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Pazopanib versus pacLitaxel in relapsed Urothelial TumOurs

Submission date	Recruitment status	[X] Prospectively registered
13/03/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/03/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
26/10/2022	Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-pazopanib-transitional-cell-urothelial-tract-cancer-pluto

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
PLUTO 2011

Study information

Scientific Title
A randomised phase II study investigating pazopanib vs weekly paclitaxel in relapsed or progressive transitional cell carcinoma (TCC) of the urothelium

Acronym
PLUTO

Study objectives
That pazopanib will provide a survival advantage over weekly paclitaxel as a second line treatment for advanced urothelial cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland REC 1, 07/11/2011, ref: 11/WS/0090

Study design
Two-arm open-label randomised control phase II trial

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Relapsed or progressive transitional cell carcinoma of the urothelium

Interventions
Patients are randomised on a 1:1 basis to either:
1. Pazopanib 800mg orally once daily until disease progression or patient toxicity or patient choice
2. Paclitaxel 80 mg/m2 three weeks out of every 4 for a maximum of 24 weeks

For the first 24 weeks of the study patients will be seen formally on a 4 weekly basis in clinic. Radiological assessments (CT or MRI scan of chest, abdomen and pelvis) will occur at 12 weekly intervals until disease progression. From week 24 onwards all patients will be seen on a 6 weekly basis until disease progression.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
Overall survival

Secondary outcome measures
1 Progression free survival
2 Clinical benefit (proportion of patients alive with stable disease, partial response or complete response) at 12 weeks after the start of treatment
3 Clinical benefit at 24 weeks after start of treatment
4 Toxicity according to Common Terminology Criteria for Adverse Events version 4 (CTCAE v4)
5 Qualiy of life assessed by FACT-Bl at weeks 1, 9, 17, 25, 37, 49, 61, 73, 85 and 97

Overall study start date
01/05/2012

Completion date
01/07/2015

Eligibility

Key inclusion criteria
1. Histologically or cytologically confirmed TCC (bladder, renal pelvis, ureter, urethra), which is locally advanced or metastatic (T4b and/or N1-3 and/or M1). Patients with mixed or differentiation pattern pathology will be permitted entry providing that TCC is a component pathology.
2. Progressive disease during or after one prior platinum-based chemotherapy regimen for advanced disease or as peri-operative therapy for muscle-invasive/node positive disease (if completed < 12 months prior to documented disease progression). The regimen must have included either cisplatin or carboplatin. Patients may have had two platinum containing regimens if one of these was given peri-operatively, and provided that there was a chemotherapy-free interval of at least 12 months between completing the 1st course and commencing the second course of chemotherapy. Chemotherapy given during radical radiotherapy as a radiosensitizer will not be considered as a chemotherapy treatment for the purposes of study eligibility.
3. Age ≥ 18 years
4. Measurable disease by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1

5. Adequate organ function as defined by the following criteria:
5.1. Total serum bilirubin ≤1.5 x upper level of normal (ULN)
5.2. Serum transaminases <2.5 x ULN. Concomitant elevations of transaminases and bilirubin are not permitted
5.3. Creatinine clearance >30ml/min (calculated by Cockcroft Gault equation) or Creatinine ≤1.5 x ULN
5.4. Absolute neutrophil count (ANC) ≥1500/mm3 without growth factor support
5.5. Platelets ≥ 100,000/mm3
5.6. Urine protein to creatinine ratio (UPC) < 110 mg/mmol (1g/g) (or total urinary protein < 1g /24hrs)
5.7. Activated partial thromboplastin time (APTT) ≤1.2 x ULN
5.8. International normalised ratio (INR) ≤ 1.2
6. Signed and dated informed consent indicating that the patient has been informed of all the pertinent aspects of the trial prior to enrolment
7. A negative pregnancy test for women of childbearing potential
8. Life expectancy of 3 months or more
9. Willingness and ability to comply with scheduled visits, treatment plans and laboratory tests and other study procedures
10. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
140

Total final enrolment
131

Key exclusion criteria
1. Congestive heart failure, myocardial infarction, coronary artery bypass graft or thrombotic cerebrovascular event in the previous six months, or ongoing severe or unstable arrhythmia requiring medication. Patients with rate controlled atrial fibrillation are permitted to enter the study
2. History of clinically significant bleeding in the 6 months prior to study initiation (including haemoptysis, cerebrovascular bleed or haematemis; patients with haematuria are permitted entry as long as there is no indication for intervention)
3. Major surgery or trauma within 28 days prior to first dose of investigational product and/or presence of any unhealed wound, fracture, or ulcer (procedures such as catheter placement not considered to be major surgery)
4. Cerebrovascular accident including transient ischemic attack (TIA), pulmonary embolism or deep venous thrombosis (DVT) within the past 6 months. Subjects with recent DVT who have

been therapeutically anti-coagulated for at least 6 weeks are eligible.
5. History of another malignancy in the last 5 years (other than treated squamous/basal cell skin cancer, treated early stage cervical cancer or treated / biochemically stable, organ confined prostate cancer)
6. Ongoing major gastrointestinal disease including unstable inflammatory bowel disease or bleeding peptic ulcer disease
7. Known endobronchial lesions which have a high risk of pulmonary haemorrhage
8. Previously identified brain, or central nervous system (CNS) metastases at baseline, with the exception of those subjects who have previously-treated CNS metastases (surgery ± radiotherapy, radiosurgery, or gamma knife) and who meet both of the following criteria: are asymptomatic and have no requirement for steroids or enzyme-inducing anticonvulsants in prior 28 days
9. Pregnant or breastfeeding. Patients must be surgically sterile or be postmenopausal, or must agree to use effective contraception during the period of therapy. Male patients must be surgically sterile or agree to use effective contraception
10. Administration of any investigational drug within 28 days or five half lives, whichever is longer, prior to receiving the first dose of study treatment
11. Treatment with any of the following anti-cancer therapies:
11.1. Radiation therapy, surgery or tumour embolisation within 14 days prior to the first dose of study medication
11.2. Chemotherapy, immunotherapy, biologic therapy, investigational therapy within 28 days or five half-lives of a drug (whichever is longer) prior to the first dose of study medication
12. Peripheral neuropathy of grade 2 or more
13. Any on-going toxicity from prior anti-cancer therapy that is >Grade 1 and/or that is progressing in severity, except alopecia
14. Other severe or uncontrolled systemic disease or evidence of any other significant clinical disorder or lab finding that makes it undesirable for the patient to participate in the study
15. Any psychological, familial, sociological or geographical consideration potentially hampering compliance with the study protocol and follow up schedule; those considerations should be discussed with the patient before registration in the trial
16. Known Human immunodeficiency virus (HIV) or other chronic immunosuppressive disease
17. QTc that is immeasurable or >480 msec on screening ECG. (Note: If a subject has a QTc interval >480 msec on screening ECG, the screen ECG may be repeated twice (at least 24 hours apart). The average QTc from the three screening ECGs must be <480 msec in order for the subject to be eligible for the study.) Patients who are receiving a drug that has a risk of Torsades de Pointes are excluded if QTc is ≥ 460 msec. The method for estimating QTc must be consistent between all time points for any individual patient.
18. History of symptomatic peripheral vascular disease within 6 months prior to trial entry
19. Uncontrolled hypertension [blood pressure (BP) >150/90] at screening visit if screening value is higher than this, then study entry will be permitted if there is evidence documented by a trained healthcare professional of controlled blood pressure during the 4 weeks prior to study entry)
20. Evidence of active bleeding or bleeding diathesis
21. Recent haemoptysis (>=½ teaspoon of red blood within 8 weeks before first dose of study drug)
22. Patients who are unable or unwilling to withdraw potent CYP3A4 inhibitors, inhibitors of P-glycoprotein or breast cancer resistance protein (BCRP)
23. Prior hypersensitivity to cremophor or known sensitivity to any component of pazopanib

Date of first enrolment
01/05/2012

Date of final enrolment
01/07/2015

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Beatson West of Scotland Cancer Centre
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Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

Sponsor details
c/o Dr Nat Brittain
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05kdz4d87

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

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2017		Yes	No
Plain English results			26/10/2022	No	Yes
HRA research summary			28/06/2023	No	No