# Phase I/II study of S 49076, a multi-target inhibitor of c-MET, AXL, FGFR in combination with bevacizumab in patients with recurrent glioblastoma multiforme

<b>Submission date</b> 05/12/2014	Recruitment status No longer recruiting	<ul><li>Prospectively registered</li></ul>		
		☐ Protocol		
Registration date 13/02/2015	Overall study status Completed	<ul><li>Statistical analysis plan</li></ul>		
		[X] Results		
Last Edited	Condition category	Individual participant data		
23/03/2018	Cancer			

## Plain English summary of protocol

Not provided at time of registration and not expected to be available in the future

# **Contact information**

# Type(s)

Public

#### Contact name

Mrs Valérie Fautrier

#### Contact details

50 rue Carnot Suresnes France 92284

# Additional identifiers

# EudraCT/CTIS number

2013-003079-37

IRAS number

ClinicalTrials.gov number

# Secondary identifying numbers

CL1-49076-002

# Study information

## Scientific Title

Phase I/II study of S 49076, a multi-target inhibitor of c-MET, AXL, FGFR in combination with bevacizumab in patients with recurrent glioblastoma multiforme

## **Acronym**

N/A

## **Study objectives**

To evaluate the safety and efficacy of S 49076 in combination with bevacizumab in patients with recurrent glioblastoma multiforme (GBM). This is a phase I, dose-finding study of S 49076 in combination with bevacizumab followed by a randomised efficacy phase II study.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Ethics approval was obtained before recruitment of the first participants

## Study design

International multicenter open-label dose-finding and non-comparative efficacy study with one-way cross-over

# Primary study design

Interventional

## Secondary study design

Dose-finding study followed by a randomised efficacy 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

Glioblastoma multiforme

#### Interventions

Capsules containing 100 mg of S 49076 (oral use). The dose will be gradually escalated, following an algorithm-based 3+3 design, from level 1 at 400 mg/day to the MTD, with the possibility to deescalate. A panel of four doses of S49076 (300, 400, 500 and 600 mg) could be tested.

Solution for infusion of bevacizumab; each ml of concentrate contains 25 mg of bevacizumab. Bevacizumab will be administered on day 1 and 15 of each cycle, 28-days/cycle.

## Intervention Type

Drug

## **Phase**

Phase I/II

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

S49076

## Primary outcome measure

## Phase I:

- 1. Dose Limiting Toxicity and recommended phase II dose in combination of bevacisumab, at end of phase I part
- 2. Safety profile:
- 2.1. Adverse Events at each visit
- 2.2. Coagulation: within 7 days prior to the first test drug administration, D1 of each cycle and Withdrawal Visit (WV)
- 2.3. Physical and clinical neurological examination, vital signs, haematology, biochemistry and urinalysis: within 7 days prior to the first test drug administration, D1 and D15 of each cycle and WV
- 2.4. ECG parameters: within 7 days prior to the first test drug administration, D1, D2 and D15 of cycle 1, after D1 and D15 of each cycle and WV
- 2.5. LVEF assessment: at inclusion, on D28 every 2 cycles from cycle 1 and WV

#### Phase II:

1. Progression-free survival rate according to RANO (Response Assessment in Neuro-Oncology) criteria: at 6 months (PFS-6)

## Secondary outcome measures

#### Phase I:

- 1. Pharmacokinetic evaluation at D1, D2, D15 and D28 of cycle 1 and D1 of cycle 2
- 2. Pharmacodynamic evaluation at D1 of each cycle
- 3. Tumour response evaluation at within 14 days prior to the first test drug administration, D28 at each cycle and WV

## Phase II:

- 1. ORR, CBR, OS, progression-free survival, response duration, duration of clinical benefit: within 14 days prior to the first test drug administration, D28 at each cycle and WV
- 2. Safety tolerance profile of the combination:
- 2.1. AE: at each visit
- 2.2. Physical and clinical neurological examinations, vital signs, ECG, Haematology, Biochemistry and Urinalysis: within 7 days prior to the first test drug administration, D1 and D15 of each visit and WV
- 2.3. Activity profile in subgroup with c-Met amplification or mutation: within 14 days prior to the first test drug administration, D28 at each cycle and WV
- 2.4. Quality of life: within 14 days prior to the first test drug administration, D28 at each cycle and WV

## Overall study start date

10/03/2014

## Completion date

03/11/2016

# **Eligibility**

## Key inclusion criteria

- 1. Male or female patient aged > or = 18 years old
- 2. Histologically confirmed diagnosis of glioblastoma multiforme (WHO grade IV). Patients will be eligible if original histology was low-grade glioma and a subsequent diagnosis of glioblastoma was made
- 3. Unequivocal evidence of first progression/recurrence after standard treatment with combined chemo-irradiation (including a possible combination of temozolomide with an investigational agent) performed by MRI within 2 weeks before the first test drug administration
- 4. No more than one prior line of treatment
- 5. Patients must have measurable tumour disease as defined by RANO
- 6. Ability to swallow oral capsules

## Participant type(s)

Patient

## Age group

Adult

## Lower age limit

18 Years

#### Sex

Both

## Target number of participants

115

## Key exclusion criteria

- 1. Pregnant or breastfeeding women
- 2. Involvement in another therapeutic interventional trial at the same time or within 3 weeks prior to the first day of test drug administration
- 3. Major surgery (including craniotomy) within 4 weeks prior to the first day of test drug administration or minor surgical procedures (e.g., core biopsy or fine needle aspiration) within 14 days
- 4. Chemotherapy within 4 weeks (6 weeks for nitroso-ureas) prior to the first day of test drug administration
- 5. Radiotherapy within 3 months prior to the diagnosis of progression
- 6. Prior treatment with bevacizumab or other VEGF-receptor targeted agent
- 7. Prior treatment with a PI3K inhibitor, HGF or Met pathways for phase II part
- 8. Prior treatment with carmustine wafer
- 9. Impaired cardiac function

## Date of first enrolment

03/10/2014

## Date of final enrolment

04/06/2016

# Locations

## Countries of recruitment

France

Switzerland

## Study participating centre AP-HP Pitié-Salpêtrière

AP-HP Pitié-Salpētrière 47-83 Boulevard de l'Hôpital Paris France 75013

# Study participating centre

University Hospital of Lausanne (Centre Hospitalier Universitaire Vaudois)

Rue du Bugnon 46 Lausanne Switzerland 1011

# **Sponsor information**

## Organisation

Institut de Recherches Internationales Servier (France)

## Sponsor details

50 rue Carnot Suresnes France 92284

## Sponsor type

Industry

## Website

http://www.servier.com/

## ROR

https://ror.org/034e7c066

# Funder(s)

## Funder type

Industry

## **Funder Name**

**ADIR** 

# **Results and Publications**

## Publication and dissemination plan

Summary results and lay summary are published on www.clinicaltrials.servier.com.

## Intention to publish date

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from www.clinicaltrials.servier.com if a Marketing Authorisation has been granted after 1st January 2014.

## IPD sharing plan summary

Available on request

## **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
Basic results				No	No