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Activity of sorafenib in schwannomas

Submission date 14/02/2012	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/02/2012	**Overall study status** Completed	
Last Edited 19/05/2022	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-sorafenib-in-skin-schwannomas

Contact information

Type(s)
Scientific

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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

Study design
Non-randomised interventional trial

Primary study design
Interventional

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 >1cm3 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 > 3.4x109/l
6.2. Platelets > 99x109/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
9.3.2. 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, phenobarbitol, 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
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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?
Basic results		03/05/2021	19/05/2022	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes