ISRCTN89118367 https://doi.org/10.1186/ISRCTN89118367

Docetaxel with or without AZD6244 in wt BRAF advanced melanoma

Submission date	Recruitment status	[_] Prospectively registered
29/10/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/10/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
26/10/2022	Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-docetaxel-with-without-AZD6244-advanced-melanoma

Contact information

Type(s)
Scientific

Contact name
Ms Linda Collins

Contact details
Old Road Campus
Roosevelt Drive
Headington
Oxford
United Kingdom
OX3 7DQ
-
Linda.Collins@clinpharm.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
2009-018153-23

IRAS number

ClinicalTrials.gov number
NCT01256359

Secondary identifying numbers
8672

Study information

Scientific Title
Docetaxel +/- AZD6244 in Melanoma - A double blind randomised phase 2 trial of docetaxel with or without AZD6244 in wt BRAF advanced melanoma

Acronym
DOC-MEK

Study objectives
This is a randomised, double-blind placebo controlled phase 2 trial. Patient will be randomly assigned 1:1 between two treatment arms. They will receive either docetaxel 75 mg/m^2 intravenously (IV) and placebo given twice daily (bd), or AZD6244 75 mg bd daily with docetaxel 75 mg/m^2 IV. Docetaxel will be administered every 3 weeks for a maximum 6 cycles, but AZD6244/placebo may be continued beyond this, until disease progression.

The objective is to assess whether the combination of AZD6244 with docetaxel is worthy of evaluation in a definitive randomised study, with the null hypothesis being that the combination has activity similar to that of docetaxel alone in this population. After consent has been obtained mutational analysis of tumour BRAF will be performed on archival tumour tissue, where this information is not already known, to assess eligibility for the study. If there is no archival tissue a fresh biopsy will be requested from the patient. A blood sample will also be taken for future genetic analysis.

Once taking part in the trial patients will need to attend their oncology unit regularly for monitoring and the delivery of treatment. Patients will undergo complete physical examination at screening, on C1D1, C1D8, C1D15, C2D1, C2D8 and day 1 of every subsequent cycle. Blood for haematology, biochemistry and clotting will be taken at each of these visits. A 12-lead electrocardiogram (ECG) will be performed at screening. Disease assessment will be by computed tomography (CT) scanning using modified Response Evaluation Criteria in Solid Tumours (RECIST) criteria after 9 and 18 weeks, then every 3 months until disease progression.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire REC A approved on 30/09/2010 (ref: 10/H0604/59)

Study design
Multicentre randomised interventional treatment trial

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
Patients will receive 75 mg AZD6244 or placebo orally twice a day on a continuous schedule. Capsules should be taken whole and not opened or crushed. They should be taken on an empty stomach (no food or drink for 2 hours before or 1 hour after treatment), with approximately 240 ml of water. Doses should be taken approximately 12 hours apart. Wherever possible doses should not be missed but if a dose is missed then the next dose should be taken at the allotted time.

Docetaxel arm: Patients will receive docetaxel 75 mg/m2, rounded to the nearest 10 mg, based on the most recent body surface area, as a 1-hour IV infusion in 250 ml of either 5% glucose solution or 0.9% sodium chloride solution. Standard pre-medication with steroids should be given, consisting of dexamethasone 8 mg b.d. for 3 days starting 1 day prior to docetaxel administration. Treatment will be given on day 1 and every 3 weeks for up to 6 cycles. The dose of docetaxel may be reduced or delayed if necessary.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Docetaxel, AZD6244

Primary outcome measure
Progression free survival, assessed at end of trial

Secondary outcome measures
Assessed at end of trial:
1. Immunohistochemistry of proteins in the MAPkinase pathway
2. Genotyping of tumours
3. Adverse events using CTCAE v4.0
4. Vital signs and weight
5. Biochemistry, haematology and urinalysis
6. Overall survival (OS)
7. Objective response rate (ORR)
8. Progression free survival at 6 months (PFS)

Overall study start date
13/10/2010

Completion date
30/10/2011

Eligibility

Key inclusion criteria
1. Aged greater than or equal to 16 years, either sex
2. Able to provide evidence from an accredited laboratory of wt BRAF status for their melanoma, or ascertainment of wt BRAF status from a sample of melanoma provided for mutational analysis in Oxford
3. Unresectable stage 3 or 4, histologically proven cutaneous or unknown primary melanoma
4. At least 1 lesion, not previously irradiated, that can be accurately measured on CT or magnetic resonance imaging (MRI) as defined by modified RECIST criteria
5. Eastern Cooperative Oncology Group (ECOG) performance score of 0 or 1
6. Life expectancy of at least 12 weeks
7. The patient is willing to give consent to the main study and able to comply with the protocol for the duration of the study, including scheduled follow-up visits and examinations
8. Haematological and biochemical indices within the ranges shown below:
8.1. Haemoglobin (Hb) greater than 10 g/dL
8.2. White blood count (WBC) greater than 3 x 10^9/L
8.3. Platelet count greater than 100,000/µL
8.4. Absolute neutrophil count greater than 1.5 x 10^9/L
8.5. Serum bilirubin less than or equal to 1.2 x upper limit of normal (ULN)
8.6. Asparate aminotransferase (AST) (SGOT) or alanine aminotranferase (ALT) less than or equal to 2.5 x ULN
8.7. Lactate dehydrogenase (LDH) less than or equal to 2 x ULN
8.8. Creatinine clearance (Cockcroft-Gault) greater than 50 ml/min

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned sample size: 80

Total final enrolment
83

Key exclusion criteria
1. Any anti-cancer therapy (including radiotherapy and participation in other clinical trials) within 28 days prior to Day 1
2. Prior DNA damaging agents or cytotoxic chemotherapy for metastatic melanoma

3. Any unresolved toxicity from prior anti-cancer therapy that is greater than CTCAE grade 2
4. Pregnancy or breastfeeding women. Female patients must have a negative urinary or serum pregnancy test or have evidence of post-menopausal status (defined as absence of menstruation for greater than 12 months, bilateral oophrectomy or hysterectomy).
5. Grade greater than or equal to 2 peripheral neuropathy at study entry
6. Patients of reproductive potential who are not willing to use adequate contraceptive measures for the duration of the study (both male and female patients)
7. Known severe hypersensitivity reactions to docetaxel or other drugs formulated in polysorbate 80
8. Ocular or mucosal malignant melanoma
9. Another active malignancy within the past five years
10. Evidence of brain metastases, unless surgically resected/stereotactic radiosurgery treated brain metastasis with no evidence of relapse on cerebral MRI, or treated brain metastasis and stable off treatment, including steroids, for 3 months
11. Clinically significant and uncontrolled major medical condition(s): such as active infection, bleeding diathesis
12. Patients who are known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus (HIV)
13. Cardiac conditions, including uncontrolled hypertension (blood pressure [BP] greater than 160/100 despite treatment), heart failure New York Heart Association (NYHA) class 2 or above, prior or current cardiomyopathy, myocardial infarction within 6 months or angina requiring nitrate therapy more than once a week
14. Previous treatment with EGFR, ras, raf or MEK inhibitors
15. Inability to swallow capsules, refractory nausea and vomiting, chronic gastrointestinal diseases (e.g., inflammatory bowel disease) or significant bowel resection that would preclude adequate absorption
16. Taking medication that significantly induces or inhibits CYP3A4

Date of first enrolment
13/10/2010

Date of final enrolment
30/10/2011

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
Roosevelt Drive
Oxford
England
United Kingdom
OX3 7BN

Sponsor type
University/education

Website
http://www.well.ox.ac.uk/home

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca UK Limited (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Results article	results	01/05/2014		Yes	No
Plain English results			26/10/2022	No	Yes
HRA research summary			28/06/2023	No	No