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

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26966

Source
Nationaal Trial Register

Brief title
Position-20 trial

Health condition

Non-small cell lung carcinoma
Niet-kleincellig longkanker

Sponsors and support

Primary sponsor: University Medical Center Groningen (UMCG)
Source(s) of monetary or material Support: AstraZeneca UK Ltd

Intervention

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, Vs4.0)

Study description

Background summary

A single arm phase II trial, patients with EGFR exon 20 mutations, deletions and/or insertions, which areT790M-ve, with advanced stage non-small cell lung carcinoma will be treated with osimertinib. Based on the safety, pharmacokinetic and preliminary efficacy data, 160 mg QD, is selected as the recommended phase II dose. Patients will be pre-treated with chemotherapy or immunotherapy. Treatment efficacy will be assessed according to RECIST 1.1 criteria.

Study objective

The study will test the hypothesis that osimertinib treatment result a partial response in 30 % of patients.

Study design

As part of the trial, patients will expected to attend several outpatient visits where they will undergo physical examinations, vital sign measurements, blood tests for safety assessment and monitoring for adverse events. In addition every 6 weeks until week 24 and then every 12 weeks patients will undergo radiographic assessment by CT of their tumors until disease progression or unacceptable toxicity. The frequency of visits and number of procedures carried out during this trial would typically 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.

Intervention

Study with the tyrosine kinase inhibitor osimertinib 160 mg once daily in patients with EGFR exon 20, T790M-ve, mutations, deletions and/or insertions.

Contacts

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Eligibility criteria

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:

o Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments

o Women under 50 years old would be consider postmenopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and with LH and FSH levels in the post-menopausal range for the institution

o Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation.

• 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). All patients must try to avoid concomitant use of any medications, herbal supplements and/or ingestion of foods with known inducer effects on CYP3A4.

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, which in the investigator's opinion makes it

undesirable for the patient to participate in the trial or which would jeopardize compliance with the protocol, or active infection including hepatitis B, hepatitis C and human immunodeficiency virus (HIV). Screening for chronic conditions is not required.

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 as demonstrated by any of the following laboratory values:

a. absolute neutrophil count <1.5 x 109/L; platelet count <100 x 109/L; haemoglobin <90 g/L

b. Alanine aminotransferase >2.5 times the upper limit of normal (ULN) if no demonstrable liver metastases or >5 times ULN in the presence of liver metastases

c. Aspartate aminotransferase >2.5 times ULN if no demonstrable liver metastases or >5 times ULN in the presence of liver metastases

d. Total bilirubin >1.5 times ULN if no liver metastases or >3 times ULN in the presence of documented Gilbert's Syndrome (unconjugated hyperbilirubinaemia) or liver metastases

e. Creatinine >1.5 times ULN concurrent with creatinine clearance <50 ml/min (measured or calculated by Cockcroft and Gault equation)

16. 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

17. 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

18. 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

19. 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

20. History of hypersensitivity active or inactive excipients of osimertinib or drugs with a similar chemical structure or class to osimertinib

Study design

Design

Study type:	Interventional
Intervention model:	Factorial
Allocation:	Non controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2018
Enrollment:	15
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL6705
NTR-old	NTR6875
Other	: ESR-16-12212

Study results