A Phase 1 Study of Combination Therapy with SAR405838 and Pimasertib in Patients with Advanced Cancer

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

Summary

ID

NL-OMON40404

Source
ToetsingOnline

Brief title
TCD13388

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
advanced cancer

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Advanced cancer, Combination therapy, Phase 1, Safety

Outcome measures

Primary outcome

* SAR405838 / pimasertib MTD (Maximum Tolerated Dose) and RP2D (Recommended Phase 2 Dose) as assessed by DLT (dose-limiting toxicity) and the biological acitivities within the tested dose range.

* In RP2D cohort expansion, tumor response and duration, as defined by RECIST 1.1.

Secondary outcome

* Overall safety profile of SAR405838 / Pimasertib (adverse events)

* PK parameters (Cmax, Tmax, AUC)

* PD biomarkers (MIC-1, IL-8, pERK, PBMC)

* In dose escalation phase, tumor response and duration.

* Genetic status of TP53/Ras in tumor tissue and ctDNA at baseline and post study drug treatment

Study description

Background summary

SAR405838 is a new anti-cancer study drug that may stop the growth of cancer by causing cancer cell death or blocking cancer cell division. SAR405838 has only shown its ability to slow or stop tumor growth or shrink tumor mass when tested in animals models. Its efficacy in humans is currently unknown.

Pimasertib has only shown its ability to slow or stop timor growth or shrink tumor mass when tested in animal models. Its efficacy in humans is currently being confirmed.

This research study is the first combination use of SAR405838 and pimasertib in the treatment of patients.

Study objective

The main purpose of the study is to evaluate the safety and tolerability (any toxicities and side effects) of SAR405838 and Pimasertib and that includes identifying the maximum safe and tolerable dose of the study drugs. Also to assess the anti-tumor activities of SAR405838/ Pimasertib in patients with advanced/ metastatic melanoma, non-small cell lung cancer (NSCLC), and colorectal cancer (CRC) based on TP53 and Ras data in tumor tissue in cohort expansion.

Other objectives of this study include evaluations of pharmacokinetics (PK) and pharmacodynamics (PD). Also the anti-tumor acitvity in response to SAR405838/Pimasertib will be investigated. In addition, TP53/Ras genetic status in tumor tissue and tumor DNA (ctDNA) derived from plasma, both at baseline and in response to SAR405838/ Pimasertib treatment.

Study design

This is a multicenter study being conducted in the Netherlands, France and United States. It is an open-label study.

Approximately 94 patients will take part in the study in dose finding and expansion phase.
The study consists of 3 parts:
* screening
* study treatment
* follow-up visit

The total duration of participation in the study will be approximately 14 to 30 weeks.

Intervention

SAR405838 will be taken at various doses orally once daily. Pimasertib will be taken at various doses orally twice daily.

Study burden and risks

Risks are related to blood sampling and possible side effects of the study drugs. The burden for the patient will be the number of visits to the research site as part of the trial.

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 a solid tumor;
Presence of locally advanced or metastatic disease with at least one measurable lesion that is not responsive to standard therapies or for which no approved or curative therapy is available.
Ability to provide written informed consent. Evidence of a personally signed informed consent;

Exclusion criteria

Age < 18 years;
Eastern Cooperative Oncology Group performance status > 1;

Inadequate functions of bone marrow, liver, and kidney;
Positive pregnancy test in women of child-bearing potential;
Pregnancy or breast-feeding;
Extensive prior radiotherapy;
The patient has retinal degenerative disease, history of uveitis, or history of retinal vein occlusion, or history of retinal detachment, or has medically relevant abnormalities identified on screening ophthalmologic examination;
Prior history of myositis or rhabdomyolysis;
Recent major surgery or trauma, unhealing/open wounds;
The patient has had congestive heart failure, unstable angina, a myocardial infarction, cardiac conduction abnormality or pacemaker or a stroke within 3 months of entering the study;
The patient has a baseline corrected QT interval (QTc) > 480 ms or left ventricular ejection fraction (LVEF) < 50% or less than the lower limit of normal;
The patient has a previously-identified allergy or hypersensitivity to components of the study treatment formulations;
Unwillingness or inability to comply with scheduled visits, drug administration plan, laboratory tests, other study procedures, and study restrictions;
Unwillingness, if not postmenopausal or surgically sterile, to abstain from sexual intercourse or employ an effective barrier or medical method of contraception during the study drug administration and follow-up periods;
Recent history of acute pancreatitis;
Clinically significant illness, medical condition, surgical history, physical finding, or laboratory abnormality that could affect the safety of the patient; alter the absorption of the study drugs; or impair the assessment of study results;

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):	06-11-2013
Enrollment:	42

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet bekend
Generic name:	Pimasertib

Ethics review

Approved WMO Date:	31-07-2013
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	05-11-2013
Application type:	First submission
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:	29-11-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-08-2014
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	01-09-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-06-2015
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	EUCTR2013-002325-33-NL
ClinicalTrials.gov	NCT01985191
CCMO	NL45409.031.13