Docetaxel with or without AZD6244 in wt BRAF advanced melanoma

Submission date	Recruitment status No longer recruiting	Prospectively registered		
29/10/2010		☐ 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

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Additional identifiers

Clinical Trials Information System (CTIS)

2009-018153-23

ClinicalTrials.gov (NCT)

NCT01256359

Protocol serial number

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

Study type(s)

Treatment

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(s)

Progression free survival, assessed at end of trial

Key secondary outcome(s))

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)

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 $3 \times 10^9/L$
- 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 $2.5 \times ULN$
- 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

Healthy volunteers allowed

No

Age group

Adult

Sex

Αll

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 United Kingdom

England

Study participating centre
Old Road Campus
Oxford
United Kingdom
OX3 7DQ

Sponsor information

Organisation

Oxford University (UK)

ROR

https://ror.org/052gg0110

Funder(s)

Funder type

Industry

Funder Name

AstraZeneca UK Limited (UK)

Results and Publications

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
HRA research summary	Participant information sheet	11/11/2025	28/06/2023		No
Participant information sheet			11/11/2025	No	Yes
Plain English results			26/10/2022	No	Yes