A Phase 1b/2 Trial of AMG 479 or AMG 102 in Combination with Platinum-based Chemotherapy as First-Line Treatment for Extensive Stage Small Cell Lung Cancer

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Primary Objective:Part 1: To identify a dose of AMG 479 in combination with etoposide plus carboplatin and/or etoposide plus cisplatin, and of AMG 102 in combination with etoposide plus carboplatin and/or etoposide plus cisplatin that can be...

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

Summary

ID

NL-OMON33131

Source
ToetsingOnline

Brief title
First-Line Treatment for Extensive Stage Small Cell Lung Cancer

Condition

- Respiratory tract neoplasms

Synonym
extensive stage Lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Extensive Stage Small Cell Lung Cancer, First- Line Treatment, previously untreated

Outcome measures

Primary outcome

Primary Endpoints

Part 1: * The incidence of adverse events and clinical laboratory abnormalities

defined as DLT

Part 2: * OS

Secondary outcome

Secondary Endpoints

Part 1:

- The incidence of adverse events and laboratory abnormalities not defined as

DLT

- The incidence of anti-AMG 479 and anti-AMG 102 antibody formation

- PK (Cmax and Cmin for AMG 479 and AMG 102)

Part 2:

- ORR, DOR, TTP, PFS, mOS, and OS rates at 10,12, 24, and 36 months

- The incidence of adverse events and laboratory abnormalities

- The incidence of anti-AMG 479 and anti-AMG 102 antibody formation

- PK (Cmax and Cmin) for AMG 479 and AMG 102

- EORTC QLQ-C30 and EORTC QLQ-LC13 scores

Study description

Background summary

Lung cancer is the leading cause of cancer-related mortality in the developed world, accounting for over 1,000,000 deaths each year globally (Parkin, Bray et al. 2005). Small cell lung cancer represents approximately 10 to 30% of all new lung cancer cases (DeVita, Hellman et al. 2005), with incidence rates declining among men but continuing to increase among women in most regions (Devesa, Bray et al. 2005). About 77,000 of the 550,000 new cases (14 %) of lung cancer diagnosed in 2004 in the United States and Europe were classified as having small cell histology. These tumors are characterized by rapid growth kinetics, early dissemination to regional lymph nodes and distant sites, and sensitivity to radiotherapy and chemotherapy (Pass 2005).
The treatment of subjects with SCLC is dependent on disease extent: limited or extensive stage disease. Limited disease includes tumors confined to one hemithorax, with or without regional lymph node metastases, including hilar, ipsilateral and contralateral mediastinal, and ipsilateral and contralateral supraclavicular lymph nodes (Stahel, Ginsberg et al. 1989), which can be safely encompassed within a tolerable radiation field (Kalemkerian, Akerley et al. 2008). Extensive disease extends beyond these boundaries and may include malignant pleural or pericardial effusion or hematogenous metastases (Shepherd, Crowley et al. 2007). Approximately 60% to 70% of subjects with SCLC present with extensive disease (Hanna, Bunn et al. 2006). Although ORRs of up to 69% have been reported in recent phase 3 trials with first-line chemotherapy for extensive disease, relapse occurs early in the majority of subjects, and virtually all (~ 95%) eventually succumb to their disease (Noda, Nishiwaki et al. 2002; Eckardt, von Pawel et al. 2006; Hanna, Bunn et al. 2006). The mOS for patients with extensive disease (7 to 9 months, with a 5-year mOS of 2%) has remained unchanged over the last several decades (Jackman and Johnson 2005).

Study objective

Primary Objective:
Part 1: To identify a dose of AMG 479 in combination with etoposide plus carboplatin and/or etoposide plus cisplatin, and of AMG 102 in combination with etoposide plus carboplatin and/or etoposide plus cisplatin that can be administered safely and is tolerated as determined by the incidence of dose-limiting toxicity (DLT)
Part 2: To estimate the relative treatment effect of AMG 479 (at the dose selected in Part 1) in combination with chemotherapy (etoposide plus carboplatin and/or etoposide plus cisplatin, as determined in part 1), and of

AMG 102 (at the dose selected in Part 1) in combination with chemotherapy, compared with placebo plus chemotherapy, as measured by the respective hazard ratios (HR) for overall survival (OS).

Study design

This study has 2 parts.
Part 1 is a multi-center, open-label dose de-escalation phase 1b segment of AMG 479 in combination with etoposide plus cisplatin (Cohort 1) or carboplatin (Cohort 2), and of AMG 102 in combination with etoposide plus cisplatin (Cohort 3) or carboplatin (Cohort 4). Once respective doses of AMG 479 and of AMG 102 have been identified that are safe and tolerated based on the incidence of DLT, Part 2 will open for enrollment.
Part 2 is a randomized, double-blind, placebo-controlled phase 2 segment of AMG 479 (at the dose selected in Part 1), and of AMG 102 (at the dose selected in Part 1), and of placebo plus platinum-based chemotherapy (etoposide plus carboplatin and/or etoposide plus cisplatin, as determined in part 1) as first-line treatment for subjects with extensive stage SCLC. Subjects (n = 180) will be randomized in a 1:1:1 ratio to each treatment arm (n = 60 per arm). Randomization will be stratified according to gender (female; male) and chemotherapy (etoposide and cisplatin; etoposide and carboplatin).
In both parts of the study, chemotherapy (etoposide plus carboplatin or cisplatin) will be administered on day 1 of each 21-day (Q3W) cycle. Etoposide will also be administered on day 2 and 3 of each Q3W cycle. Premedication (see Section 6.2.2.3), vigorous hydration and diuresis (see Section 6.2.2.4) will be required for chemotherapy treatment. Investigational product (IP; AMG 479 [Part 1, Cohorts 1 and 2; Part 2, Arm A] or AMG 102 [Part 1, Cohorts 3 and 4; Part 2, Arm B] or placebo [Part 2, Arm C]) will be administered after the chemotherapy infusion on day 2 of the initial cycle, and day 1 of each Q3W cycle thereafter. Four cycles of chemotherapy will be given. Patients with best tumor response (maximum tumor regression, per RECIST) after thesecond on-study treatment tumor assessment will receive an additional 2 cycles (a total of 6 cycles) of chemotherapy. Subjects who complete 4 to 6 cycles of chemotherapy or who discontinue chemotherapy early will continue to receive IP (AMG 479, or AMG 102, or placebo) single agent maintenance therapy on day 1 of each Q3W cycle for up to 24 months from the date of first study treatment administration (study day 1). Subjects who have completed 24 months of IP may be eligible for continued treatment with IP by extension protocol or as provided for by the local country*s regulatory mechanism (see Section 13). Study treatment will cease if a subject experiences progressive disease (PD), death, unacceptable toxicity, withdraws consent, or due to an administrative decision (by the investigator or Amgen).
Radiological imaging to assess PD (per modified RECIST) will be performed every 6 weeks (± 7 days) during the first 6 months of the study, and every 9 weeks (± 7 days) thereafter, until subjects develop PD (per modified RECIST) or begin a new cancer treatment.
A follow-up visit will occur 30 days (+ 7 days) and 60 days (+ 14 days) after

the last dose of protocol-specified treatment. Subjects will be contacted every 3 months (± 2 weeks) in the long-term follow-up, for up to 36 months from the date of the last subject randomized, to assess survival. Please refer to the Study Schema for an overview of the 2-part study design.

Intervention

Investigational Product:
Part 1: Cohorts 1a and 2a: AMG 479 18 mg/kg intravenous (IV) on day 2 of the initial cycle, and day 1 of each Q3W cycle thereafter AMG 479 18 mg/kg IV on day 1 of each Q3W cycle during IP maintenance treatment
Cohort 3a and 4a:
AMG 102 15 mg/kg IV on day 2 of the initial cycle, and day 1 of each Q3W cycle thereafter
AMG 102 15 mg/kg IV on day 1 of each Q3W cycle during IP maintenance treatment
Lower doses of AMG 479 and/or AMG 102 may be explored based on safety and PK data, to determine the maximum tolerated dose. Refer to Section 6.1.1.1 for details.
Part 2: AMG 479 (Arm A), AMG 102 (Arm B), at the respective doses selected in Part 1,
or matching placebo (Arm C), IV Q3W:
day 2 of the initial cycle, and day 1 of each Q3W cycle thereafter

Study burden and risks

An individual subject may receive IP treatment for up to 24 months from study day 1. Study treatment will cease if a subject experiences PD, death, unacceptable toxicity, withdraws consent, or due to an administrative decision (by the investigator or Amgen). After stopping study treatment, subjects will be followed every 3 months for up to 36 months to assess disease status and survival. Subjects who have completed 24 months of IP may be eligible for continued treatment with IP by extension protocol or as provided for by the local country*s regulatory mechanism.
The subject accrual period is estimated to be approximately 6 to 12 months for Part 1, and approximately 18 months for Part 2. The end of the clinical study is when all subjects have completed the study treatment and long-term follow-up (up to a maximum of 36 months from the date the last subject is randomized). The maximum duration of the study is approximately 66 months (from the first subject enrolled in Part 1 until approximately 36 months from the last subject enrolled in Part 2).

Contacts

Public

Amgen

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Key Inclusion Criteria:
- Histologically or cytologically confirmed SCLC
- Extensive disease, defined by at least one of the following criteria:
- No limited disease (ie, no disease confined to the ipsilateral hemithorax, which can be safely encompassed within a tolerable radiation field)
- Extrathoracic metastases
- Malignant pericardial or pleural effusion
- Contralateral hilar adenopathy
- Measurable or non-measurable disease, as defined by modified RECIST
- Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
- >= 18 years old
- Life expectancy (with therapy) >= 3 months
- Adequate hematologic, hepatic, coagulation, renal, and metabolic function
- Diabetes, if present, must be controlled, with glycosylated hemoglobin (HgbA1c) <= 8% and fasting blood glucose level <= 160 mg/dL

Exclusion criteria

Key Exclusion Criteria
- Prior chemotherapy, chemo-radiation, or investigational agent for SCLC
- Prior radiotherapy to > 25% of the bone marrow
- Symptomatic or untreated central nervous system (CNS) metastasis (with exceptions)
- Currently or previously treated with biological, immunological or other therapies for SCLC
- Current serious or non-healing wound or ulcer
- History of prior or concurrent other malignancy (with exceptions)
- Any clinically significant medical condition other than cancer (eg, cardiovascular disease or chronic obstructive pulmonary disease), which could interfere with the safe delivery of study treatment or increase risk of toxicity
- pregnancy or breast feeding

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-02-2010
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	carboplatin

Generic name:	carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Platin
Generic name:	Platin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Toposin
Generic name:	Etoposide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-11-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-01-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-03-2013
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	EUCTR2008-003292-42-NL
CCMO	NL26393.042.09
Other	www.clinicaltrials.gov en www.amgentrials.com