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A randomised trial evaluating the vascular endothelial growth factor inhibitor, bevacizumab (AVASTin®), as adjuvant therapy following resection of American Joint Committee on Cancer (AJCC) stage IIB (T4aN0M0), IIC (T4bN0M0) and III (TxN1-2M0) cutaneous Melanoma

Submission date
03/01/2007

Recruitment status
No longer recruiting

Registration date
30/03/2007

Overall study status
Completed

Last Edited
26/10/2018

Condition category
Cancer

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

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-bevacizumab-after-surgery-for-melanoma-skin-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2006-005505-64

Protocol serial number
2006-005505-64

Study information

Scientific Title
A randomised trial evaluating the vascular endothelial growth factor inhibitor, bevacizumab (AVASTin®), as adjuvant therapy following resection of American Joint Committee on Cancer (AJCC) stage IIB (T4aN0M0), IIC (T4bN0M0) and III (TxN1-2M0) cutaneous Melanoma

Acronym
AVAST-M

Study objectives
To determine the overall survival of patients treated with bevacizumab, compared with standard observation after resection of high risk melanoma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxford C Multi-centre Research Ethics Committee, ref: 07/Q1606/15 - approval pending

Study design
Randomised phase III multi-centre prospective clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cutaneous melanoma

Interventions
After resection of the high risk melanoma, patients will be given 7.5 mg per Kg bevacizumab by Intravenous (IV) infusion (30 minutes +/- 10 minutes). Bevacizumab infusions will be administered every three weeks for 51 weeks (maximum of 17 infusions) versus standard observation. The following samples will be taken/performed:
1. Venepuncture: blood samples will be taken at each visit, observation arm frequency equivalent to routine clinical care (n = 11), bevacizumab arm frequency higher (n = 33). The volume of blood taken on nine occasions in all will be greater, to collect blood for research purposes
2. Tissue/bodily sample: urinanalysis at baseline in all patients, then at intervals over ten years

for patients receiving bevacizumab
3. Biopsy material: excision biopsy of accessible recurrent tumour tissue and adjacent normal tissue from consenting patients
4. Imaging Investigations with radiation: Computed Tomography (CT) (or Magnetic Resonance Imaging [MRI]) scan of head pre-randomisation
5. Day-case attendance: patients receiving bevacizumab will attend an appropriate clinic for drug administration
6. Questionnaire: quality of life questionnaire

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Overall survival

Key secondary outcome(s))
1. Disease-free interval
2. Distant metastasis-free interval
3. Quality of life
4. Safety and toxicity

Completion date
05/03/2017

Eligibility

Key inclusion criteria
1. Written informed consent
2. Age more than or equal to 18 years
3. Able to comply with the protocol
4. Patients with histological confirmation of completely resected American Joint Committee on Cancer (AJCC) stage IIB (T4aN0M0), IIC (T4bN0M0) and III (TxN1-2M0) cutaneous melanoma
5. Patients may or may not have undergone sentinel lymph node dissection and/or elective lymph node dissection
6. Patients must be randomised within 12 weeks of completing primary surgery (wide local excision and lymphadenectomy)
7. Eastern Cooperative Oncology Group (ECOG) performance status zero to one
8. Life expectancy more than or equal to six months
9. Adequate haematological function:
a. Absolute Neutrophil Count (ANC) more than or equal to 1.5 x 10^9/L, and
b. platelet count more than or equal to 100 x 10^9/L, and
c. haemoglobin more than or equal to 9 g/dL (may be transfused to maintain or exceed this level)
10. Adequate liver function:
a. total bilirubin less than 1.5 x Upper Limit of Normal (ULN), and
b. Aspartate aminotransferase (AST), and/or Alanine aminotransferase (ALT) less than 2 x ULN

11. Adequate renal function:
a. serum creatinine less than or equal to 1.25 x ULN or calculated creatinine clearance more than or equal to 50 mL/min, and
b. urine dipstick for proteinuria less than 2+. Patients discovered to have more than or equal to 2+ proteinuria on dipstick urinalysis at baseline should undergo a 24 hour urine collection and must demonstrate less than or equal to 1 g of protein in 24 hours
c. International Normalised Ratio (INR) less than or equal to 1.5 and Partial Prothrombin Time (PPT) less than or equal to 1.5 x ULN

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any evidence of distant or non-regional lymph node metastases
2. Evidence of Central Nervous System (CNS) metastases, even if previously treated
3. Incomplete surgical resection of the disease
4. Prior chemotherapy, immunotherapy, hormonal therapy or radiotherapy for melanoma
5. Any surgery (including open biopsy, but excluding insertion of an indwelling catheter), or significant traumatic injury within 28 days prior to randomisation, or anticipation of the need for surgery during study treatment
6. Current or recent (within seven days of randomisation) use of aspirin (more than 325 mg/day)
7. Current or recent (within seven days of randomisation) use of full-dose oral or parenteral anticoagulants or thrombolytic agent for therapeutic purposes. Prophylactic use of anticoagulants is allowed
8. History or evidence of inherited bleeding diathesis or coagulopathy with the risk of bleeding
9. Uncontrolled hypertension (blood pressures: systolic more than 150 mmHg and/or diastolic more than 100 mmHg)
10. Clinically significant (i.e. active) cardiovascular disease for example Coronary Vascular Accident (CVA) (less than or equal to six months before randomisation), myocardial infarction (less than or equal to six months before randomisation), unstable angina, congestive heart failure New York Heart Association (NYHA) class more than or equal to II, serious cardiac arrhythmia requiring medication during the study and might interfere with regularity of the study treatment, or not controlled by medication
11. Non-healing wound, active peptic ulcer or bone fracture
12. History of abdominal fistula, gastrointestinal perforation or intra-abdominal abscess within six months of randomisation
13. Pregnant or breast-feeding females
14. Women with an intact uterus (unless amenorrhoeic for the last 24 months) not using, or do not agree to use, effective non-hormonal means of contraception (intrauterine contraceptive

device, barrier method of contraception in conjunction with spermicidal jelly or surgically sterile) if randomised to the treatment arm and for a period of six months following the last administration of bevacizumab. Men who do not agree to use effective contraception if randomised to the treatment arm and for a period of 60 days following the last administration of bevacizumab
15. Treatment with any other investigational agent, or participation in another clinical trial within 28 days prior to randomisation
16. Known hypersensitivity to bevacizumab or any of its excipients
17. Evidence of any other disease, neurological or metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or puts the patient at high risk for treatment-related complications
18. Any condition, which, in the opinion of the investigator, might interfere with the safety of the patient or evaluation of the study objectives

Date of first enrolment
05/03/2007

Date of final enrolment
05/03/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrooke's Hospital
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (ref: C7535/A6408) (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

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2014		Yes	No
Results article	results	01/02/2018		Yes	No
Plain English results				No	Yes