

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 27/02/2009	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 11/09/2023	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-looking-axitinib-advanced-soft-tissue-sarcoma-Axi-STS>

Contact information

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01140737

Secondary identifying numbers
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

Secondary study design

Non randomised study

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

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 measure

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

Secondary outcome measures

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.

Overall study start date

01/07/2009

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) $\geq 1.5 \times 10^9/L$, platelets $\geq 100 \times 10^9/L$, international normalised ratio (INR) ≤ 1.2
 - 9.3. Hepatic: bilirubin within normal range, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) $\leq 3 \times$ 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

Age group

Adult

Sex

Both

Target number of participants

Between 72 and 164

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 \geq 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 metastasis 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

England

Scotland

United Kingdom

Wales

Study participating centre

Weston Park Hospital

Sheffield

United Kingdom

S10 2SJ

Study participating centre

Aberdeen Royal Infirmary

Aberdeen

United Kingdom

AB25 2ZN

Study participating centre

Western General Hospital
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
Clatterbridge Centre for Oncology
Bebington
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CH63 4JY

Study participating centre
Bristol Haematology & Oncology Centre
Bristol
United Kingdom
BS2 8ED

Study participating centre
St. James's Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
Royal Marsden Hospital
London
United Kingdom
SW3 6JJ

Study participating centre
University College London Hospitals
London
United Kingdom
NW1 2BU

Study participating centre

Christie Hospital
Manchester
United Kingdom
M20 4BX

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Ninewells Hospital
Dundee
United Kingdom
DD2 1UB

Study participating centre
Singleton Hospital
Swansea
United Kingdom
SA2 8QA

Study participating centre
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation

Sheffield Teaching Hospitals NHS Foundation Trust (UK)

Sponsor details

Pegasus House
463a Glossop Road
Sheffield
England
United Kingdom
S10 2QD

Sponsor type

Hospital/treatment centre

Website

<http://www.sth.nhs.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, 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

Funding Body Type

Government organisation

Funding Body Subtype

For-profit companies (industry)

Location

United States of America

Results and Publications

Publication and dissemination plan

Planning to submit main trial results to a peer reviewed journal by end of Q4 2020 (updated 05/03/2020, previously: Q2 2018).

Intention to publish date

31/12/2022

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?
Basic results	version 1.0	02/09/2022	08/09/2022	No	No
Results article		08/09/2023	11/09/2023	Yes	No