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Continuous selumetinib versus continuous or interrupted selumetinib in combination with weekly paclitaxel in metastatic uveal melanoma

Submission date 17/06/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 17/06/2015	**Overall study status** Completed	
Last Edited 30/01/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-selumetinib-and-paclitaxel-for-a-type-of-eye-cancer-called-uveal-melanoma-selpac

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2014-004437-22

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19090

Study information

Scientific Title
A randomised three arm, open label, phase II study of continuous selumetinib versus continuous or interrupted selumetinib in combination with weekly paclitaxel in metastatic uveal melanoma

Acronym
SelPac

Study objectives
This study aims to compare continuous single agent selumetinib to combination paclitaxel and selumetinib in either a continuous or intermittent schedule.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - City & East Research Ethics Committee, 08/04/2015, ref: 15/LO/0159

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Topic: Cancer; Subtopic: Melanoma; Disease: Melanoma

Interventions
1. Paclitaxel, IMP
2. Selumetinib, IMP

Intervention Type

Other

Phase
Phase II

Primary outcome measure
Progression Free Survival (PFS) time.; Timepoint(s): Progression

Secondary outcome measures
1. GNAQ/GNA11 mutation status
2. RECIST Response
3. Safety and toxicity

Overall study start date
01/08/2015

Completion date
04/08/2020

Eligibility

Key inclusion criteria
Histologically or cytologically confirmed metastatic uveal melanoma
1. Patients must have measurable disease, defined by RECIST 1.1
2. Age at least18 years
3. ECOG performance status 0-2
4. Life expectancy of greater than 3 months
5. Able to swallow and retain orally-administered medication and does not have any clinically significant gastrointestinal abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach or bowels
6. All prior treatment-related toxicities must be CTCAE v4 grade = 1 (except alopecia) at the time of randomization
7. Laboratory values as listed below (SI units):
7.1. Total bilirubin = 1.5 X institutional upper limit of normal (ULN)
7.2. Aspartate aminotransferase or alanine aminotransferase >2.5 x ULN (or =5 ULN in presence of liver metastases)
7.3. Haemoglobin =9.0 g/dL
7.4. Platelets >100x109/L (100,000 per mm3)
7.5. Absolute neutrophil count >1.5x109/L (1500 per mm3)
7.6. Creatinine = 1.5 mg/dL OR calculated creatinine clearance (Cockroft-Gault formula) =50 mL /min OR 24-hour urine creatinine clearance =50 mL/min
8. Female patients of child-bearing potential should have a negative pregnancy test

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
Sample Size: 77 evaluable patients will be randomised to arms A, B and C across 13 UK centres and 1 German centre. Subjects will be randomised 1:1:1 between the 3 arms.

Key exclusion criteria
1. Patients may not have received prior chemotherapy for uveal melanoma. This includes patients who have received isolated hepatic perfusion of chemotherapy. Patients who have received prior immunotherapy or non-chemotherapy locoregional therapy for liver metastases, but who have documented evidence of progression of metastatic disease would however be eligible
2. Patients who have a known or suspected brain metastases or spinal cord compression, unless asymptomatic, has been treated with surgery and / or radiation, and has been stable without requiring corticosteroids nor anti-convulsant medications for at least 4 weeks prior to the first dose of study medication
3. Prior exposure to MEK, Ras, or Raf inhibitors or history of hypersensitivity to any excipient agents.
4. History of another malignancy unless disease-free for 3 years. Patients, who have had a completely resected nonmelanoma skin cancer, are eligible
5. Any permitted previous treatment must have been greater than 21 days prior to study treatment starting and all toxicities from previous treatments should have resolved
6. Symptomatic or untreated leptomeningeal or brain metastases or spinal cord compression. Treated brain metastases must have been stable for at least 1 month
7. Current use of a prohibited medication
8. Cardiac conditions as follows:
8.1. Uncontrolled hypertension (BP =150/95 mmHg despite medical therapy)
8.2. Acute coronary syndrome within 6 months prior to starting treatment
8.3. Baseline Left ventricular ejection fraction (LVEF) below the LLN or <55% measured by echocardiography or institution's LLN for MUGA
8.4. Atrial fibrillation with a ventricular rate >100 bpm on ECG at rest
8.5. Symptomatic heart failure NYHA Class II-IV, prior or current cardiomyopathy, or severe valvular heart disease
8.6. Prior or current cardiomyopathy including but not limited to the following:
8.7. Known hypertrophic cardiomyopathy
8.8. Known arrhythmogenic right ventricular cardiomyopathy
8.9. Previous moderate or severe impairment of left ventricular systolic function (LVEF <45% on echocardiography or equivalent on MuGA) even if full recovery has occurred
8.10.Uncontrolled angina (Canadian Cardiovascular Society grade II-IV despite medical therapy)
8.11. Acute coronary syndrome within 6 months prior to starting treatment
8.12. QTcF >450ms or other factors that increase the risk of QT prolongation
9. Ophthalmological conditions as follows (unless in the eye involved by uveal melanoma):
9.1. Intra-ocular pressure >21 mmHg, or uncontrolled glaucoma (irrespective of intra-ocular pressure)
9.2. Current or past history of retinal pigment epithelial detachment (RPED)/central serous retinopathy(CSR) or retinal vein occlusion
10. Uncontrolled intercurrent illness or uncontrolled systemic disease including, but not limited to, ongoing or active infection – including any patient known to have hepatitis B, hepatitis C or

human immunodeficiency virus (HIV), symptomatic congestive heart failure, unstable /uncontrolled angina pectoris, uncontrolled cardiac arrhythmia, QTc prolongation, active bleeding diatheses, renal transplant or psychiatric illness/social situations that would limit compliance with study requirements
11. Female patients who are breast-feeding
12. Male or female patients of reproductive potential who are not employing an effective method of contraception

Date of first enrolment
01/08/2015

Date of final enrolment
28/11/2018

Locations

Countries of recruitment
England

Germany

United Kingdom

Study participating centre
Liverpool Clinical Trials Centre
University of Liverpool
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Sponsor information

Organisation
University of Liverpool

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
04/08/2021

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		19/09/2021	16/06/2022	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 7	13/05/2020	30/01/2024	No	No