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A study of pazopanib efficacy and safety in patients with advanced clear-cell renal cell carcinoma and ECOG Performance Status 2 (PaZ02)

Submission date
29/03/2012

Recruitment status
No longer recruiting

Registration date
29/03/2012

Overall study status
Completed

Last Edited
23/10/2020

Condition category
Cancer

[X] Prospectively registered
[_] 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-study-looking-advanced-kidney-cancer

Study website
https://www.birmingham.ac.uk/research/activity/mds/trials/crctu/trials/paz02/index.aspx

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2011-001211-31

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11827

Study information

Scientific Title
A study of PaZopanib efficacy and safety in patients with advanced clear-cell renal cell carcinoma and ECOG Performance Status 2 (PaZ02): A non-randomised phase II trial

Acronym
PaZ02

Study objectives
New treatments which are active and well tolerated are needed for patients with advanced renal cancer who suffer from symptoms that are bad enough to affect their quality of life and ability to carry on with their daily routine. These patients are classed as 'Performance Status 2'. The objective of this study is to see if a new drug called pazopanib can prevent the renal cancer from growing and see if it is well tolerated by patients with advanced renal cancer who are classed as 'Performance Status 2'.

Pazopanib works by disrupting the capillaries and blood vessels which supply the tumour tissue with blood and nutrients. In previous clinical trials pazopanib has demonstrated a significant effectiveness in advanced renal cell cancer patients who are less affected by their symptoms and is currently used for their treatment. It has not yet been tested in patients with 'Performance Status 2'.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Nottingham 2 Committee First MREC approval date 24th February 2012, ref: 11 /EM/0450

Study design
Early phase II non-randomised single arm multicentre study

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Treatment

Participant information sheet
Not available, trial now closed to recruitment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Renal Cancer; Disease: Kidney

Interventions
Pazopanib, Patients will receive pazopanib 800 mg once daily (OD) orally continuous dosing.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
Current primary outcome measures as of 05/02/2019:
1. Tolerability: proportion of patients at 6 months of treatment who were free from drug-related grade 3-4 toxicities resulting in an SAE or drug discontinuation >3 weeks.
2. Efficacy: Proportion of patients progression free (as per RECIST guidelines version 1.1) and alive at 6 months.

Previous primary outcome measures:
Efficacy and tolerability
1. Efficacy: proportion of patients who are progression free and alive at 6 months
2. Tolerability: Ratio of patients free of grade 3, grade 4 adverse events which are related to the study medication and deemed to be clinically relevant

Secondary outcome measures
Current secondary outcome measures as of 05/02/2019:
1. Overall Survival (OS) - will be measured at 12 months post registration as the number of whole days from date of entry into the trial until death by any cause or censor.
2. Progression Free Survival (PFS) - will be measured at 12 months post registration as the number of whole days from the date of entry into trial until evidence of radiological disease progression or death by any cause, or censor date.
3. Response and clinical benefit rates - Response Rate will be defined as the proportion of patients who achieve either a complete or partial Radiological Response and Clinical benefit rate will be defined as the proportion of patients who achieve either a complete, partial or stable radiological response as defined by the RECIST 1.1 Criteria.
4. Duration of response - will be measured as the number of whole days between date of first evidence of response (CR or PR) until date of Progression of the Disease (PD) or death as defined by the RECIST1.1 Criteria.
5. Treatment safety - defined as the proportion of patients developing Adverse Events (AEs). AEs

will be collected from the date of entry in the trial until 28 days after drug discontinuation and graded according the NCI-CTC version 4. AEs will be classified by causality, grade, type, duration and system involved.
6. Drug dose administered - defined by dose intensity, incidences of dose reductions, interruptions, escalations and discontinuations.

Previous secondary outcome measures as of 05/02/2019:
1. Overall Survival (OS)
2. Progression Free Survival (PFS)
3. Response and clinical benefit rates
4. Duration of response
5. Treatment safety
6. Drug dose administered

Previous secondary outcome measures:
1. Overall survival
2. Progression Free Survival (PFS)
3. Response and clinical benefit rates
4. Duration of response
5. Treatment safety dose

Overall study start date
01/04/2011

Completion date
31/12/2018

Eligibility

Key inclusion criteria
1. Written informed consent
2. Histologically confirmed diagnosis of renal cell carcinoma with clear cell component
3. Locally advanced (defined as not amenable of curative surgery) or metastatic disease
4. Measurable disease as per Response Evaluation Criteria In Solid Tumors (RECIST) Criteria 1.1
5. Performance Status 2 assessed using the ECOG scale
6. No prior systemic therapy
7. Female patients of childbearing potential will be eligible if they agree to adequate contraception. Pregnancy test must be negative 1 week before first drug dose
8. Adequate organ function as defined by the following criteria:
8.1. Total serum bilirubin ≤1.5 x upper limit normal (ULN). Patients with Gilberts disease are eligible if the total bilirubin is <3.0 x ULN and direct bilirubin is ≤ 35%.
8.2. Serum transaminases (AST and ALT) <2.5 x ULN, unless liver metastases are documented in which case AST and ALT must be ≤ 5 x ULN
8.3. Calculated creatinine clearance ≥ 30mL/min (Cockroft Gault method)
8.4. Urine Protein to Creatinine Ratio (UPC) < 1. If UPC ≥ 1 then a 24 hour urine protein must be assessed. Only patients with 24 hour urine protein < 1g will be eligible
8.5. Total serum calcium concentration < 2.9 mmol/l
8.6. Absolute neutrophil count (ANC) ≥ 1500/mm3
8.7. Haemoglobin ≥ 9g/dl
8.9. Platelets ≥ 100,000/mm3
8.10. INR (International Normalised ratio) ≤ 1.2 x ULN. Subjects receiving anticoagulant therapy

are eligible if their INR is stable and within the recommended range
9. Age ≥18
10. Life expectancy ≥ 12 weeks
11. Willingness and ability to comply with scheduled visits, treatment plans, 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: 75; UK Sample Size: 75

Total final enrolment
75

Key exclusion criteria
1. Pregnant or lactating female patients. Patients who agree to discontinue nursing 14 days prior to commencing treatment and do not nurse throughout all the treatment period are eligible
2. Previous systemic treatment for renal cell carcinoma (RCC) (licensed or investigational) including adjuvant or neoadjuvant therapy
3. Major surgery or trauma < 4 weeks or radiotherapy and/or presence of any nonhealing wound, fracture, or ulcer. Radiotherapy < 2 weeks prior to starting treatment
4. History or clinical evidence of brain metastases or active seizure disorders
5. Previous malignancies within the last 5 years, with the exception of successfully treated superficial or in situ carcinomas and of invasive tumours treated with curative intent and in remission for at least 5 years
6. Current use of drugs which are known strong CYP4A inhibitors (7.10)
7. Use of any prohibited medications within 14 days of the first dose of study medication (
8. Uncontrolled hypertension defined as systolic blood pressure ≥ 150 mm Hg or diastolic blood pressure ≥ 95 mm Hg. Initiation or adjustment of antihypertensive medication(s) is permitted prior to study entry
9. Presence of uncontrolled infection
10. Prolongation of the QT interval (QTc) > 480 msecs
11. History of malabsorption, major gastrointestinal tract resection or other pathology likely to affect study drug absorption
12. History of any one or more of the following cardiovascular conditions within the past 6 months:
12.1. Cardiac angioplasty or stenting
12.2. Myocardial infarction
12.3. Unstable angina
12.4. Coronary artery bypass graft surgery
12.5. Symptomatic peripheral vascular disease

12.6. Class III or IV congestive heart failure, as defined by the New York Heart Association (NYHA) Functional Classification
13. History of cerebrovascular accident (CVA) including transient ischemic attack (TIA) within the past 12 months
14. History of pulmonary embolism or untreated deep venous thrombosis (DVT) within the past 6 months. Patients with recent DVT who have been treated with therapeutic anticoagulating agents for at least 6 weeks are eligible
15. Evidence of active bleeding or bleeding diathesis
16. Known endobronchial lesions and/or lesions infiltrating major pulmonary vessels
17. Any serious and/or unstable preexisting medical, psychiatric, or other conditions that could interfere with subjects safety, obtaining informed consent or compliance to the study
18. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drug chemically related to pazopanib

Date of first enrolment
21/02/2013

Date of final enrolment
12/08/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
PaZ02 trials office
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham

Sponsor details
Research Support Group
University of Birmingham
Edgbaston
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B15 2TT

Sponsor type
University/education

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

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

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

Funder Name
Novartis

Alternative Name(s)
Novartis AG, Novartis International AG

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan

Results of this trial will be submitted for publication in a peer reviewed journal. The manuscript will be prepared by the Trial Management Group (TMG) and authorship will be determined by mutual
agreement.
Any secondary publications and presentations prepared by Investigators must be reviewed by the TMG. Manuscripts must be submitted to the TMG in a timely fashion and in advance of being submitted for publication, to allow time for review and resolution of any outstanding issues.
Authors must acknowledge that the trial was performed with the support of University of Birmingham.
Intellectual property rights will be addressed in the Clinical Study Site Agreement between Sponsor and site.

Intention to publish date

30/09/2020

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		22/10/2018		No	No
Basic results		20/10/2020		No	No
HRA research summary			28/06/2023	No	No