Combining Afatinib and Concurrent Chemotherapy, Followed by Osimertinib and Concurrent Chemotherapy, in Untreated EGFR Positive NSCLC Tumors

Gepubliceerd: 15-10-2020 Laatst bijgewerkt: 15-05-2024

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28617

Bron
NTR

Verkorte titel
COMBINATION

Aandoening

Non small cell lung cancer

Ondersteuning

Primaire sponsor: Amsterdam UMC
Overige ondersteuning: The translational research part is supported by Boehringer Ingelheim

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Disease control rate (DCR) at 18 months, defined as the rate of patients that are still on treatment using either afatinib or osimertinib without radiological disease progression according to RECIST (v1.1). If patients develop oligo-progressive disease that is amenable to local treatments such as stereotactic radiotherapy and if the patient has clinical benefit of the ongoing TKI treatment, the treating physician may (in the best interest of the patient) treat the oligo-progressive site(s) locally and continue the TKI (in part-1 and part-2) beyond progression, as per current standard of care guidelines. The efficacy of this sequential approach will be compared to the front-line osimertinib outcome data, as reported by the FLAURA trial.

Toelichting onderzoek

Achtergrond van het onderzoek

Osimertinib monotherapy is now the preferred treatment option in EGFR mutation positive non-small cell lung cancer (NSCLC). However, a sequential combination strategy using first line afatinib in with a short course of chemotherapy, followed by osimertinib with a short course of chemotherapy (in T790M positive tumors) could increase the targeted therapy efficacy option for these patients.
Study design: this is a single arm, open label, multicenter phase II study. A total of 21 evaluable patients are needed.
Study population: TKI-naïve advanced EGFRm+ del19/L858R NSCLC patients who are eligible for treatment with EGFR TKI and chemotherapy. Patients with CNS metastases will be excluded.

Doel van het onderzoek

We hypothesized that treating advanced stage EGFR mutation positive NSCLC in first line with afatinib and osimertinib in second line (in T790M positive tumors) will cause an apoptotic cell death in a large part of TKI-sensitive cancer cells, resulting in a large reduction of the tumor bulk. Adding cytotoxic chemotherapy after 6 weeks of EGFR-TKI will destroy remaining TKI-resistant subclones at an early stage, when the TKI-resistance tumor volume is the smallest and most vulnerable. We will administer only 2 cycles of chemotherapy to limit toxicity, while maintaining a substantial anti-cancer effect. After progression on afatinib-chemotherapy combination, the majority of patients will develop T790M and will be able treated by osimertinib-chemotherapy combination.
So, this strategy will allow us to timely sequence the most appropriate drugs (afatinib and osimertinib with chemotherapy) to get the highest anti-cancer efficiency. In this way, we will avoid long periods of maintenance treatments with chemotherapy or anti-VEGFR treatments that are associated with toxicity, costs, and necessitate the patients to come into the ward

for intravenous medication. The limited cycles of chemotherapy also allows the treating physician to again treat the patient with the same chemotherapy regimen once progression occurs after all sensible targeted therapy options have been used. Therefore, we hypothesize that this sequential combination strategy will be more effective than other available strategies and will improve the quality of patient care as compared to current general practice.

Onderzoeksopzet

The primary endpoint will be evaluated at 18 months of inclusion using RECIST1.1. The secondary and explorary endpoints will be evaluated using RECIST1.1 every six weeks, survival data, molecular analysis of histologic specimen at baseline and upon progression, and blood samples dd-PCR every six weeks initially and upon progression.

Onderzoeksproduct en/of interventie

This study consists of 2 parts. Part 1 is defined as a first line treatment with afatinib orally (30 mg once a day) for the first 6 weeks, followed by concurrent use of afatinib (20mg once a day, part 1B) plus 2 cycles of carboplatin and pemetrexed (21 days per cycle); followed by afatinib monotherapy (30mg once a day). Part 2 comprises a 2nd line treatment with osimertinib (80 mg once daily) after failure of part 1, only in T790M positive patients for the first 6 weeks, followed by concurrent use of osimertinib (80mg once a day) plus 2 cycles of carboplatin and pemetrexed (21 days per cycle); followed by osimertinib monotherapy (80mg once a day).

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Histologically confirmed NSCLC, positive for EGFR exon 19 deletion or EGFR exon 21 L858R
2. WHO PS 0-2
3. Be willing and able to provide written informed consent for the trial.
4. Be above 18 years of age on day of signing informed consent.
5. Patients must have radiological measurable disease
6. Demonstrate adequate organ function, as deemed acceptable by the treating physician in the context of metastatic NSCLC:
a. Leukocytes ≥ 3,000/mm3
b. Absolute neutrophil count (ANC) ≥ 1500/mm3
c. Platelet count ≥ 100,000/mm3
d. Hemoglobin ≥ 6 mmol/L
e. Creatinine ≤ 1.5 x ULN or creatinine clearance (CrCl) ≥40 mL/min (if using the Cockcroft-Gault formula below):
i. Female CrCl = [(140 - age) x weight x 0.85]/(0.85 x creat in mmol/L)
ii. Male CrCl = [(140 - age) x weight x 1.00]/(0.81 x creat in mmol/L)
f. Total Bilirubin ≤ 1.5 x ULN (except subjects with Gilbert Syndrome)
g. AST and ALT ≤ 3 times the upper limit of normal

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Inability to provide informed consent
2. Inability to take study medications
3. Patients with CNS metastases
4. Prior EGFR TKI or platinum-doublet therapy for advanced stage NSCLC. Prior (neo)adjuvant treatments are allowed when the last administration is one year or more.
5. Evidence of interstitial lung disease or active, non-infectious pneumonitis.
6. Active infection requiring systemic therapy.
7. Active Hepatitis B or C.
8. Psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
9. Patient is pregnant or breastfeeding, or expecting to conceive within the projected duration of the trial, starting with the screening visit.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	14-10-2020
Aantal proefpersonen:	21
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	15-10-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 52389
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8985
CCMO	NL74383.029.20
OMON	NL-OMON52389

Resultaten