

# A study of pazopanib in metastatic merkel cell carcinoma

<b>Submission date</b> 26/03/2013	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 26/03/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 11/12/2014	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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

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### Contact details

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B15 2TT

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## 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  $\geq 18$  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  $\leq 150 \mu\text{mol/L}$ . If serum creatinine is  $>150 \mu\text{mol/L}$ , calculated creatinine clearance must be  $\geq 30 \text{ ml/min}$  Urine Protein to Creatinine ratio (UPC)  $<1$ . If UPC  $\geq 1$ , then a 24-hour protein must be assessed. Patients must have 24-hour protein value  $<1 \text{ g}$  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  $\leq 1.5 \times$  Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same test to be used for study duration)  $\leq 2.5 \times$  ULN (or  $\leq 5 \times$  ULN if liver metastases are present)
  - 7.3. Haematology: Absolute Neutrophil Count (ANC)  $\geq 1.5 \times 10^9/\text{L}$ , Serum creatinine  $\leq 150 \mu\text{mol/L}$ . If serum creatinine  $>150 \mu\text{mol/L}$ , calculated creatinine clearance must be  $\geq 30 \text{ ml/min}$ , Urine Protein to Creatinine ratio (UPC)  $<1$ . If UPC  $\geq 1$ , then a 24-hour protein must be assessed. Patients must have 24hour protein value  $<1 \text{ g}$  to be eligible
  - 7.4. Liver function tests: Total serum bilirubin  $\leq 1.5 \times$  Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same test to be used for study duration)  $\leq 2.5 \times$  ULN (or  $\leq 5 \times$  ULN if liver metastases are present)
  - 7.5. Haematology: Absolute Neutrophil Count (ANC)  $\geq 1.5 \times 10^9/\text{L}$  Haemoglobin  $\geq 10 \text{ g/dL}$  Platelets  $\geq 100 \times 10^9/\text{L}$
  - 7.6. Coagulation test: International Normalized Ratio  $\leq 1.2 \times$  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  $\geq 18$  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  $\leq 150 \mu\text{mol/L}$ . If serum creatinine  $>150 \mu\text{mol/L}$ , calculated creatinine clearance must be  $\geq 30 \text{ ml/min}$  Urine Protein to Creatinine ratio (UPC)  $<1$ . If UPC  $\geq 1$ , then a 24-hour protein must be assessed. Patients must have 24-hour protein value  $<1 \text{ g}$  to be eligible
  - 7.2. Liver function tests: Total serum bilirubin  $\leq 1.5 \times$  Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same test to be used for study duration)  $\leq 2.5 \times$  ULN (or  $\leq 5 \times$  ULN if liver metastases are present)
  - 7.3. Haematology: Absolute Neutrophil Count (ANC)  $\geq 1.5 \times 10^9/\text{L}$ , Serum creatinine  $\leq 150 \mu\text{mol/L}$ . If serum creatinine  $>150 \mu\text{mol/L}$ , calculated creatinine clearance must be  $\geq 30 \text{ ml/min}$ , Urine Protein to Creatinine ratio (UPC)  $<1$ . If UPC  $\geq 1$ , then a 24-hour protein must be assessed. Patients must have 24hour protein value  $<1 \text{ g}$  to be eligible
  - 7.4. Liver function tests: Total serum bilirubin  $\leq 1.5 \times$  Upper Limit Normal (ULN), Alanine Aminotransferase or Aspartate Aminotransferase (in accordance with institutional policy, same

test to be used for study duration)  $\leq 2.5 \times \text{ULN}$  (or  $\leq 5 \times \text{ULN}$  if liver metastases are present)

7.5. Haematology: Absolute Neutrophil Count (ANC)  $\geq 1.5 \times 10^9/\text{L}$  Haemoglobin  $\geq 10 \text{ g/dL}$

Platelets  $\geq 100 \times 10^9/\text{L}$

7.6. Coagulation test: International Normalized Ratio  $\leq 1.2 \times \text{ULN}$

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  $\geq 140 \text{ mm Hg}$  or diastolic blood pressure  $\geq 90 \text{ mm Hg}$ . 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