 25/10/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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

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Public

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## **Additional identifiers**

**EudraCT/CTIS number**  
2011-000961-10

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
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

**Study design**

Non-randomised; Interventional; Design type: Treatment

**Primary study design**

Interventional

**Secondary study design**

Non randomised study

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet

**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 measure**

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

**Secondary outcome measures**

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

**Overall study start date**

02/04/2012

**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  $\geq 18$  years
5. Eastern Cooperative Oncology Group (ECOG) Performance Status  $\leq 2$
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 x normal
10. International Normalized Ratio (INR)  $<$  2
11. Cr  $\leq 1.5$  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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 25; UK Sample Size: 25

**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**

England

United Kingdom

**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)

**Sponsor details**

The Walton Centre for Neurology and Neurosurgery

Prescot Street

Liverpool

England

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L7 8XP

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.rlbuht.nhs.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, CRUK

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

To be submitted to an ophthalmology journal in June 2018.

**Intention to publish date**

31/12/2018

**Individual participant data (IPD) sharing plan**

Not provided at time of registration

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
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<a href="#">Plain English results</a>			07/11/2019	No	Yes
<a href="#">Results article</a>	results	01/02/2020	07/11/2019	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No