ISRCTN18183156 https://doi.org/10.1186/ISRCTN18183156

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

Registration date
14/09/2017

Overall study status
Completed

Last Edited
16/06/2023

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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

Study website
https://cctu.org.uk/portfolio/cancer/trials-closed-to-recruitment-in-follow-up/interim

Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2016-005228-27

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

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
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 measure
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

Secondary outcome measures
1. Safety is assessed using the standard cancer National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) V4.03 criteria thoughout the trial
2. Objective Response Rate will be assessed according to RECIST v1.1
T3. ime 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 oucome 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

Overall study start date
23/01/2017

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 150; UK Sample Size: 150

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
England

Scotland

United Kingdom

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

Sponsor details
Addenbrookes Hospital
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ

Sponsor type
Hospital/treatment centre

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

Publication and dissemination plan
It is planned that the main trial results will be presented at national and international conferences and published in peer-reviewed journal, within a year of the overall trial end date.

Intention to publish date
26/11/2022

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
Protocol file	version 4.0	01/08/2019	14/10/2022	No	No
HRA research summary			28/06/2023	No	No