Patients on osimertinib with EGFR mutation exon 20, non-T790M in lung cancer. The position-20 trial.

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To determine the efficacy (as assessed by best response) of osimertinib in patients with locally advanced or metastatic NSCLC and only an EGFR exon 20 mutation, deletion and/or insertion, which are T790M-ve.

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

Summary

ID

NL-OMON55798

Source
ToetsingOnline

Brief title
The position-20 trial

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Astra Zeneca,unrestricted grant

Intervention

Keyword: EGFR exon 20, Non-small cell lung cancer, osimertinib

Outcome measures

Primary outcome

Best response defined by RECIST 1.1

Secondary outcome

- Progression free survival (PFS) is defined by RECIST 1.1

- Duration of response

- Overall survival

- Treatment- related adverse events (CTC-AE, v4.0)

Study description

Background summary

Osimertinib is an oral, potent, irreversible EGFR-TKI selective for sensitizing (EGFRm) and T790M resistance mutation with a significant selectivity margin against wild-type EGFR. As a result, osimertinib can effectively block EGFR signalling both in EGFR single mutant cells with activating EGFR mutations and in double mutant cells bearing the resistance T790M mutation. Osimertinib is registered in patients with advanced T790M positive NSCLC and is currently under investigation as a treatment option in: 1) Patients with advanced EGFRm NSCLC who are treatment naïve; 2) In combination with novel agents for patients with EGFR TKI resistant NSCLC. Data from the ongoing phase I AURA study (D5160C00001) in patients with T790M positive NSCLC who were previously treated with EGFR TKI, have achieved promising efficacy with osimertinib; 54.2% 95% CI (40.8%, 67.3%) of subjects achieved a response, 91.5% 95% CI (81.3%, 97.2%) achieved disease control, medium duration of response of 12.4 months 95% CI (8.3, NC) and median PFS based on 38% maturity of data was 13.5 months 95% CI (8.3, NC), as assessed by blinded independent central review. Promising evidence of efficacy was also observed in patients with EGFRm treatment naïve NSCLC treated with osimertinib as first line EGFR TKI. Across the clinical development programme, osimertinib has demonstrated a manageable safety profile.

Study objective

To determine the efficacy (as assessed by best response) of osimertinib in patients with locally advanced or metastatic NSCLC and only an EGFR exon 20 mutation, deletion and/or insertion, which are T790M-ve.

Study design

Based on the safety, pharmacokinetic and preliminary efficacy data, 160 mg once daily is selected as the recommended phase II dose. No dosage adjustment is required due to patient age, body weight, gender, ethnicity and smoking status.

Intervention

See study design

Study burden and risks

As part of the trial, patients will be expected to attend multiple clinic visits, where they will undergo physical examinations, vital sign measurements, blood tests for safety assessment, pregnancy testing (for females of child bearing potential), and monitoring for adverse events. In addition, every 6 weeks (until week 24) and then every 12 weeks, patients will undergo radiographic assessment of their tumors (by CT) until disease progression. Blood will also be collected at certain visits for research purposes. The frequency of visits and number of procedures carried out during this trial would be considered as standard of care. These procedures are conducted by medically trained professionals and every effort will be made to minimise any risks or discomfort to the patient.

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. Provision of informed consent prior to any study specific procedures
2. Patients must be >= 18 years of age.
3. Locally advanced or metastatic non-small cell lung cancer, not amenable to curative surgery or radiotherapy
4. Presence of an EGFR exon 20, non-T790M, mutation, deletions and/or insertion only,
5. ECOG performance score of 0-2
6. Patients must have a life expectancy >= 12 weeks.
7. Females should be using adequate contraceptive measures, should not be breast feeding and must have a negative pregnancy test prior to start of dosing if of child-bearing potential or must have evidence of non-child-bearing potential by fulfilling one of the following criteria two weeks before screening. Male patients should be willing to use barrier contraception.
8. Patient is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up.
9. At least one lesion, not previously irradiated, that can be accurately measured at baseline as >= 10 mm in the longest diameter (except lymph nodes which must have short axis >= 15 mm) with computed tomography (CT) or magnetic resonance imaging (MRI) and which is suitable for accurate repeated measurements.
10. Brain metastasis, if asymptomatic, are allowed. In case of symptomatic brain metastasis, patient must have had radiotherapy and stable for at least 2 weeks.

Exclusion criteria

1. Presence of a T790M mutation or other tumour driven mutations, translocations or amplifications (e.g. common EGFR mutations, KRAS, BRAF V600E, ALK, ROS1)
2. Patient is unwilling and unable to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up
3. Previous treatment with EGFR-TKI
4. Patients currently receiving (or unable to stop use prior to receiving the first dose of study treatment) medications or herbal supplements known to be potent inducers of CYP3A4 (at least 3 weeks prior).
5. Any unresolved toxicities from prior therapy greater than Common Terminology Criteria for Adverse Events (CTCAE) grade 1 at the time of starting study treatment with the exception of alopecia and grade 2, prior platinum-therapy related neuropathy or immune mediated pneumonitis or hepatitis previously treated with IO therapy.
6. Any evidence of severe or uncontrolled systemic diseases, including uncontrolled hypertension and active bleeding diatheses.
7. Patients with symptomatic central nervous system (CNS) metastases who are neurologically unstable
8. Past medical history of interstitial lung disease (ILD), drug-induced ILD, radiation pneumonitis requiring steroid treatment, or any evidence of clinically active ILD
9. Inadequate bone marrow reserve or organ function.
10. Any of the following cardiac criteria:
- Mean resting corrected QT interval (QTc) > 470 msec obtained from 1 electrocardiograms, using the screening clinic ECG machine derived QTc value
- Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g., complete left bundle branch block, third degree heart block, second degree heart block)
- Any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, hypokalemia, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age in first degree relatives or any concomitant medication known to prolong the QT interval
11. Refractory nausea and vomiting, chronic gastrointestinal diseases, inability to swallow the formulated product or previous significant bowel resection that would preclude adequate absorption of osimertinib
12. Males and females of reproductive potential who are not using an effective method of birth control and females who are pregnant or breastfeeding or have a positive (urine or serum) pregnancy test prior to study entry
13. Judgment by the Investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions and requirements
14. History of hypersensitivity active or inactive excipients of osimertinib or drugs with a similar chemical structure or class to osimertinib

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-08-2018
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tagrisso
Generic name:	osimertinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	31-05-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-02-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-05-2020

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-08-2021
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	EUCTR2017-004734-28-NL
CCMO	NL64116.042.17
Other	NTR, nummer volgt