A phase I, open-label, multi-center, dose escalation study of oral BGJ398, a pan FGF-R kinase inhibitor, in adult patients with advanced solid malignancies

Published: 06-11-2009
Last updated: 04-05-2024

Primary: To determine the maximum tolerated dose (MTD) and thus the recommended phase IIdose and schedule of single agent oral BGJ398 in patients with advanced solid tumors with FGFR1 or FGFR2 amplification or FGFR3 mutation.Secundary objectives* to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON45230

Source
ToetsingOnline

Brief title
A phase I study with BGJ398 (pan FGF-R inhibitor) in solid malignancies.

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Advanced and/or metastatic cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Financiering door de sponsor Novartis Pharma BV (farmaceutisch bedrijf)

Intervention

Keyword: BGJ398, pan FGF-R inhibitor, solid tumors, Urothelial carcinoma

Outcome measures

Primary outcome

Incidence rate and category of Dose Limiting Toxicities

Secondary outcome

* Efficacy arm 4: Overall response Rate assessed by RECIST

* Safety: (Serious) Adverse drug reactions, changes in hematology and chemistry values, specifically those associated with calcium/ phosphate homeostasis and renal function; and assessments of physical examinations, vital signs and electrocardiograms.

* PK: Time vs. concentration profiles, PK parameters of BGJ398 and known active metabolite(s).

* PD: Pre- vs. post treatment serial changes in FGF23 plasma levels.

* Efficacy: Rate of objective tumor response and PFS assessed by investigator per RECIST

Study description

Background summary

In 2002, 11 million new cancer cases and 7 million cancer deaths were estimated worldwide
(Parkin et al., 2005). Solid malignancies are the most commonly diagnosed and most
common causes of cancer death. Patients with advanced solid malignancies often have limited therapeutic options beyond institutional standard of care. For patients whose cancer has become refractory to all available treatments and who have no further treatment options, there is a significant unmet therapeutic need

Study objective

Primary: To determine the maximum tolerated dose (MTD) and thus the recommended phase II
dose and schedule of single agent oral BGJ398 in patients with advanced solid tumors with FGFR1 or FGFR2 amplification or FGFR3 mutation.

Secundary objectives
* to assess prelimanary anti-tumor activity of BGJ398 in expansion arm 4 in patients with UCC with FGFR3 alterations
* To characterize the safety and tolerability of oral BGJ398 at the recommended phase II dose
* To determine the pharmacokinetic profiles of oral BGJ398 including known pharmacologically active metabolites BHS697 and BQR917.
* To evaluate the effect of BGJ398 on FGF23 plasma level.
* To assess any preliminary anti-tumor activity of BGJ398.

Study design

The study has been designed as a Phase IA dose-escalation trial including a MTD dose expansion arm in patients with advanced solid tumors, in which oral BGJ398 will be administered once daily on a continuous schedule.
The initial dose level will be 5 mg /day. A minimum of 3 evaluable patients will be treated per dose level.
Before a drug dosage can be declared to be the MTD, at least 6 patients will have to be treated at this dose level for one at least 21 days. Once MTD has been declared, the MTD cohort will be expanded to enroll a total of appr.20 patients with lung SCC and appr. 20 patients with other advanced solid tumors.

Intervention

BGJ398 as an oral formulation available as hard gelatin capsules. MTD = 125 mg/dag
Dosing schedule: continous dosing (arm 1 and 2) or 3 weeks on 1 week off (arm 3 and 4)

Study burden and risks

The main side effects and observations seen in laboratory studies with BGJ398 or potential side effects concluded from laboratory tests include the following:
* Elevation of some electrolytes: Phosphorus and calcium which potentially can cause tissues calcifications in various body sites.
* Reduction of kidney function.
* Impaired intactness of the cornea
* Reproductive risks for both women and men. The risks to an unborn human fetus or a nursing child from BGJ398 are not known.

Taking blood and tumorbiopsies may cause pain, bleeding, and/or bruising.

Patients will be exposed to radiation (CT-scan and X-rays). The radiation exposure will not exceed the maximum ranges that are set within the Netherlands.

Ophthalmologic examinations: The patient will receive eyedrops in order to dilate (expand) the pupils. Some lightsensitivity may be experienced for a few hours after this examination. The dilating drops may also rarely cause increased pressure in the eye, leading to nausea and pain.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patients with histologically/cytologically confirmed advanced solid tumors with FGFR1 or FGFR2 amplification or FGFR3 mutation, for which no further effective standard anticancer treatment exits. Patients with advanced solid tumors carrying any FGFR mutation or amplification identified locally may be enrolled
2. Measurable or non-measurable disease, for arm 4 measurable disease
3. * 18 years of age.
4. WHO performance status 0-2.
5. Adequate bone marrow function:
6. Adequate hepatic and renal function:
7. Calcium-phosphate homeostasis:
* Normal serum inorganic phosphorus (Pi).
* Normal serum total (t) and ionized (i) calcium (Ca).
8. Adequate cardiovascular function
* NYHA grade * 2.
* Ejection fraction * 50%.
* QTc interval * 470 msec.
* BP systolic in rest * 100 mmHg and * 150 mmHg.
* BP diastolic in rest * 100 mmHg.
* Heart rate in rest > 50/min and < 100/min.
9. Recovery from all adverse events of previous systemic anti-cancer therapies to Grade * 1 except for alopecia and stable neuropathy of Grade *2 which was induced by prior cancer treatment.
10. Contraception:
* Women of childbearing potential and men must use adequate contraceptive regimen during and for 3 months after the treatment period; women must have a negative pregnancy test and must not be nursing.
* For men must use adequate contraceptive regimen during and for 3 months after the treatment period.

Exclusion criteria

1. Prior treatment with FGFR-inhibitor or MEK-inhibitor with the exception of prior treatment with TKI258.
2. Patients with primary CNS tumor or CNS tumor involvement.
3. Patients with history and/or current evidence of endocrine alteration of calcium/phosphate homeostasis
4. History and/or current evidence of ectopic mineralization/ calcification with the exception of calcified lymphnodes and asymptomatic coronary calcification.
5. Current evidence of corneal disorder/ keratopathy
6. Concomitant therapies that are known to prolong the QT interval and/or are associated with a risk of Torsades de Pointes < 7 days before the first dose; however amiodarone is not permitted <90 days before the first dose.
7. Medication or supplements to increase serum levels of phosphorus and/or calcium levels within 28 days before the first dose.
8. Active or unstable cardio/cerebro-vascular disease.
9. History or current evidence of cardiac arrhythmia and/or conduction abnormality CTCAE Grade * 1.
10. History of congenital long QT- syndrome and/or hypokalaemia CTCAE Grade * 3.
11. Chest x-ray/CT with evidence of lung calcifications with the exception of calcified

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-12-2009
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet van toepassing
Generic name:	Nog niet van toepassing

Ethics review

Approved WMO Date:	06-11-2009
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-12-2009
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-08-2010
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-12-2010
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-07-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-08-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	15-12-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-04-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-11-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-01-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-02-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	07-05-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-11-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	05-12-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-01-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-05-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-06-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-09-2014

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-10-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-04-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-07-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-06-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-02-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-010876-73-NL
ClinicalTrials.gov	NCT01004224

Register	ID
CCMO	NL29778.031.09