Randomized Phase 3 Trial of Gemcitabine/Carboplatin With or Without Iniparib (SAR240550) (a PARP1 Inhibitor) in Subjects with Previously Untreated Stage IV Squamous Non Small Cell Lung Cancer (NSCLC)

Published: 09-08-2010
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON39236

Source
ToetsingOnline

Brief title
Gemcitabine/Carboplatin With or Without Iniparib in subjects with NSCLC.

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non small cell lungcarcinoma/lungcancer

Research involving

Human

Sponsors and support

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

Intervention

Keyword: disease progress, Non-small cell lung cancer, PARP1 inhibitor

Outcome measures

Primary outcome

To evaluate the overall survival (OS) of patients with stage IV squamous NSCLC

receiving gemcitabine/carboplatin either with or without iniparib.

Secondary outcome

· Progression free survival (PFS)

· Time to progression (TTP)

· Objective response rate (ORR)

· Safety and tolerability of the treatment regimen

· Quality of life as measured by EORTC QLQ-30 and QLQ-LC13

Study description

Background summary

Non-small cell lung cancer (NSCLC) accounts for approximately 80% of these cancer cases.
The majority of these cases present with unresectable locally advanced (stage IIIB) or metastatic
disease (stage IV) at diagnosis. Patients with advanced disease rarely survive 5 years, and over
half die within the first year of diagnosis. Combination chemotherapy can extend survival,
palliate symptoms of progressive disease, and improve the quality of life in

patients with
advanced disease. Doublet chemotherapy regimens are considered standard front-line treatment
for advanced disease. Randomized trials using modern doublet regimens have reported median
overall survivals (OS) of 8 to 10 months (Kelly et al. 2001; Schiller et al. 2002; Scagliotti et al.
2002; Smit et al. 2003; Alberola et al. 2003; Gronberg et al. 2009).

Study objective

The purpose of this study is to find out if the combination of gemcitabine plus carboplatin and iniparib works better than gemcitabine and carboplatin alone in subjects with stage IV squamous non-small-cell lung cancer (NSCLC) that have not previously been treated.

Study design

Patients will be randomized in a 1:1 fashion to receive either
gemcitabine/carboplatin with iniparib (Arm A) or
gemcitabine/carboplatin alone (Arm B).

See page 25 of the study protocol

Intervention

The study treatment schedules for group A and B are different, as decribed below

Group A:

• Gemcitabine on day 1 and 8
• Carboplatine on day 1
• iniparib on day 1, 4, 8 and 11

Group B:

• Gemcitabine on day 1 and 8
• Carboplatine on day 1

Study burden and risks

This is decribed in the patient information and consent form

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

1. Newly diagnosed, stage IV squamous NSCLC. This includes patients who present with disseminated metastases, and those with a malignant pleural or pericardial effusion (i.e., formerly stage IIIB in the 6th TNM staging system).
2. Patients who have received prior adjuvant therapy for early-stage lung cancer are eligible if at least 12 months have elapsed from that treatment.
3. Histologically confirmed squamous cell bronchogenic carcinoma. Patients whose tumors have mixed non-small cell histologies are eligible, as long as squamous carcinoma is the predominant histology. Mixed tumors with small cell anaplastic elements are not eligible. Cytologic specimens obtained by brushings, washings, or needle aspiration of the defined lesion are acceptable.
4. Patients with previous thoracic radiotherapy as definitive therapy for locally advanced nonsmall

cell lung cancer are eligible, as long as the recurrence is outside the original radiation therapy port. Radiation therapy must have been completed >4 weeks prior to the initiation of study treatment.
5. Presence of evaluable (measureable or non-measureable) disease.
6. ECOG Performance Status of 0 or 1 (see Appendix A).
7. Laboratory values as follows:
· Absolute neutrophil count (ANC) >=1,500/mL and platelet count >=100,000/mL (<=72 hours prior to initial treatment)
· Hemoglobin >9 g/dL (Note: patients may be transfused or receive erythropoietin to maintain or exceed this level).
· Bilirubin < ULN.
· Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <=2.5 times the upper limit of normal if no liver involvement or <=5 times the upper limit of normal with liver involvement.
· Creatinine <=2.0 mg/dL, or creatinine clearance >=40 mL/min (as calculated by the Cockcroft-Gault method (see Section 8.3.3). Calculated creatinine clearance will be used to calculate carboplatin dose.
8. Women of childbearing potential must have a negative serum pregnancy test performed within 7 days prior to start of treatment. Women of childbearing potential or men with partners of childbearing potential must use effective birth control measures during treatment, and at least 6 months after the last dose of study treatment. If a woman becomes pregnant or suspects she is pregnant while participating in this study, she must agree to inform her treating physician immediately. Sexually active men must agree to use a medically acceptable form of birth control during treatment and at least 6 months after the last dose. If a female partner becomes pregnant during the course of study the treating physician should be informed immediately.
9. 18 years of age or older.
10. Ability to understand the nature of this study, give written informed consent, and comply with study requirements.
11. Patients entering this study must be willing to provide tissue from a previous tumor biopsy (if available) for correlative testing. If tissue is not available/accessible, a patient will still be eligible for enrollment into the study.

Exclusion criteria

1. Prior treatment with gemcitabine, carboplatin (except in the adjuvant setting), or BSI-201.
2. Past or current history of neoplasm other than the entry diagnosis, with the exception of t1) reated non-melanoma skin cancer, 2) treated non-invasive or in-situ carcinoma of any primary site or 3) invasive cancers treated definitively, with treatment ending >5 years previously and no evidence of recurrence.
3. A history of active cardiac disease, within the previous 6 months, including any of the following:
· Malignant hypertension;

· Unstable angina;
· Congestive heart failure;
· Myocardial infarction within the previous 6 months;
· Symptomatic unstable or uncontrolled cardiac arrhythmias.
4. Active brain metastases. Patients with treated brain metastases are eligible if (1) radiation therapy was completed at least 2 weeks prior to study treatment; (2) followup scan shows no disease progression; (3) patient does not require steroids.
5. Women who are pregnant or lactating.
6. Any serious, active infection (> grade 2) at the time of treatment.
7. A serious underlying medical condition that would impair the ability of the patient to receive protocol treatment.
8. A major surgical procedure, or significant traumatic injury -28 days of beginning treatment, or anticipation of the need for major surgery during the course of the study.
9. Uncontrolled or intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, or cardiac arrhythmia.
10. History of any medical or psychiatric condition or laboratory abnormality that, in the opinion of the investigator, may increase the risks associated with the study participation or administration of the investigational products, or that may interfere with the interpretation of the results.
11. Known or suspected allergy/hypersensitivity to any agent given in the course of this trial.
12. Use of any non-approved or investigational agent <=30 days prior to administration of the first dose of study drug. Patients may not receive any other investigational or anti-cancer treatments while participating in this study

Study design

Design

Study phase:	3
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):	03-05-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	/
Generic name:	iniparib
Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gemcitabine
Generic name:	Gemcitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-08-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-09-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-11-2010
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-04-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	19-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-02-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-02-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-08-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2010-019255-22-NL
CCMO	NL32530.060.10