A multicenter, open-label, randomized phase II study to evaluate the efficacy of AUY922 vs pemetrexed or docetaxel in NSCLC patients with EGFR mutations who have progressed on prior EGFR TKI treatment (CAUY922A2207)

Published: 11-09-2012
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Primary: Progression Free Survival (PFS) in patients treated with AUY922 versus pemetrexed or docetaxel.Secondary: Overall response rate, disease control rate, overall survival, safety and tolerability, PK.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON39976

Source
ToetsingOnline

Brief title
CAUY922A2207

Condition

- Respiratory tract neoplasms

Synonym
lung cancer, non-small cell lung cancer

Research involving

Human

Sponsors and support

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

Intervention

Keyword: AUY922, EGFR TKI, HSP90, NSCLC

Outcome measures

Primary outcome

Progression free survival.

Secondary outcome

Overall response rate, disease control rate, overall survival, toxicity, PK.

Study description

Background summary

Lung cancer is the leading cause of cancer deaths in the US with 215.000 new cases and 160.000 deaths in 2008. Non-small cell lung cancer (NSCLC) accounts for roughly 85% of all lung cancer cases. Epidermal growth factor receptors (EGFR) have been shown to be over-expressed in an approximately 40 to 90% of NSCLC patients. Recent development of targeted agents such as EGFR tyrosine kinase inhibitors erlotinib and gefitinib have opened up new treatment options in NSCLC. However, a large majority of NSCLC patients, including patients with certain KRAS mutations, and a constitutively active PI3K/AKT pathway, and even some mutations in EGFR, are insensitive to targeted therapy, necessitating development of newer agents. Heat shock protein 90 (HSP90) is an ATP-dependent molecular chaperone that assists in the structural folding and stabilization of a wide range of cellular proteins including IGF-1R, EGFR, AKT, and RAS. AUY922, an isoxazole, is one of the most potent non-geldanamycin HSP90 inhibitors currently under clinical development. AUY922 exerts its activity by binding to the ATP-ase domain of the HSP90 N-terminus preventing HSP90 from forming the closed conformation, and performing its functions on client proteins.
Pre-clinical studies have shown AUY922 to be active in a wide range of NSCLC cell lines, including cell lines with EGFR and K-ras mutations. As a majority of the oncogenic proteins involved in NSCLC proliferation such as IGFR-1,

c-Met, KRAS and EGFR are HSP90 client proteins AUY922 treatment may have significant therapeutic potential in patients with advanced NSCLC.
The purpose of this phase II trial is to evaluate the safety and efficacy of treatment with AUY922 in comparison with pemetrexed and docetaxel in NSCLC patients who progressed on prior EGFR-TKI treatment.

Study objective

Primary: Progression Free Survival (PFS) in patients treated with AUY922 versus pemetrexed or docetaxel.
Secondary: Overall response rate, disease control rate, overall survival, safety and tolerability, PK.

Study design

Multicenter randomized open-label placebo controlled parallel group phase II study.
Randomization (1:1) to treatment with:
* AUY922 IV infusion 70 mg/m2 of 1 h every week
* Pemetrexed IV infusion 500 mg/m2 of 1 h every 3 weeks or docetaxel IV infusion 75 mg/m2 of 1 h every 3 weeks . The investigator will make the choice between pemetrexed and docetaxel on a patient by patient basis.
Treatment until progression or unacceptable toxicity.
108 patients.

Intervention

Treatment with AUY922, docetaxel or pemetrexed.

Study burden and risks

Risk: Adverse events of study medication.
Burden: Study duration in principle until disease progression. Thereafter follow-up for survival. AUY-group: weekly visits (course 1: 5 visits), control group every 3 weeks.
I.v. infusions weekly (AUY, 500 ml in 1 h) or every 3 weeks (control group, 500 ml in 1 h).
Physical examination day 1 of every course.
Blood draws screening approx. 40 ml, every course 25 ml, final visit 20 ml.
Pregnancy test at screening.
ECG every visit (AUY) of at start and end.
Echocardiography or MUGA-scan start and end.
Tumor evaluations conform regular treatment.
Eye examination in AUY group 3 times.
Tumor biopsy at screening (if no archived tumor material available).
Optional tumor biopsy at the end of treatment.

Optional donation of left-over tumor tissue for future testing.

Contacts

Public
Novartis

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* 18 years and above.
* Histologically or cytologically documented stage IIIB or IV NSCLC.
* EGFR gene mutation in the tumor.
* Documented clinical benefit (CR, PR, or SD for *6 months) on prior EGFR TKI followed by documented progression.
* Patients must have received platinum based prior treatment.
* WHO performance status 0-1.
* Measurable disease.

Exclusion criteria

* More than two prior lines of antineoplastic therapy for advanced disease.
* Evidence of CNS involvement. Brain CT/MRI mandatory. Note: treated and stable CNS metastasis allowed.
* Radiation therapy for management of local disease within four weeks (RT for palliative pain management is allowed).
* Prior treatment with an HSP90 inhibitor.
* Impaired cardiac function (see protocol page 34 for details).
* Women of childbearing potential not using adequate contraception, pregnancy, lactation.
* Sexually active men not using adequate contraception.

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):	28-01-2013
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	pemetrexed
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	AUY922
Generic name:	AUY922
Product type:	Medicine
Brand name:	Taxotere
Generic name:	docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-09-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-11-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-02-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	12-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-07-2014
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
Other	clinicaltrials.gov, registratienummer NCT01646125
EudraCT	EUCTR2012-001050-25-NL
CCMO	NL41751.042.12