ISRCTN10125877 https://doi.org/10.1186/ISRCTN10125877

A study of pazopanib in metastatic merkel cell carcinoma

Submission date	Recruitment status	[ ] Prospectively registered
26/03/2013	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
26/03/2013	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
11/12/2014	Cancer	[ ] Record updated in last year

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-of-pazopanib-for-merkel-cell-carcinoma-ukmcc-01

Study website
http://www.birmingham.ac.uk/crctu

Contact information

Type(s)
Scientific

Contact name
Dr Joshua Savage

ORCID ID
http://orcid.org/0000-0003-0599-0245

Contact details
Cancer Research UK Clinical Trials Unit
School of Cancer Studies
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
-
UKMCC-01@trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number

2011-003226-27

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13736

Study information

Scientific Title
A Phase II study of pazopanib in metastatic merkel cell carcinoma

Acronym
UKMCC-01

Study objectives
Merkel cell carcinoma (MCC) is a rare neuroendocrine cancer of the skin with poor prognosis. The annual incidence is thought to be 0.6 per 100,000 of population, with approximately 400 cases per year in the UK. In this study we aim to determine if pazopanib is clinically active, as determined by response rate using the RECIST scoring, in advanced MCC and thus warrants further investigation in a phase III trial. Furthermore, through a translational sub-study, we aim to explore the biological features of MCC and relate these to clinical outcome in order to identify possible clinical biomarkers and therapeutic targets.

More details can be found at: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=13736

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Haydock, 02/11/2012, ref: 12/WM/0182

Study design
Non-randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Non randomised study

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
Treatment with Pazopanib, 4 x 200 mg tablets once daily by mouth for 28 days. Treatment will continue until disease progression.

Follow Up Length: 60 month(s)

Study Entry Details: Registration, followed by trial entry on completion of successful screening

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Pazopanib

Primary outcome measure
Clinical response rate; Timepoint(s): Proportion of patients with complete response or confirmed partial response throughout trial

Secondary outcome measures
1. Disease control rate; Timepoint(s): % of patients that have stable disease, a PR, or a CR for more than 12 weeks
2. Duration of response; Timepoint(s): Time from date of first response (partial/complete) to date of progression or death from any cause
3. Overall survival; Timepoint(s): Time from entry into the trial until death from any cause
4. PFS; Timepoint(s): Time from entry into the trial until disease progression or death from any cause

Overall study start date
02/11/2012

Completion date
01/08/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 17/01/2014:
1. Patients with histologically proven, unresectable, MCC that is metastatic and/or for which durable control cannot be achieved with surgery or radiotherapy
2. RECIST measurable disease, as per RECIST version 1.1
3. Age ≥18 years, either sex

4. Performance status 0, 1 or 2 assessed using the Eastern Cooperative Oncology Group scale
5. Received previous first line chemotherapy or considered unsuitable for chemotherapy
6. Toxicities from first line chemotherapy resolved to at least grade 1
7. Adequate end organ function
7.1. Renal function tests: serum creatinine ≤150 µmol/L. If serum creatinine is >150 µmol/L, calculated creatinine clearance must be ≥30 ml/min Urine Protein to Creatinine ratio (UPC) <1. If UPC ≥1, then a 24-hour protein must be assessed. Patients must have 24-hour protein value <1 g to be eligible. Alternatively, Albumin/Creatinine ratio may be measured (in accordance with institutional policy, same test to be used for study duration)
7.2. Liver function tests: Total serum bilirubin ≤1.5 X Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same test to be used for study duration) ≤2.5 X ULN (or ≤5 X ULN if liver metastases are present)
7.3. Haematology: Absolute Neutrophil Count (ANC) ≥1.5 X 109/L, Serum creatinine ≤150 µmol /L. If serum creatinine >150 µmol/L, calculated creatinine clearance must be ≥30 ml/min, Urine Protein to Creatinine ratio (UPC) <1. If UPC ≥1, then a 24-hour protein must be assessed. Patients must have 24hour protein value <1 g to be eligible
7.4. Liver function tests: Total serum bilirubin ≤1.5 X Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same test to be used for study duration) ≤2.5 X ULN (or ≤5 X ULN if liver metastases are present)
7.5. Haematology: Absolute Neutrophil Count (ANC) ≥1.5 X 109/L Haemoglobin ≥10 g/dL Platelets ≥100 X 10 to the power of 9/L
7.6. Coagulation test: International Normalized Ratio ≤1.2 X ULN, unless on therapeutic anticoagulation. For patients on therapeutic anticoagulation, INR should be stable and in target range
8. Able to give written informed consent
9. Women of childbearing potential, or men in a relationship with a woman of childbearing age, prepared to adopt adequate contraceptive measures if sexually active
10. Willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures

Previous inclusion criteria:
1. Patients with histologically proven, unresectable, MCC that is metastatic and/or for which durable control cannot be achieved with surgery or radiotherapy
2. RECIST measurable disease, as per RECIST version 1.1
3. Age ≥18 years, either sex
4. Performance status 0, 1 or 2 assessed using the Eastern Cooperative Oncology Group scale
5. Received previous first line chemotherapy or considered unsuitable for chemotherapy
6. Toxicities from first line chemotherapy resolved to at least grade 1
7. Adequate end organ function
7.1. Renal function tests: Serum creatinine ≤150 µmol/L. If serum creatinine >150 µmol/L, calculated creatinine clearance must be ≥30 ml/min Urine Protein to Creatinine ratio (UPC) <1. If UPC ≥1, then a 24-hour protein must be assessed. Patients must have 24-hour protein value <1 g to be eligible
7.2. Liver function tests: Total serum bilirubin ≤1.5 X Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same test to be used for study duration) ≤2.5 X ULN (or ≤5 X ULN if liver metastases are present)
7.3. Haematology: Absolute Neutrophil Count (ANC) ≥1.5 X 109/L, Serum creatinine ≤150 µmol /L. If serum creatinine >150 µmol/L, calculated creatinine clearance must be ≥30 ml/min, Urine Protein to Creatinine ratio (UPC) <1. If UPC ≥1, then a 24-hour protein must be assessed. Patients must have 24hour protein value <1 g to be eligible
7.4. Liver function tests: Total serum bilirubin ≤1.5 X Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same

test to be used for study duration) ≤2.5 X ULN (or ≤5 X ULN if liver metastases are present)
7.5. Haematology: Absolute Neutrophil Count (ANC) ≥1.5 X 109/L Haemoglobin ≥10 g/dL Platelets ≥100 X 10 to the power of 9/L
7.6. Coagulation test: International Normalized Ratio ≤1.2 X ULN
8. Able to give written informed consent
9. Women of childbearing potential, or men in a relationship with a woman of childbearing age, prepared to adopt adequate contraceptive measures if sexually active
10. Willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 25; UK Sample Size: 25

Key exclusion criteria
1. Previous malignancies. (Unless agreed in writing by the Chief Investigator or a clinical Coinvestigator, investigators are advised to call the Trial Office).
2. Known brain metastases unless radically treated with surgery or radiotherapy >6 months prior to study entry and without evidence of central nervous system progression since treatment
3. History in the past 6 months of cerebral or clinically significant gastrointestinal haemorrhage
4. Haemoptysis within 6 weeks prior to first dose of study medication
5. Evidence of active bleeding or bleeding diathesis
6. Uncontrolled hypertension defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg. Initiation or adjustment of antihypertensive medication(s) is permitted prior to trial entry
7. Presence of uncontrolled infection
8. History of malabsorption, major gastrointestinal tract resection or other pathology likely to affect absorption of study medication
9. Prolongation of the QT interval (QTc) >480 milliseconds
10. History of any one or more of the following cardiovascular conditions within the past 6 months: Cardiac angioplasty or stenting Myocardial infarction Unstable angina Coronary artery bypass graft surgery Symptomatic peripheral vascular disease Class III or IV congestive heart failure, as defined by the New York Heart Association Functional Classification
11. History of cerebrovascular accident including transient ischemic attack within the past 12 months
12. History of pulmonary embolism or untreated deep venous thrombosis within the past 6 months. Patients with a history of thromboembolic disease who are on treatment with therapeutic anticoagulating agents are eligible
13. Known endobronchial lesions and/or lesions infiltrating major pulmonary vessels
14. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drug chemically

related to pazopanib
15. Major surgery or trauma <4 weeks prior to starting study medication and/or presence of any nonhealing wound, fracture, or ulcer
16. Radiotherapy <2 weeks prior to starting study medication
17. Known HIV, Hepatitis B or C infection
18. Pregnant (female patients of child bearing potential should have a urine or blood Human Chorionic Gonadotropin test performed to rule out pregnancy prior to trial entry)
19. Lactating females. Patients who agree to discontinue nursing 14 days prior to commencing treatment and do not nurse throughout all the treatment period are eligible
20. The use of the following medication is prohibited: Previous therapy with agents that target the Vascular Endothelial Growth Factor (VEGF) or Platelet derived Growth Factor (PDGF) pathways Chemotherapy, immunotherapy, biologic therapy, investigational therapy, hormone therapy or use of any prohibited medications within 14 days prior to the first dose of study medication Use of drugs which are known strong CYP3A4 inhibitors or inducers within 14 days prior to the first dose of study medication
21. Any serious and/or unstable preexisting medical, psychiatric, or other conditions that could interfere with patients safety, obtaining informed consent or compliance to the study
22. Other contraindications to study medication

Date of first enrolment
21/12/2012

Date of final enrolment
21/12/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cancer Research UK Clinical Trials Unit
School of Cancer Studies
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham (UK)

Sponsor details
Research Support Group
Aston Webb Building
Edgbaston
Birmingham
England
United Kingdom
B15 2TT

Sponsor type
University/education

Website
http://www.birmingham.ac.uk/

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Cancer Research UK (UK) ; Grant Codes: C17955/A12806; CTAAC

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GSK

Funding Body Type

Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We intend to publish protocol, trial results and translational sub-study results.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available