

A research study to compare treatment with dabrafenib and trametinib, either taken continuously every day, or intermittently (with planned treatment breaks in each cycle), in patients with metastatic Melanoma

Submission date 04/09/2017	Recruitment status No longer recruiting	☒ Prospectively registered ☒ Protocol
Registration date 14/09/2017	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 16/06/2023	Condition category Cancer	☐ Individual participant data

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-comparing-2-ways-of-giving-dabrafenib-and-trametinib-for-advanced-melanoma-interim>

Contact information

Type(s)

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Additional identifiers**Clinical Trials Information System (CTIS)**

2016-005228-27

Protocol serial number

33584

Study information**Scientific Title**

INTERIM: a randomised phase II feasibility study of INTERmittent versus continuous dosing of oral targeted combination therapy In patients with BRAFV600 mutant stage 3 unresectable or metastatic Melanoma

Acronym

INTERIM

Study objectives

This feasibility study aims to determine if intermittent dosing is deliverable, based on patient and professional willingness to take part in a randomised trial evaluating less rather than standard durations of treatment. The trial will evaluate treatment compliance, Progression Free Survival and Quality of Life, to inform whether a subsequent definitive trial is justified and how it should be designed.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Cambridge South Research Ethics Committee, ref: 17/EE/0340

Study design

Randomised; Interventional; Design type: Treatment, Drug, Imaging

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Melanoma

Interventions

All participants receive standard Dabrafenib+Trametinib, either taken continuously every day (continuous arm), or with planned treatment breaks in each 28 day cycle (intermittent arm).

Eligible patients are randomly assigned to either the continuous arm or the intermittent arm in a 1:1 ratio using the minimisation with random element method.

1. Stratification parameters are:
2. Eastern Cooperative Oncology Group (ECOG) performance status
3. Disease stage
4. Presence or absence of brain metastases
5. Lactate Dehydrogenase (LDH) levels

Patients will continue on allocated treatment as long as they benefit from the treatment and it is tolerable.

Follow-up for survival will be a minimum of 9 months to a maximum of 5 years from date of randomisation of the last patient.

Intervention Type

Other

Phase

Phase II

Primary outcome(s)

1. Recruitment rate will be measured as the average number of patients recruited per site per two months. To be assessed once the trial has been recruiting for 15 months, or when 15 sites have been open for 6 months whichever is sooner
2. Treatment compliance is the percentage of patients completing the allocated treatment at 6 months from randomisation
3. Overall Quality of Life, defined as the global health status score derived from European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire at 6 months from randomisation
4. Progression Free Survival (assessed according to standard Response Criteria In Solid Tumours (RECIST v1.1), calculated as the duration from the date of randomisation to the date of first progression or death from any cause, which ever occurs first

Key secondary outcome(s)

1. Safety is assessed using the standard cancer National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) V4.03 criteria throughout the trial
2. Objective Response Rate will be assessed according to RECIST v1.1
3. Time to treatment failure will be the time from starting drug treatment on day 1 of cycle 1 until the date of day 1 of the last cycle +28 days
3. Overall survival will be calculated as the duration from the date of randomisation to the date of death from any cause
4. Patient Reported outcomes focussing on skin toxicity evaluation will be assessed using skin-specific patient reported outcome measures throughout the trial
5. Patient experience will be assessed by a survey of patients in each arm of the trial, 9 months from randomisation. Also, semi-structured interviews in a subset of patients who have

volunteered at a later time point

6. Quality of Life and Health Economics Evaluation using the EORTC QLQ-C30 and EQ5D questionnaires throughout the trial

Completion date

27/11/2020

Eligibility

Key inclusion criteria

1. Signed informed consent
2. Age ≥ 18 years old
3. Histologically or cytologically confirmed BRAFV600 mutant stage 3 unresectable or metastatic melanoma
4. Measurable disease by RECIST
5. ECOG performance status 0-2
6. Minimum life expectancy 12 weeks
7. Adequate bone marrow, renal and liver function
8. Received no prior BRAF or MEK inhibitor therapy for metastatic disease
9. Willing and able to comply with the scheduled visits, treatment plans, laboratory tests, completion of QoL questionnaires and other study procedures
10. Archival tumour tissue sample available
11. Women of child-bearing potential and all sexually active male patients must agree to use effective contraception methods throughout treatment

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

79

Key exclusion criteria

1. Concomitant immunotherapy being administered to treat advanced melanoma
2. Other invasive malignancies diagnosed within the last year which are not in complete remission, or for which additional therapy is required
3. Significant acute or chronic medical or psychiatric condition, disease or laboratory abnormality which in the judgment of the investigator would place the patient at undue risk or interfere with

the trial

4. Women who are pregnant, plan to become pregnant or are lactating during the trial period

5. Other investigational anti-cancer drugs

6. Use of strong inducers and inhibitors of CYP3A or CYP2C8

Date of first enrolment

23/10/2017

Date of final enrolment

28/03/2020

Locations

Countries of recruitment

United Kingdom

England

Scotland

Study participating centre

Addenbrookes Hospital

Oncology Centre

Box 193

Hills Road

Cambridge

United Kingdom

CB2 0QQ

Study participating centre

Churchill Hospital

Oxford Cancer Centre

Headington

Oxford

United Kingdom

OX3 7LE

Study participating centre

The Christie Hospital

Wilmslow Road

Manchester

United Kingdom

M20 4BX

Study participating centre

The Royal Marsden

Fulham Road
London / Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre

Norfolk & Norwich University Hospital

Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre

Royal Preston Hospital

Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre

Charing Cross Hospital

Imperial College Healthcare NHS Trust
Fulham Place Road
London
United Kingdom
W6 8RF

Study participating centre

University Hospital Birmingham (Queen Elizabeth)

Heritage Building
Mindelsohn Way
Edgebaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Weston Road
Glasgow
United Kingdom
G12 OYN

Study participating centre
Edinburgh Cancer Centre
Western General Hospital
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
University College London Hospital
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Weston Park Hospital
Whitham Road
Sheffield
United Kingdom
S10 2SJ

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
University Hospital Southampton
Medical Oncology
MP307 Level D East Wing
Southampton General Hospital

Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Bristol University Hospitals
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Study participating centre
Royal Free Hospital
Academic Oncology
Upper 4th Floor
Room U4/10,
Pond Street
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
<https://ror.org/04v54gj93>

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and analysed during the current study will be available upon request from the Cambridge Clinical Trials Unit - Cancer Theme (CCTU-CT) (cctu.cancer@addenbrookes.nhs.uk). Fully anonymised data linked only to relevant samples collected will be shared. Data will only be available following submission of the full end of trial report, initial publications of the data, and upon approval of the CCTU-CT and Sponsor.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		13/12/2021	16/06/2022	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 4.0	01/08/2019	14/10/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes