

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

<b>Submission date</b> 20/01/2009	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 27/02/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 11/09/2023	<b>Condition category</b> 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

### Type(s)

Scientific

### Contact name

Prof Penella Woll

### Contact details

Weston Park Hospital  
Whitham Road  
Sheffield  
United Kingdom  
S10 2SJ

-

p.j.woll@sheffield.ac.uk

### Type(s)

Scientific

### Contact name

Ms Ana Hughes

### Contact details

Cancer Research UK Clinical Trials Unit (CRCTU)  
Institute of Cancer and Genomic Sciences

University of Birmingham  
Birmingham  
United Kingdom  
B15 2TT  
+44 (0)121 414 3793  
a.i.hughes@bham.ac.uk

## **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  $\geq 16$
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  $\geq 50$  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)  $\leq 1.2$
  - 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)  $\geq 150$  mmHg or diastolic BP  $\geq 90$  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  
United Kingdom  
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?
<a href="#">Basic results</a>	version 1.0	02/09/2022	08/09/2022	No	No
<a href="#">Results article</a>		08/09/2023	11/09/2023	Yes	No