ISRCTN60791336 https://doi.org/10.1186/ISRCTN60791336

A phase II study of axitinib in patients with advanced angiosarcoma and other soft tissue sarcomas

Submission date 20/01/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/02/2009	**Overall study status** Completed	
Last Edited 11/09/2023	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-axitinib-advanced-soft-tissue-sarcoma-Axi-STS

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01140737

Protocol serial number
STH15195

Study information

Scientific Title
Axitinib in patients with advanced angiosarcoma and other soft tissue sarcomas: a phase II open-label parallel-group (non-randomised) study

Acronym
Axi-STS

Study objectives
The study objective is to evaluate the therapeutic activity, safety and tolerability of axitinib in patients with advanced/metastatic soft tissue sarcoma who have relapsed after standard chemotherapy. The therapeutic activity will be separately assessed in angiosarcoma, synovial sarcoma, leiomyosarcomas and other sarcomas.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands REC, 15/12/2009

Study design
Phase II open-label non-randomised multi-centre parallel-group study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Advanced angiosarcoma and other soft tissue sarcomas

Interventions

All participants will receive the same treatment. However, they will be grouped according to the four pathological subtypes: angiosarcoma, synovial sarcoma, leiomyosarcoma and other (sarcoma, not otherwise specified [NOS]), and each group (stratum) will be analysed separately (parallel-group analysis).

Patients will take axitinib tablets 5 mg by mouth twice daily continuously. There may be one dose reduction to 3 mg twice daily. A four-week dosing period will be considered as 1 cycle of treatment. Axitinib treatment will be continued until disease progression, or the development of limiting toxicity.

Disease evaluation will be carried out 12 weeks after study entry (even if the study treatment has already been discontinued) then every 12 weeks until disease progression. After disease progression, patients should be followed up every 3 months for survival. Patients will be followed-up until death or the end of the trial. It is expected to complete accrual in 2 years and the study in 3 years.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Proportion of patients progression-free 12 weeks after starting treatment, defined according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria.

Key secondary outcome(s))
1. Tumour response rate (using RECIST criteria) at end of treatment
2. Time to progression, defined as the interval in whole days between the date of registration into the trial and the earliest date of detection of disease progression
3. Progression-free survival, defined as the interval in whole days between the date of registration into the trial and the earliest of date of detection of disease progression or date of death from any cause. For those patients who do not experience disease progression or die during the course of the trial, progression-free survival times will be censored at the last follow-up date.
4. Overall survival, defined as the interval in whole days between the date of registration into the trial and date of death from any cause; patients who do not die during the course of the trial will be censored at the last follow-up date.
5. Changes in performance status, assessed at screening, weekly during cycle 1, monthly from cycle 2 and at the end of treatment
6. Adverse events, graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v3.0. Report from date of patient enrolment into the study until 30 days after last exposure to the trial treatment.
7. Biomarkers of angiogenesis in blood and tumour biopsy samples. A paraffin-fixed block will be requested from relevant histopathology departments for the pathological and biological studies, for angiosarcomas only, fresh tumour material will be required. If not already available, a core biopsy will be required.

Completion date
08/01/2019

Eligibility

Key inclusion criteria
1. Pathologically confirmed soft tissue sarcoma, including:
1.1. Angiosarcoma, including intermediate and malignant vascular tumours (World Health Organization [WHO] classification, 2002) and Kaposi's sarcoma
1.2. Leiomyosarcoma, including uterine, skin or non organ origin
1.3. Synovial sarcoma
1.4. Other eligible subtypes of soft tissue sarcoma of Trojani intermediate or high grade, including fibroblastic, fibrohistiocytic, adipocytic, rhabdomyosarcoma, malignant peripheral nerve sheath, and NOS. See exclusion criteria for ineligible subtypes
2. Locally advanced or metastatic disease incurable by surgery or radiotherapy
3. Measurable disease according to Response Evaluation Criteria in Solid Tumours (RECIST) criteria
4. Evidence of objective disease progression in the past 6 months, without anticancer treatment since progression
5. Patients ineligible for chemotherapy (e.g., through age, clinical condition or patient refusal) or who have received no more than two prior chemotherapy regimens
6. Both males and females, age >=16
7. WHO performance status 0, 1 or 2
8. At least 4 weeks from prior anticancer treatment (surgery, radiotherapy and systemic therapies) and full recovery from all their adverse effects
9. Adequate physiological function:
9.1. Renal : calculated or measured creatinine clearance >=50 ml/min
9.2. Haematological: absolute neutrophil count (ANC) >=1.5 x 109/L, platelets >=100 x 109/L, international normalised ratio (INR) <=1.2
9.3. Hepatic: bilirubin within normal range, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <=3 x upper limit of normal
9.4. Cardiac: left ventricular ejection fraction (LVEF) (measured by echocardiography [ECHO] or multiple uptake gated acquisition scan [MUGA]) within normal range
10. Negative pregnancy test and agrees to comply with contraceptive measures
11. Able to swallow oral medication

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
145

Key exclusion criteria

Current exclusion criteria as of 18/10/2011:
1. Ineligible pathological subtypes including:
1.1. Osteosarcoma
1.2. Ewings/primitive neuroectodermal tumour (PNET) sarcomas
1.3. Chondrosarcoma
1.4. Gastrointestinal stromal tumours (GIST)
1.5. Dermatofibrosarcoma protuberans (DFSP)
1.6. Malignant mesothelioma
1.7. Mixed mesodermal tumours of uterus
2. Known central nervous system metastases
3. Age <16 years
4. Current use or anticipated need for treatment with drugs that are known CYP3A4 or CYP1A2 inducers (i.e. carbamazepine, dexamethasone, felbamate, omeprazole, phenobarbital, phenytoin, primidone, rifabutin, rifampicin, and St. John's Wort)
5. Current use or anticipated need for treatment with drugs that are known potent CYP3A4 inhibitors
6. Previous malignancies (except curatively treated non-melanoma skin cancer or carcinoma in situ of the cervix or breast) within the past 3 years
7. Uncontrolled or poorly controlled hypertension: systolic blood pressure (BP) >=150 mmHg or diastolic BP >=90 mmHg. Hypertension may be treated prior to study entry, but 3 consecutive readings less than 150/90 must be obtained, at least 24 h apart prior to study entry
8. Heart failure >=NYHA class II
9. History within the previous 6 months of any blood clots in the sputum or streaky haemoptysis that was persistent (> 2 weeks) or recurrent (> 3 episodes).
10. Any of the following within the 12 months prior to study drug administration: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident or transient ischemic attack, deep vein thrombosis or pulmonary embolism
11. Therapeutic dose warfarin. Low molecular weight heparin is permitted.
12. History of malabsorption or major gastrointestinal tract resection likely to affect study drug absorption
13. Pregnancy or breastfeeding. Female patients must be surgically sterile or be postmenopausal, or must agree to use two effective contraception measures during the period of therapy which should be continued for 4 weeks after the last dose of study therapy. Male patients must be surgically sterile or must agree to use effective contraception during the period of therapy. The definition of effective contraception will be based on the judgment of the principal investigator or a designated associate.
Added 18/10/2011:
14. Regular treatment with antiplatelet medication, including aspirin >325 mg/day or NSAIDs.
15. Patients with cavitating lung metastases or any metatstasis abutting or invading a major pulmonary blood vessel on baseline CT or MRI scan.
16. History of bleeding diathesis or coagulopathy within 12 months of study entry.

Previous exclusion criteria:
9. History of hemoptysis >1/2 teaspoon (2.5 ml) of blood in any 24-hour period within prior 2 weeks of enrolment

Points 1-8 and 10-13 remained unchanged.

Date of first enrolment

31/08/2010

Date of final enrolment
01/01/2016

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Weston Park Hospital
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Study participating centre
Aberdeen Royal Infirmary
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Study participating centre

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LS9 7TF

Study participating centre
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SW3 6JJ

Study participating centre
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Study participating centre
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M20 4BX

Study participating centre
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NG5 1PB

Study participating centre

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Southampton General Hospital
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Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (UK) (ref: C5410/A10910)

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
Pfizer (USA) (supplementary funding)

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen, Pfizer Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The current 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		08/09/2023	11/09/2023	Yes	No
Basic results	version 1.0	02/09/2022	08/09/2022	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes