A randomized, open-label, multi-center phase II study to compare AUY922 with docetaxel or irinotecan in adult patients with advanced gastric cancer, who have progressed after one line of chemotherapy

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Primary objective: * To assess the treatment effect on progression-free survival in patients who receive AUY922 on a once-weekly schedule versus patients who receive docetaxel or irinotecanSecondary Objectives* To estimate the overall survival...

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

Summary

ID

NL-OMON34887

Source
ToetsingOnline

Brief title
Compare AUY922 with docetaxel or irinotecan in gastric cancer

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
Advanced gastric cancer

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis

Intervention

Keyword: advanced gastric cancer, AUY922, docetaxel or irinotecan, HSP90 inhibitor

Outcome measures

Primary outcome

Primary endpoint

* Progression-free survival (PFS).

Progression-free survival (PFS) is the time from the date of randomization to the date of event defined as the first documented progression or death due to any cause. If a patient has not had an event, PFS is censored at the date of last tumor assessment

Secondary outcome

Secondary endpoints

* Efficacy: Overall survival and Objective response rate

* Safety: Incidence of adverse drug reactions and serious adverse drug reactions as assessed by CTCAE Version 4.0

* PK: Exposure of AUY922 and parameters: e.g. Cmax, and Ctrough

* Biomarkers: Temporal and magnitude changes in blood and tissue marker levels

Study description

Background summary

Gastric cancer is one of the most common cancer globally, and the second leading cause of cancer death, accounting for 866,000 deaths in 2007 (World Health Organization 2008). Gastric cancer remains a difficult-to-cure disease. Even after curative gastrectomy, 40%-60% patients will develop advanced disease with local and/or distant recurrences. Because the disease is asymptomatic in early stages, more patients are diagnosed at an advanced stage either with unresectable, locally advanced or metastatic disease (approximately 84%). Prognosis after first-line treatment for advanced gastric cancer is still very poor. There is no widely accepted standard, or approved second-line treatment. New drugs with novel mechanisms of action may bring more significant benefits to advanced gastric cancer patients in the second-line setting.

AUY922 is an isoxazole-based compound which competitively inhibits the ATPase activity of heat shock protein 90. (Hsp90). Heat shock proteins (HSP) are molecular chaperones that assist in the structural formation and folding of a wide variety of client proteins including a broad panel of critical signaling proteins and oncoproteins.
Pre-clinical experiments have demonstrated that AUY922 inhibits proliferation of gastric cancer cells.

Study objective

Primary objective:
* To assess the treatment effect on progression-free survival in patients who receive AUY922 on a once-weekly schedule versus patients who receive docetaxel or irinotecan

Secondary Objectives
* To estimate the overall survival treatment effect

Additional Secondary Objectives
* To estimate the objective response rate
* To evaluate safety and tolerability
* Pharmacokinetics of AUY922
* To investigate the pharmacodynamic effect of AUY922 on HSP90 client proteins in tumor tissue and blood
* To investigate cellular anti-tumor activity of AUY922 in tumor tissue and blood

Study design

A randomized, open-label, multi-center phase lla trial in approximately 120 patients. Randomization will be on a 1:1 ratio.
Sixty (60) patients will receive AUY922 and 60 patients will receive either docetaxel or irinotecan.

Intervention

AUY922
AUY922 will be administered via IV once weekly . The dose to be administered will be 70 mg/m2.

Docetaxel
Docetaxel will be administered via IV once every 3 weeks. The dose to be administered will be 75 mg/m .

Irinotecan
Irinotecan will be administered via IV once every 3 weeks. The dose to be administered will be 350 mg/m2.

Study burden and risks

Possible risks and side effects of AUY922 or docetaxel or irinotecan.
The main sie effects seen from use of the study drug treatments include skin irritation at the side of the infusion, diarrhea, nausea and vomiting, decrease in the number of white blood cells, decrease in the number of red blood cells, abnormal heart rhythms.
For AUYy922 vision changes may occur (reversible).

Risks and inconveniences due to blood draw.
Some discomfort due to eye examinations (some irritation in the eye).
The risks of a tumorbiopsy are related of the site where the tumor biopsy is taken.
Additional radiation load due to CT-scans and PET-scans. The additional radiotion load is 4-6 mSv (FDG-PETscan) * 3.5 mSv (MUGA scan) en 8 mSv (CTscan).

Contacts

Public
Novartis

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NL

Scientific
Novartis

Raapopseweg 1
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients with cytological or histological confirmed gastric adenocarcinoma or gastroesophageal junction adenocarcinoma.
- Patients with progressive disease (radiological confirmed) after one line of chemotherapy for advanced gastric cancer.
- At least one measurable lesion as defined by RECIST.
- Patients who meet the following criteria will be eligible for PET assessments:
o At least one lesion must be measurable (>2cm)
o Able to lie still and flat on the PET table.
- WHO Performance Status of < 1
- Life expectancy of > 12 weeks
- Patients must have the following laboratory values:
o Absolute Neutrophil Count *1.5x109/L
o Hemoglobin * 9 g/dl <= 5.58 mmol/l
o Platelets *100x109/L
o Potassium, total calcium (corrected for serum albumin) and phosphorus within normal limits
o Magnesium above LLN
o Adequate liver function defined as:
AST/SGOT and ALT/SGPT * 1.5 x Upper Limit of Normal if Alkaline Phosphatase > 2.5 ULN or AST/SGOT and ALT/SGPT * 2.5 x Upper Limit of Normal (ULN) if Alkaline Phopaphatse * 5.0 x ULN if liver metastases are present
o Serum bilirubin * 1.5 x ULN

o Serum creatinine * 1.5 x ULN or 24-hour clearance * 50 ml/min.
o Negative serum pregnancy test.

Exclusion criteria

- Patients with CNS metastasis which are symptomatic or require treatment for symptom control and/or gowing.
- Prior treatment with any HSP90 or HDAC inhibitor
- Systemic anti-cancer treatment prior to the first dose of studymedication within the following timeframes:
o Radiotherapy, conventional chemotherapy and monoclonal antibodies, such as trastuzumab: within 4 weeks
o Palliative radiotherapy: within 2 weeks
o Nitrosoureas, mitomycin: within 6 weeks
o Any continuous-dosing of systemic anti-cancer therapiefor which the recovery period is not known, or investigational drugs within a duration of * 5 half lives of the agent and their active metabolites (if any)
- Treatment with therapeutic doses of coumarin-type anticoagulants. Maximum daily dose of 2mg allowed.
- Known sensitivity to taxanes, drugs formulated with polusorbate 80 or patients with Acute Myeloid Leukemia.
- Concomitant use of agents that induce, inhibit or are metabolized by CYP3A4, neuromuscular blocking agenst and Atazanavir sulfate.
- Unresolved diarrhea * CTCAE grade 1
- Patients with malignant ascites that requires invasive treatment.
- No archival tumor sample available or unwilling to have a fresh tumor sample collected at baseline.
- Acute or chronic liver or renal disease.
- Other concurrent severe and/or uncontrolled medical conditions that could cause unacceptable safety risks or compromise compliance with the protocol.
- Impaired cardiac function, including any one of the following:
o History (or family history) of long QT syndrome.
o QTc * 450 msec on screening ECG.
o Clinically manifested ischemic heart disease * 6 months prior to study start.
o History of heart failure or left ventricular (LV) dysfunction (LVEF * 45%) by MUGA or ECHO.
o Clinically significant ECG abnormalities.
o History or presence of atrial fibrillation, atrial flutter or ventricular arrhythmias including ventricular tachycardia or Torsades de Pointes.
o Other clinically significant heart disease (e.g congestive heart failure, uncontrolled hypertension)
o Clinically significant resting bradycardia (< 50 beats per minute).
o Treatment with any medication which has a relative risk of prolonging the QTcF interval or inducing Torsades de Pointes.
o Cardiac pacemaker
- Known diagnosis of HIV infection

- history of another primary malignancy that is currently clinically significant or currently requires active intervention.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-12-2010
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Irinotecan, campto
Generic name:	CPT-11
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Nog niet beschikbaar
Generic name:	Nog niet beschikbaar
Product type:	Medicine
Brand name:	Taxotere®
Generic name:	Docetaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-03-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-10-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-09-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-10-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2011

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2009-015407-47-NL
CCMO	NL30760.042.10