A Phase 3 Multicenter, Randomized, Open Label, Active-controlled, Study of AMG 510 Versus Docetaxel for the Treatment of Previously Treated Locally Advanced and Unresectable or Metastatic NSCLC Subjects With Mutated KRAS p.G12C

Published: 05-03-2020
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This study has been transitioned to CTIS with ID 2023-508214-42-00 check the CTIS register for the current data. Primary: To compare the efficacy of AMG 510 versus docetaxel as assessed by progression-free survival (PFS) in previously treated...

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

Summary

ID

NL-OMON56228

Source
ToetsingOnline

Brief title
20190009_NSCLC Subjects With KRAS p.G12C

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lung cancer, Lung tumor

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG 510, Non small cell lung cancer, Phase 3

Outcome measures

Primary outcome

Progression will be based on blinded independent central review (BICR) of

disease response per RECIST version 1.1.

Secondary outcome

• Overall survival - defined as time from randomization until death from any

cause.

• ORR Response will be assessed by BICR.

• Dyspnea as measured by QLQ-LC13

• Cough as measured by QLQ LC13

• Chest Pain as measured by QLQ-LC13

Refer to section 3 of the protocol.

Study description

Background summary

Lung cancer is the most common type of cancer occurring in both males and females worldwide (WHO statistics, 2018), and the 5-year survival rate for advanced NSCLC is low (between 6% and 33%, depending on the stage (American Cancer Society, 2019).
While the role of KRAS mutations in human cancers has been known for decades, no anti-cancer therapies specifically targeting KRAS mutations have been successfully developed, largely because the protein has been intractable for inhibition by small molecules (McCormick, 2016). AMG 510 is a small molecule that specifically and irreversibly inhibits the KRAS G12C mutated protein. Nonclinical studies of AMG 510 have demonstrated inhibition of growth and regression of cells and tumors harboring KRAS p.G12C, and in clinical Study 20170543, AMG 510 demonstrated antitumor activity in KRAS p.G12C mutated NSCLC. These data suggest that inhibition of KRAS G12C may have therapeutic benefit for subjects with KRAS p.G12C driven cancers. Therefore, the aim of Study 20190009 is to evaluate the efficacy, safety, and tolerability of AMG 510 compared to docetaxel in subjects with previously treated, locally advanced, and unresectable or metastatic NSCLC with KRAS p.G12C mutation.

The target population is subjects with pathologically documented, locally-advanced unresectable or metastatic lung malignancy with KRAS p.G12C mutation identified through molecular testing and no other previously identified driver mutation (eg, epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) fusion).
Amgen considers that docetaxel is the appropriate comparator for this study because:
• Docetaxel is indicated for the treatment of NSCLC in patients who have progressed after checkpoint inhibitor and platinum-based doublet therapy and is regionally widely available.
• Alternative choices are not widely available or would be appropriately used in only a narrower population of younger, healthier patients.
• Compared with the overall population of patients with NSCLC, the subjects enrolled in this study must have better performance status (ECOG status * 1). Docetaxel mortality in clinical studies was increased in subjects with ECOG status of 2. In addition, because AMG 510 is expected to have better tolerability than docetaxel, enrolling subjects with better performance status is expected to maximize the tolerability of the docetaxel control group compared with AMG 510.

Study objective

This study has been transitioned to CTIS with ID 2023-508214-42-00 check the CTIS register for the current data.

Primary: To compare the efficacy of AMG 510 versus docetaxel as assessed by progression-free survival (PFS) in previously treated subjects with KRAS p.G12C mutated non-small cell lung cancer (NSCLC)

Key Secondary:
-To compare the efficacy of AMG 510 versus docetaxel as assessed by: Overall Survival (OS) Objective response rate (ORR)
-To compare patient-reported outcomes (PRO) as assessed by: European Organization for Research and Treatment of Cancer Quality-of life Questionnaire Core 13 (EORTC QLQ-LC13) and European Organization for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORTC QLQ-C30)

Refer to section 3 of the protocol.

Study design

This is a phase 3, multicenter, randomized, open label, active-controlled, study to evaluate the efficacy, safety, and tolerability of AMG 510 versus docetaxel in subjects with previously treated locally advanced and unresectable or metastatic NSCLC with KRAS p.G12C mutation. The study will be conducted at approximately 290 sites globally. The study will consist of a screening period, a treatment period, a safety follow-up (SFU) period, and long term follow up period. See Section 8.1.6 and Section 8.1.7 for AMG 510 and Docetaxel treatment beyond radiologic progression. See Section 8.1.8 for crossover. Approximately 330 previously treated subjects with locally advanced and unresectable or metastatic NSCLC with centrally confirmed KRAS p.G12C mutation will be enrolled. Subjects must have documentation of KRAS p.G12C mutation identified by central laboratory testing with the Qiagen KRAS therascreen® KRAS Rotor-Gene Q (RGQ) PCR Kit through Amgen Study 20190294 or through this protocol. Subjects will be randomized 1:1 to receive either AMG 510 or docetaxel and stratified by number of prior lines of therapy in advanced disease (1versus 2 versus > 2), race (Asian versus non-Asian), and history of CNS involvement (present or absent). As designed, the trial will not be terminated at PFS analyses and subjects will continue to be followed for OS data until the targeted number of events are reached to enable OS analyses and a robust description of the totality of the data.

Intervention

AMG510 vs docetaxel

Study burden and risks

The FIH study, Study 20170543 demonstrated that AMG 510 was well tolerated at the 180 mg QD to 960 mg QD dose levels tested.

Based on nonclinical toxicity studies of AMG 510, the key safety information to be monitored in clinical studies of AMG 510 includes renal toxicity, anemia, leukocytosis, and splenomegaly. Clinical signs and symptoms of these toxicities observed in nonclinical studies, along with relevant laboratory parameters,

will be monitored during the study to mitigate against possible risks to subjects.

Contacts

Public
Amgen

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Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Histologically or pathologically documented, locally-advanced and unresectable or metastatic NSCLC.
104. Have documentation of KRAS p.G12C mutation confirmed by central testing through the current protocol or have documentation of KRAS p.G12C mutation through Amgen Study 20190294 prior to enrollment.
105. Subjects will have received and progressed or experienced disease recurrence on or after at least 1 prior systemic therapy for locally advanced and unresectable or metastatic disease. Prior treatment must include a

platinum-based doublet chemotherapy and checkpoint inhibitor for advanced or metastatic disease, either given as one line of therapy or as individual lines of therapy unless the subject has a medical contraindication to one of the required therapies. If the subject has a medical contraindication to a required therapy, the subject may be enrolled only after the investigator discusses and obtains approval from the Amgen medical monitor.
a) Adjuvant therapy will count as a line of therapy if the subject progressed on or within 6 months of adjuvant therapy administration.
b) In locally advanced and unresectable NSCLC, disease progression on or within 6 months of end of prior curatively intended multimodal therapy will count as a line of therapy. If chemoradiation is followed by planned systemic therapy without documented progression between chemoradiation and systemic therapy, the entire treatment course counts as one line
of therapy.
c) Maintenance therapy following platinum doublet-based chemotherapy is not considered as a separate line of therapy.
106. Subjects must have archived tumor tissue samples collected within 5 years or be willing to undergo pre-treatment tumor biopsy for tissue prior to enrollment.
107. Measurable disease per RECIST v1.1 criteria. Lesions previously radiated are not considered measurable unless they have progressed after radiation.
108. ECOG Performance Status of =< 1
109. Adequate hematologic laboratory assessments, defined as the following within 10 days prior to start of study therapy:
110. Life expectancy of > 3 months, in the opinion of the investigator

Please refer to section 5.1 of the protocol.

Exclusion criteria

Subjects have received prior docetaxel in unresectable or metastatic setting (including subjects who received prior docetaxel in first line for metastatic disease, but not including subjects who received prior docetaxel neoadjuvantly or adjuvantly and did not progress within 6 months of end of therapy).
202. Mixed small-cell lung cancer or mixed NSCLC histology
203. Previously identified driver mutation (according to local standard of care or guidelines) other than KRAS p.G12C for which an approved therapy is available (including EGFR, ALK, etc).
204. Active brain metastases. Subjects who have had brain metastases resected or have received whole brain radiation therapy ending at least 4 weeks (or stereotactic radiosurgery ending at least 2 weeks) prior to study day 1 are eligible if they meet all of the following criteria:
a) residual neurological symptoms grade =< 2; b) on stable doses of dexamethasone or equivalent for at least 2 weeks, if applicable; and c) follow-up MRI performed within 30 days prior to enrollment shows no progression

or new lesions appearing.
Active brain metastases are defined as: Untreated brain lesions (new or progressing) and/or symptomatic brain lesions (symptoms as determined by the investigator), present at the time of study entry.
205. Leptomeningeal disease.
206. Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures at a frequency greater than monthly. Subjects with PleurX catheters in place may be
considered for the study with Medical Monitor approval.
-Other Medical Conditions, Prior/Concomitant Therapy, Prior/Concurrent Clinical Study Experience and Other Exclusions are listed in protocol page 52-55

Please refer to section 5.2 of the protocol.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2020
Enrollment:	56
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	AMG510

Generic name:	AMG510
Product type:	Medicine
Brand name:	Taxetere
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	05-03-2020
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-04-2020
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-01-2021
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-01-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-04-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-07-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-07-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-12-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-01-2022
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-02-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-05-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-05-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-07-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-07-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-09-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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
EU-CTR	CTIS2023-508214-42-00
EudraCT	EUCTR2019-003582-18-NL
ClinicalTrials.gov	NCT04303780
CCMO	NL72293.028.20