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A phase II trial of Cediranib in the treatment of patients with Alveolar Soft Part Sarcoma

Submission date 08/12/2010	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 07/02/2011	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 24/01/2025	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-cediranib-alveolar-soft-part-sarcoma-casps

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01337401

Clinical Trials Information System (CTIS)
2010-021163-33

Protocol serial number
ICR-CTSU/2010/10027 (Trials Unit) CCR3448 (Sponsor)

Study information

Scientific Title
A randomised phase II multi-centre double-blind placebo-controlled clinical trial of Cediranib in the treatment of patients with Alveolar Soft Part Sarcoma

Acronym
CASPS

Study objectives
Alveolar soft part sarcoma (ASPS) is rare, with an incidence in the region of 0.5 - 1% of all sarcomas. Given an approximate annual incidence of sarcomas for the UK of 2,500 (excluding advanced gastrointestinal stromal tumour) a reasonable estimate of incidence for ASPS is 15 cases per annum. However, within this number the incidence of metastatic disease is high; patients typically survive for well in excess of 3 years with slowly progressive metastatic disease.

There is no standard accepted therapy for this patient group. The only report of clinical benefit concerned a similar agent, sunitinib, also an inhibitor of vascular endothelial growth factor receptor (VEGFR), as well as of other targets. The limited evidence available suggests that cediranib has unprecedented activity in ASPS and as such, this needs to be confirmed. Owing to the indolent nature of the disease in many cases, and hence the difficulty in proving that disease stabilisation is due to treatment, a formal prospective comparative study is required. The randomised design proposed in CASPS represents the best way of proving that the drug is active in this disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
UK South London Research Ethics Committee (4), 23/01/2011, ref: 10/H0806/118

Primary study design
Interventional

Study design
Randomised phase II multi-centre double-blind placebo-controlled clinical trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Alveolar soft part sarcoma

Interventions
Group 1: Cediranib tablets 30 mg oral once daily until week 24
Group 2: Placebo tablets 30 mg oral once daily until week 24

At week 24 all patients unblinded and may continue with open label cediranib until disease progression or study withdrawal for other reason.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Efficacy of cediranib in the treatment of ASPS by measuring the percentage change in the sum of target marker lesion diameters from randomisation to week 24 (or progression if sooner) compared to treatment with placebo

Key secondary outcome(s)
Secondary outcomes:
1. Response rate at week 24, best response using RECISTv1.1 and best reduction (%) in tumour size
2. Progression-free survival and percentage alive and progression-free at 12 months (APF12)
3. Overall survival
4. The safety and tolerability profile of cediranib in patients with ASPS

Exploratory objectives:
1. To explore the utility and applicability of Choi response criteria8 in ASPS patients treated with cediranib
2. To explore tissue markers of tumour response to cediranib in original archived biopsies, and optional pre- and post-treatment biopsies
3. To evaluate the changes in circulating markers of angiogenesis from blood samples in response to cediranib
4. To evaluate the changes in circulating endothelial cells/endothelial precursor cells in response to cediranib

Completion date
15/01/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/11/2014:
1. Histologically confirmed diagnosis of ASPS (central confirmation not required at study entry)
2. Age 16 years and older
3. Availability of archived tissue blocks to enable confirmation of t(X;17) translocation
4. ECOG Performance Status of 0-1
5. Life expectancy of >12 weeks
6. Progressive disease as defined by RECIST v1.1 within 6 months prior to randomisation
7. Measurable metastatic disease using RECIST v1.1, i.e. at least one lesion 10 mm in diameter (15 mm in short axis for nodal lesions) assessable by CT (or MRI for brain metastases).
8. Patients with brain metastases are permitted provided disease is controlled with a stable dose of corticosteroid and/or non-enzyme inducing anticonvulsant
9. The capacity to understand the patient information sheet and ability to provide written informed consent
10. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests and other study procedures
11. Able to swallow and retain oral medication

Previous inclusion criteria:
1. Histologically confirmed diagnosis of ASPS (central confirmation not required at study entry)
2. Aged 16 years and older
3. Availability of archived tissue blocks or unstained slides to enable confirmation of t(X;17) translocation
4. Eastern Cooperative Oncology Group (ECOG) performance status of 0 - 1
5. Life expectancy of greater than 12 weeks
6. Progressive disease within 6 months prior to randomisation
7. Measurable metastatic disease using Response Evaluation Criteria in Solid Tumours (RECIST) v1.1, i.e. at least one lesion 10 mm in diameter (15 mm in short axis for nodal lesions) assessable by spiral computed tomography (CT) (or magnetic resonance imaging [MRI] for brain metastases)
8. Patients with brain metastases are permitted provided disease is controlled with a stable dose of corticosteroid and/or non-enzyme inducing anticonvulsant
9. The capacity to understand the patient information sheet and ability to provide written informed consent
10. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests and other study procedures
11. Able to swallow and retain oral medication

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 Years

Sex
All

Total final enrolment
48

Key exclusion criteria
Current exclusion criteria as of 11/11/2014:
1. Inadequate bone marrow reserve as demonstrated by an absolute neutrophil count ≤1.5 x 109 /L or platelet count ≤100 x 109/L
2. Serum bilirubin ≥ 1.5 x ULN (unless Gilberts syndrome)
3. ALT or AST ≥ 2.5 x ULN. If liver metastases are present, ALT or AST > 5 x ULN
4. Serum creatinine > 1.5 x ULN or a creatinine clearance (calculated or measured) of ≤ 50mL/min
5. Greater than +1 proteinuria unless urinary protein < 1.5g in a 24 hr period or protein /creatinine ratio < 1.5.
6. History of significant gastrointestinal impairment, as judged by the Investigator, that would significantly affect the absorption of cediranib.
7. Patients with a history of poorly controlled hypertension with resting blood pressure >150 /100 mmHg in the presence or absence of a stable regimen of anti-hypertensive therapy.
8. Any evidence of severe or uncontrolled co-morbidities e.g. unstable or uncompensated respiratory, cardiac, hepatic or renal disease, or active and uncontrolled infection.
9. Evidence of prolonged QTc >480 msec (using Bazetts correction, for which the formula is: QTc = QT/√RR) or history of familial long QT syndrome.
10. Significant recent haemorrhage (>30mL bleeding/episode in previous 3 months) or haemoptysis (>5 mL fresh blood in previous 4 weeks).
11. Major thoracic or abdominal surgery in the 14 days prior to entry into the study, or a surgical incision that is not fully healed.
12. Pregnant or breast-feeding women; women of childbearing potential with a positive pregnancy test prior to receiving study medication; women the intention of pregnancy during study treatment; women of child bearing potential unwilling to have a urine or serum pregnancy test prior to study entry (even if surgically sterilised).
13. Men and women of childbearing potential unwilling to use adequate birth control measures (e.g. abstinence, oral contraceptives, intrauterine device, barrier method with spermicide, implantable or injectable contraceptives or surgical sterilisation) for the duration of the study and should continue such precautions for 2 weeks after receiving the last study treatment.
14. History of anticancer (including investigational, non-registered) treatment in the four weeks prior to first dose of cediranib, with the exception of palliative radiotherapy for symptom control.
15. Previous treatment with cediranib.
16. Known hypersensitivity to any excipient of cediranib.
17. History of other malignancies (except for adequately treated basal or squamous cell carcinoma or carcinoma in situ) within 5 years, unless the patient has been disease free for 2 years and there is a tissue diagnosis of the primary cancer of interest from a target lesion.
18. Other concomitant anti-cancer therapy (including LHRH agonists) except steroids
19. Recent history of thrombosis
20. Patients with brain metastases if they are symptomatic requiring increasing steroids in the previous six weeks to study entry or those with evidence of recent and/or active bleeding, or those causing uncontrolled seizures.

Previous exclusion criteria:
1. Inadequate bone marrow reserve as demonstrated by an absolute neutrophil count less than or equal to 1.5 x 10^9/L or platelet count less than or equal to 100 x 10^9/L
2. Serum bilirubin greater than or equal to 1.5 x upper limit of normal (ULN) (unless Gilbert's syndrome)
3. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) greater than or equal to 2.5 x ULN. If liver metastases are present, ALT or AST greater than 5 x ULN.
4. Serum creatinine greater than 1.5 x ULN or a creatinine clearance (calculated or measured) of less than or equal to 50 mL/min
5. Greater than +1 proteinuria unless urinary protein less than 1.5 g in a 24 hour period or protein /creatinine ratio less than 1.5
6. History of significant gastrointestinal impairment, as judged by the Investigator, that would significantly affect the absorption of cediranib
7. Patients with a history of poorly controlled hypertension with resting blood pressure greater than 150/100 mmHg in the presence or absence of a stable regimen of anti-hypertensive therapy
8. Any evidence of severe or uncontrolled co-morbidities, e.g. unstable or uncompensated respiratory, cardiac, hepatic or renal disease, or active and uncontrolled infection
9. Evidence of prolonged QTc greater than 480 msec (using Bazetts correction, for which the formula is: QTc = QT/vRR) or history of familial long QT syndrome
10. Significant recent haemorrhage (greater than 30 ml bleeding/episode in previous 3 months) or haemoptysis (greater than 5 ml fresh blood in previous 4 weeks)
11. Major thoracic or abdominal surgery in the 14 days prior to entry into the study, or a surgical incision that is not fully healed
12. Pregnant or breast-feeding women; women of childbearing potential with a positive pregnancy test prior to receiving study medication; women the intention of pregnancy during study treatment; women of child bearing potential unwilling to have a urine or serum pregnancy test prior to study entry (even if surgically sterilised)
13. Men and women of childbearing potential unwilling to use adequate birth control measures (e.g. abstinence, oral contraceptives, intrauterine device, barrier method with spermicide, implantable or injectable contraceptives or surgical sterilisation) for the duration of the study and should continue such precautions for 2 weeks after receiving the last study treatment
14. History of anticancer (including investigational, non-registered) treatment in the four weeks prior to first dose of cediranib, with the exception of palliative radiotherapy for symptom control
15. Known hypersensitivity to cediranib or any of its excipients
16. History of other malignancies (except for adequately treated basal or squamous cell carcinoma or carcinoma in situ) within 5 years, unless the patient has been disease free for 2 years and there is a tissue diagnosis of the primary cancer of interest from a target lesion
17. Other concomitant anti-cancer therapy (including LHRH agonists) except steroids
18. Recent history of thrombosis
19. Patients with brain metastases if they are symptomatic requiring increasing steroids in the previous six weeks to study entry or those with evidence of recent and/or active bleeding, or those causing uncontrolled seizures

Date of first enrolment
11/05/2011

Date of final enrolment
29/07/2016

Locations

Countries of recruitment
United Kingdom

England

Australia

Spain

Study participating centre
Sycamore House (SRMSYC), DF29
Surrey
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Study participating centre
Royal Marsden Hospital
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Study participating centre
The Christie Hospital
Wilmslow Rd
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M20 4BX

Study participating centre
Bristol Haematology and Oncology Centre
Horfield Rd
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BS2 8ED

Study participating centre
University College London Hospital
235 Euston RD

London
United Kingdom
NW1 2BU

Study participating centre
Royal Victoria Infirmary
Queen Victoria Rd
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NE1 4LP

Study participating centre
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NE7 7DN

Study participating centre
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NSW 2050

Study participating centre
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Study participating centre
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Sponsor information

Organisation
The Institute of Cancer Research/Royal Marsden Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) (ref: CRUK/10/021)

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
AstraZeneca (UK) (ref: ISSRECE0036)

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

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?
Results article	results	01/07/2019	05/06/2019	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results		24/01/2025	24/01/2025	No	Yes