A Phase III, Open Label, Randomized Study of AZD9291 versus Platinum-Based Doublet Chemotherapy for Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer whose Disease has Progressed with Previous Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Therapy and whose Tumours harbour a T790M mutation within the Epidermal Growth Factor Receptor Gene (AURA3)

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To assess the safety and efficacy, measured as progression free survival, of AZD9291 compared with platinum-based doublet chemotherapy in patients with EGFR mutation positive en T790M mutation positive, locally advanced or metastatic non small cell...

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

Summary

ID

NL-OMON42148

Source
ToetsingOnline

Brief title
AURA3

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, Non small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Opdrachtgever/sponsor AstraZeneca

Intervention

Keyword: AZD9291, EGFR, Non Small Cell Lung Cancer, T790M

Outcome measures

Primary outcome

Progression Free Survival (PFS)

Secondary outcome

- Objective Response Rate (ORR)

- Duration of response (DOR)

- Disease Control Rate (DCR)

- Tumor shrinkage

- Overall survival (OS)

- To assess the effect of AZD9291 compared to platinum-based doublet

chemotherapy on disease related symptoms and quality of life

- To characterise the pharmacokinetics of AZD9291 and metabolites in subjects

receiving AZD9291

- Safety

- Tolerability

Study description

Background summary

Lung cancer has been the most common cancer in the world for several decades, and by 2008, there were an estimated 1.61 million new cases, representing 12.7% of all new cancers. It was also the most common cause of death from cancer, with 1.38 million deaths (18.2% of the total).
NSCLC represents approximately 80% to 85% of all lung cancers. Unfortunately, at the time of diagnosis approximately 70% of NSCLC patients already have advanced or metastatic disease not amenable to surgical resection. Furthermore, a significant percentage of early stage NSCLC patients who have undergone surgery subsequently develop distant recurrence and die as a result of their lung cancer. Patients presenting with advanced NSCLC have a median overall survival (OS) of 10 to 12 months.
Treatment of advanced NSCLC can be guided by the presence of certain molecular drivers
such as EGFR, anaplastic lymphoma kinase (AnLK) and KRAS mutations. The incidence of
Epidermal Growth Factor Receptor mutation positive (EGFRm+) NSCLC is approximately
10-15% and 30-40% of patients in the West and Asia, respectively.
Although first- (eg, erlotinib, gefitinib) and second-generation (eg, afatinib) Epidermal
Growth Factor Receptor Tyrosine Kinase Inhibitors (EGFR TKIs) are established therapies for patients with NSCLC known to have activating mutations in EGFR (EGFRm+), the
emergence of a secondary T790M mutation in patients treated with an EGFR TKI agent has
been described as a major route of development of resistance to this class of therapy
in approximately 60% of patients.
Selective inhibition of EGFR tyrosine kinase has demonstrated clinical benefit in
approximately 70% of patients with advanced NSCLC.
AZD9291 is a potent irreversible inhibitor of both the single EGFRm+ (TKI sensitivity
conferring mutation) and dual EGFRm+/T790M+ (TKI resistance conferring mutation) receptor forms of EGFR with a significant selectivity margin over wild-type EGFR.
Therefore AZD9291 has the potential to provide clinical benefit to patients with advanced

NSCLC harbouring both the single sensitivity mutations and the resistance mutation following prior therapy with an EGFR-TKI.

Study objective

To assess the safety and efficacy, measured as progression free survival, of AZD9291 compared with platinum-based doublet chemotherapy in patients with EGFR mutation positive en T790M mutation positive, locally advanced or metastatic non small cell lung cancer, who have progressed following treatment with an approved EGFR Tyrosine Kinase Inhibitor (EGFR-TKI).

Study design

Phase III, open-label, randomised study
Randomised in a ratio of 2:1:
- AZD9291 (80 mg orally, once daily)
- Pemetrexed (500 mg/m2) + carboplatin (AUC5) / cisplatin (75mg/m2) (intravenously, administered on day 1 of each 21 day cycle)

Intervention

Patient will be dosed with AZD9291 (80 mg orally, once daily) or with Pemetrexed (500 mg/m2) + carboplatin (AUC5) / cisplatin (75mg/m2) (intravenously, administered on day 1 of each 21 day cycle).

Study burden and risks

On several days during the study patients will undergo the following assessments:
- anamnesis (at screening also medical history)
- physical examination
- WHO performance status
- vital signs (blood pressure, pulse)
- length
- weight
- CT or MRI scan
- ECG
- ophthalmolgic assessment
- blood and urine assessments
- MUGA/echocardiogram
- questionnaires (EORTC QLQ C-30, QLQ-LC13, EQ-5D-5L and PRO CTCAE) (by e-device)
- pregnancy test

Adverse events that may be caused by AZD9291 are: diarrhea, rash and acne, dry skin, nail changes, nail infections or changes to eyelashes, heart problems,

dryness of the eyes or thinning of the front layer of the eye, changes to the lining of the gut and inflammation of the lungs.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Subjects with histologically- or cytologically-documented NSCLC.
- Locally advanced or metastatic NSCLC.
- Radiological documentation of disease progression following 1st line EGFR TKI Treatment without any further treatment.
- Eligible to receive treatment with the selected doublet-chemotherapy.
- Confirmation of EGFR mutation.
- Central confirmation of T790M+ mutation status.
- World Health Organisation (WHO) performance status 0-1.

- At least one lesion, not previously irradiated.

Exclusion criteria

- Treatment with more than one prior line of treatment for advanced NSCLC.
- Treatment with an approved EGFR-TKI (eg, erlotinib, gefitinib, afatinib) within 8 days or approximately 5 x half-life of the first dose of study treatment.
- Any cytotoxic chemotherapy, investigational agents or other anticancer drugs from a previous treatment regimen or clinical study within 14 days of the first dose of study treatment.
- Previous treatment with an unapproved EGFR-TKI.

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:	Recruiting
Start date (anticipated):	10-10-2014
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	15-07-2014

Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	06-08-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-03-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-03-2015

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-07-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-08-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-08-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-04-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-12-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-03-2017

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-04-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-02-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Not approved Date:	23-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-08-2019
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2014-000594-39-NL
ClinicalTrials.gov	NCTnummernognietbekend
CCMO	NL49354.031.14