

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

Rationale

- Limited number of active agents available for the treatment of soft tissue sarcoma.
- New agents are needed.
- Pazopanib has 7% RR in STS (excl. liposarcoma) and 12 week PFR of 44% - now in phase III trial.
- Prospective trials in angiosarcoma show:
 - 17% RR with paclitaxel
 - 14% RR with sorafenib
 - 12% RR with bevacizumab
- Angiosarcomas are endothelial tumours – so it is attractive to use vascular targeted drugs.
- Axitinib is a potent VEGFR inhibitor, given by mouth.
- Systematic study of angiogenic pathways is needed.

Objectives

To evaluate the activity, safety and tolerability of axitinib in patients with advanced/metastatic soft tissue sarcoma who are unsuitable for or have relapsed after standard chemotherapy.

Trial design

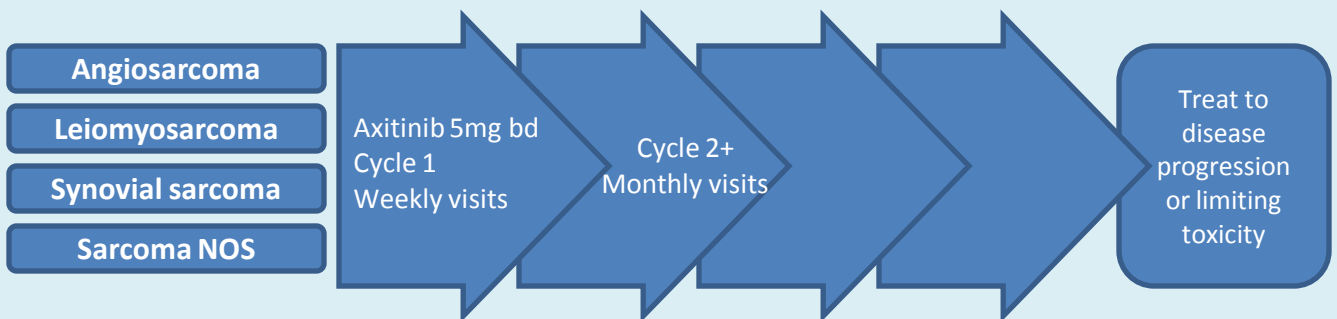
- Open label, multicentre, stratified, phase II trial.
- Four strata: angiosarcoma, leiomyosarcoma, synovial sarcoma, other soft tissue sarcomas.
- Simon's 2-stage design is applied separately to each of the four patient group (strata).
- Each stratum will recruit 18 or 38 patients.

Main inclusion criteria

- Age \geq 16.
- Pathologically confirmed soft tissue sarcoma.
- Locally advanced or metastatic disease incurable by surgery or radiotherapy.
- Measurable disease according to RECIST criteria.
- Evidence of objective disease progression in the past 6 months, without anticancer treatment since progression.
- Patients ineligible for chemotherapy, eg. through age, clinical condition or patient refusal.
- No more than two prior chemotherapy regimens.
- At least 4 weeks from prior anticancer treatment (surgery, radiotherapy and systemic therapies) and full recovery from all their adverse effects.
- WHO performance status 0, 1 or 2.

Main exclusion criteria

- Ineligible pathological subtypes (defined in the protocol).
- Known central nervous system metastases.
- Previous malignancies (except curatively treated non-melanoma skin cancer or carcinoma in situ of the cervix or breast) within the past 3 years.
- Uncontrolled or poorly controlled hypertension.
- Heart failure \geq NYHA class II.
- Thromboembolic events (arterial or venous thrombosis, myocardial infarction, unstable angina, cardiac angioplasty or stenting) within the past 3 months.
- Therapeutic dose warfarin.
- History of malabsorption or major gastrointestinal tract resection likely to affect trial drug absorption.



Primary endpoint

- Progression-free survival rate at 12 weeks (RECIST criteria).

Biological endpoints

- Biomarkers of angiogenesis in blood and tumour samples.

Secondary endpoints

- Tumour response rate (RECIST criteria).
- Progression free interval.
- Progression free survival.
- Overall survival.
- Toxicities.
- Changes in performance status.