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Neoadjuvant intraviTreal ranibizumab treatment in high-risk ocular melanoma patients

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

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-ranibizumab-eye-cancer-nitro

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Scientific

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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, intravitreous fluid sample and tumour biopsy). A second tumour biopsy and intravitreous 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 intravitreous 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 intravitreous 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 >=18 years
5. Eastern Cooperative Oncology Group (ECOG) Performance Status ≤ 2
6. Platelets ≥100,000mm3
7. White cell count (WCC) ≥ 3.0 x 109/L
8. Absolute neutrophil count (ANC) ≥ 1.0 x 109/L
9. Bilirubin < twice normal, Alkaline Phosphatase < 5 x 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 4weeks
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 ≥ 10g/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
United Kingdom
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?

Plain English results	results	01/02/2020	07/11/2019	No	Yes
Results article			07/11/2019	Yes	No
HRA research summary			28/06/2023	No	No