

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 07/02/2011	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 24/01/2025	Condition category Cancer	<input type="checkbox"/> 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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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2010-021163-33

ClinicalTrials.gov (NCT)

NCT01337401

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

Study design

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

Primary study design

Interventional

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 $\leq 1.5 \times 10^9$ /L or platelet count $\leq 100 \times 10^9$ /L
2. Serum bilirubin $\geq 1.5 \times$ ULN (unless Gilberts syndrome)
3. ALT or AST $\geq 2.5 \times$ ULN. If liver metastases are present, ALT or AST $> 5 \times$ ULN
4. Serum creatinine $> 1.5 \times$ ULN or a creatinine clearance (calculated or measured) of ≤ 50 mL/min
5. Greater than +1 proteinuria unless urinary protein < 1.5 g 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: $QTc = QT/\sqrt{RR}$) or history of familial long QT syndrome.
10. Significant recent haemorrhage (> 30 mL 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 $1.5 \times 10^9/L$ or platelet count less than or equal to $100 \times 10^9/L$
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: $QTc = QT/\sqrt{RR}$) 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

United Kingdom

SM2 5PT

Study participating centre

Royal Marsden Hospital

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London

United Kingdom

SW3 6JJ

Study participating centre

The Christie Hospital

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M20 4BX

Study participating centre

Bristol Haematology and Oncology Centre

Horfield Rd

Bristol

United Kingdom

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
Newcastle-upon-Tyne
United Kingdom
NE1 4LP

Study participating centre
Freeman Hospital
Freeman Rd
Newcastle-upon-Tyne
United Kingdom
NE7 7DN

Study participating centre
Chris O'Brien Lifehouse
119-143 Missenden Rd
Camperdown
Sydney
Australia
NSW 2050

Study participating centre
Princess Alexandra Hospital
199 Ipswich Rd
Woolloongabba
Brisbane
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QLD 4102

Study participating centre
Hospital de la Santa Creu i Sant Pau
Carrer de Sant Quintí 89
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Hospital Puerta de Hierro
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Study participating centre
Hospital Miguel Servet
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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