A Phase 1/2, Ascending Multiple-Dose Study to Evaluate the Safety, Efficacy and Pharmacokinetics of BMS-753493 in Subject with Advanced Cancer

Published: 25-01-2008
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To determine the maximum tolerated dose, dose limiting toxicity and recommended Phase 2 dose of BMS-753493 in subjects with advanced cancer.

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

Summary

ID

NL-OMON33965

Source
ToetsingOnline

Brief title
CA190-001

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
advanced cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb

Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: BMS-753493, Cancer, Phase 1/2

Outcome measures

Primary outcome

The primary outcome measure is to evaluate the safety of BMS-753493 by determining maximum tolerated dose, any dose limiting toxicities, and the recommended Phase II dose.

Secondary outcome

The secondary outcome measures are to describe the overall safety profile of BMS-7535493, to measure the levels of drug in the blood at various times (pharmacokinetics), to evaluate impact of BMS-753493 on heart rhythm, and to describe any preliminary evidence of anti-tumor activity of BMS-753493.

Study description

Background summary

BMS-753493 is a a folate-receptor targeted epothilone and it is hoped its anti-neoplastic properties will selectively target tumour cells that over-express folate receptors. This study will explore the use of BMS-753493 in humans for the first time.

Study objective

To determine the maximum tolerated dose, dose limiting toxicity and recommended Phase 2 dose of BMS-753493 in subjects with advanced cancer.

Study design

This is an open-label study of BMS-753493. Subjects will progress through the following periods of the study:

* Screening period: lasting up to 28 days
* Treatment period: Patients will receive BMS-753493 infusions in 21 day treatment cycles and undergo a variety of procedures to monitor the safety and efficacy of BMS-753493.
* End of Treatment visit and follow-up visits every 30 days until all study related toxicities resolve to baseline, stabilise or are deemed irreversible.

This is a dose-escalation study with a starting dose of 5mg. Groups of 3 - 6 subjects will receive increasing doses of BMS-753493 until the maximum tolerated dose and recommended dose for Phase 2 is established.

Subjects will also be asked to consider taking part in an optional sub-study (amendment 1). This involves the collection of one blood sample for pharmacogenetic analysis.

Intervention

Administration of BMS-753493 as a 3 to 5 minute bolus intravenous infusion on Days 1, 4, 8 and 11 of every 21 day cycle until disease progression or unacceptable toxicity occurs.

Study burden and risks

There is a possibility that BMS*753493 may be an effective treatment for some types of cancer. However, it is not known if individual patients entering the trial will benefit directly. The information gained from this study may help future patients with advanced cancer. Patients will have the inconvenience of more frequent interventions/procedures and longer visits to the hospital than would be usual for routine clinical care. They will also have to undergo additional procedures. As this is the first time BMS-753493 has been given to humans, the potential side effects are unknown. A list of potential side is included in the informed consent document. Additional unforeseen side effects could occur and some side effects could be life-threatening or fatal. Robust safety monitoring in included throughout the protocol. At all times throughout the study, the patient has the right to withdraw consent without their usual standard of care being affected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Histologically or cytologically confirmed diagnosis of solid tumour which has progressed on standard therapy or for whom no standard therapy is known - Minimum of 10 archived tumour tissue slides required, or subject*s willingness and ability to undergo tumour biopsy collection for IHC analysis
• Measurable or non-measurable disease
• Men and women, aged 18 or greater
• ECOG performance status 0*1 (generally fit and mobile)
• Adequate recovery from recent surgery and radiation therapy - one week for minor surgery and 3 weeks for major surgery and radiation therapy
• At least four weeks since last dose of carboplatin, immunotherapy or chemotherapy, (six weeks for nitrosoureas, or mitomycin C), prior to beginning protocol therapy. Hormonal anti*cancer agents and nontraditional cytotoxic agents, such as trastuzumab, gefitinib, erlotinib, cetuximab, bevacizumab, are not considered chemotherapy regimens when administered alone, and at least 4 weeks must have elapsed from the last dose of this class of agents before study drug administration.
• Subjects must have recovered to baseline or Grade 1 from the toxicities resulting from previous therapies.
• Women of child-bearing potential must be using an adequate method of contraception to avoid pregnancy throughout and for 4 weeks after the study.

Exclusion criteria

• Symptomatic brain metastases or sign or symptoms suggestive of them.
• Current grade 2 motor or sensory Neuropathy or a prior history of grade 3 or greater neuropathy.
• Uncontrolled or significant cardiovascular disease: Myocardial Infarction within 6 months; uncontrolled angina or conjestive heart failure within 3 months; history of significant arrhythmias; any QT problems;
pacemaker; 2nd degree AV block or any form of bundle branch block; troponin (T or I) above upper limit of normal; left ventricular ejection fraction lower than limit of normal as determined by MUGA or echocardiogram; inadequate cardiac function as defined by a New York Heart Association (NYHA) classification of > Class I
• Inadequate blood results: haem/hepatic/renal/thyroid function
• Known methylenetetrahydrofolate reductase (MTHFR) mutations or known impaired regulation of homocysteine levels
• Uncontrolled thyroid disorder, including hypo and hyper*thyroidism, Grave*s disease or Hashimoto*s disease. Subjects with hypothyroidism who are on thyroid replacement therapy and whose symptoms of thyroiditis are resolved to Grade 1 before enrollment are eligible
• Inadequate haematological, hepatic, renal or thyroid function.
• Use of multi*vitamins and/or folic acid supplements for 1 week prior to first day of treatment and throughout the course of the trial
• Use of steroids except for anti*emetic purposes and/or continuing therapy for controlled brain metastases, chronic steroid use if required for disease, appetite stimulation, treatment of hypersensitivity reactions and for prevention of same, premedication prior to CT scan requiring IV contrast in subjects with IV contrast allergy
• Use of known P-glycoprotein inhibitors for 1 week prior to first day of treatment and throughout the course of the trial
• Inability to provide an archived tumour sample (10 slides) for analysis within 28 days of study drug Administration
• Women of child-bearing potential who are unwilling or unable to use an acceptable method of contraception.
• Sexually active fertile men not using effective birth control if their partners are of child-bearing potential.
• Women who are pregnant or breastfeeding.
• Exposure to any investigational drug or placebo within 4 weeks of study drug administration.
• Other concurrent anti-cancer therapy
• Prior radiation including more than 25% of major bone marrow containing areas

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):	28-04-2008
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	geen
Generic name:	epothilone folate

Ethics review

Approved WMO Date:	25-01-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	11-04-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	10-06-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	25-06-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-07-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-07-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-09-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-09-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-10-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-11-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	13-08-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2007-001432-31-NL
ClinicalTrials.gov	NCT-00546247
CCMO	NL20776.078.07