

# Activity of sorafenib in schwannomas

|                                        |                                                   |                                                                                                   |
|----------------------------------------|---------------------------------------------------|---------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>14/02/2012   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>14/02/2012 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>19/05/2022       | <b>Condition category</b><br>Cancer               | <input type="checkbox"/> Individual participant data                                              |

## Plain English summary of protocol

<http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-sorafenib-in-skin-schwannomas>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2011-001789-16

### Protocol serial number

10563

## Study information

**Scientific Title**

Investigation of the intratumoural concentration and activity of sorafenib in cutaneous schwannomas

**Study objectives**

In this study we will assess the delivery and biological activity of sorafenib in cutaneous schwannomas. As cutaneous schwannomas are the hallmark in the patient group of interest- patients with multiple merlin deficient tumours- we have focused our research initially on schwannomas in NF2 patients. Tumours caused by NF2 gene mutation, especially in NF2 patients, present considerable management problems, with current treatment options limited to surgery and radiosurgery. Currently there is no proven drug treatment for merlin deficient tumours. However consensus recommendations to accelerate clinical trials in NF2 have recently been published and include the recommendation of phase 0 trials. We have been investigating potential therapeutic targets in merlin deficient tumours for many years. After detailed target identification, our own studies have shown that PDGFR is massively over expressed and activated in schwannomas. We showed that sorafenib substantially decreases cell proliferation in human primary schwannoma cells by inhibiting PDGFR. Sorafenib is an approved tyrosine kinase inhibitor. There is extensive literature on the pharmacokinetics, pharmacodynamics and safety of sorafenib and considerable experience with its use, mainly in the treatment of renal cell carcinoma and hepatocellular carcinoma. Pharmacokinetic studies show that sorafenib is rapidly absorbed and shows steady state levels after 7-10 days. This phase 0 study of 14 patients with cutaneous schwannomas amenable to biopsy is designed to investigate the intra-tumoural penetration and molecular activity of sorafenib in cutaneous schwannoma tissue after 11 days of daily sorafenib dosing compared to pre-treatment levels. It will provide evidence for a drug candidate to be used in Phase II/III multi-centre randomised clinical trials (RCTs) with NF2 patients and patients with merlin deficient tumours, for example inoperable meningiomas, and inoperable schwannomas.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

London Bloomsbury NRES Committee, 26/08/2011, ref: 11/LO/0771

**Primary study design**

Interventional

**Study design**

Non-randomised interventional trial

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Brain and Nervous System Tumour

**Interventions**

One arm only. Treatment is Sorafenib (Nexavar - made by Bayer HealthCare, BayerSchering Pharma) administered as 2 x 200mg tablets (400mg) twice daily for 10 days (i.e. 800mg per day), plus 2 x 200mg (morning only) on the 11th day. Depending on an interim analysis of drug concentration and activity at the recruitment halfway stage, the second 7 participants may

receive a lower dose of 400mg per day instead of 800mg. Note that this is an experimental study to determine the action of Sorafenib in the blood and skin tumours of patients with NF2; there are no intended or anticipated clinical benefits of taking part.

## **Intervention Type**

Drug

## **Phase**

Phase IV

## **Drug/device/biological/vaccine name(s)**

Sorafenib

## **Primary outcome(s)**

Target inhibition by sorafenib in CS biopsies measured at Day 11.

## **Key secondary outcome(s)**

No secondary outcome measures

## **Completion date**

31/12/2015

# **Eligibility**

## **Key inclusion criteria**

1. Written informed consent
2. Diagnosis of NF2
3. Over 18 years in age
4. Presence of more at least two cutaneous schwannomas >1cm<sup>3</sup> in area and accessible for biopsy
5. WHO/ECOG Performance Status 0 or 1
6. Adequate bone marrow function within 28 days prior to the baseline visit and:
  - 6.1. WBC > 3.4x10<sup>9</sup>/l
  - 6.2. Platelets > 99x10<sup>9</sup>/l
7. Adequate renal function within 28 days prior to the baseline visit
  - 7.1. creatinine < 2.5 x upper limit of normal
8. Adequate hepatic function within 28 days prior to the baseline visit
  - 8.1. LFT < 1.5 x upper limit of normal
  - 8.2. Serum amylase < 1.5 x upper limit of normal
  - 8.3. Prothrombin (PT) or INR (International Normalized Ratio) and Prothrombin Time (PTT) < 1.5 x upper limit of normal
    - 8.3.1. Able to swallow tablets
    - 8.3.2. Ppatients with the potential for pregnancy or impregnating their partner must agree to use acceptable methods of birth control to avoid conception
  - 8.4. Female patients who are not using hormonal contraception must agree to employ two barrier methods of contraception (e.g. condom, diaphragm with spermicidal jelly) during the study and for 3 months following the end of their study participation
  - 8.5. Female patients who are using hormonal contraception must agree to use an additional barrier method (e.g. condom or diaphragm with spermicidal jelly) during the study and for 3 months following the end of study participation
  - 8.6. Post menopausal women must be amenorrheic for at least 12 months to be considered of

nonchildbearing potential.

9. Women of childbearing potential with a negative serum pregnancy test at screening and a negative urine pregnancy test at the baseline visit

10. Male and female

11. Lower Age Limit 18 years

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

All

### **Key exclusion criteria**

1. Hypersensitivity to sorafenib or any of its excipients
2. Cardiac arrhythmias requiring antiarrhythmics (betablockers and digoxin are allowed)
3. Symptomatic coronary artery disease or ischemia
4. Myocardial infarction (MI) within the last six months; congestive cardiac failure > NYHA Class II
5. Active clinically serious bacterial or fungal infections
6. Known history of human immunodeficiency virus (HIV) infection or chronic hepatitis B or C
7. Pregnant or breastfeeding
8. Patients with uncontrolled hypertension
9. Serious uncontrolled concomitant medical or psychiatric illness
- 9.1. Concomitant medications which have adverse interactions with sorafenib: rifampicin, ritonavir, ketoconazole, itraconazole and St Johns Wort
10. Treatment with strong CYP3A4 inhibitors (e.g., erythromycin, ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin, ritonavir, mibefradil) which has not been discontinued or switched to a different medication at least 2 weeks prior to starting the study drug.
11. Treatment with strong CYP3A4 inducers (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St Johns Wort), which has not been discontinued or switched to a different medication at least 2 weeks prior to starting the study drug.
12. Grade 3 or higher impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drug (e.g., ulcerative disease, uncontrolled nausea, vomiting, diarrhoea, malabsorption syndrome)
13. History of acute pancreatitis within one year of study entry or medical history of chronic pancreatitis
14. History of another primary malignancy that is currently clinically significant or currently requires active intervention.
15. Any other clinically significant medical or surgical condition which, according to the CI/PIs discretion, should preclude participation
16. History of significant congenital or acquired bleeding disorder
17. Patients taking warfarin or cytotoxic drugs

**Date of first enrolment**

06/02/2012

**Date of final enrolment**

31/12/2015

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

Peninsula College of Medicine & Dentistry

Plymouth

United Kingdom

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## Sponsor information

**Organisation**

Plymouth Hospitals NHS Trust (UK)

**ROR**

<https://ror.org/05x3jck08>

## Funder(s)

**Funder type**

Charity

**Funder Name**

Samantha Dickson Brain Tumour Trust (UK)

**Alternative Name(s)**

The Samantha Dickson Brain Tumour Trust (SDBTT), SDBTT

**Funding Body Type**

Private sector organisation

## Funding Body Subtype

Other non-profit organizations

## Location

United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

Not provided at time of registration

## IPD sharing plan summary

## Study outputs

| Output type                          | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|--------------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Basic results</a>        |         | 03/05/2021   | 19/05/2022 | No             | No              |
| <a href="#">HRA research summary</a> |         |              | 28/06/2023 | No             | No              |