# Phase IV trial of afatinib followed by osimertinib versus osimertinib alone as first-line treatment in patients with advanced *EGFR* mutation-positive NSCLC

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## Introduction

- EGFR TKIs are the standard first-line treatment for patients with advanced *EGFR*m+ NSCLC[1]
- The T790M mutation is the most common resistance mechanism to the second-generation TKI afatinib[2]
- The third-generation TKI osimertinib has shown efficacy in patients with T790M+ NSCLC[3]
- Consequently, a sequential treatment strategy of afatinib followed by osimertinib has been proposed for patients who develop T790M[4]
- This sequential approach was associated with a median time on EGFR TKI treatment of 27.7 months in the observational GioTag study[4] but has not been assessed in a prospective clinical trial

*EGFR*m+, EGFR mutation-positive; T790M+, T790M mutation-positive; TKI, tyrosine kinase inhibitor

## Objectives

**Primary objective**

- Time to EGFR TKI treatment failure within 24 months for afatinib followed by osimertinib in T790M+ patients versus osimertinib alone†

**Secondary objectives**

- Time to EGFR TKI failure
- Progression-free survival
- Overall survival
- Response rate at 12 and 24 months
- Safety and tolerability
- Symptom control assessed by patient-reported quality of life

†Analysis of primary endpoint will be performed 24 months after randomisation of the last patient

**References**

1. Planchard D, et al. Ann Oncol 2018;29:iv192-iv237
2. Shah R and Lester JF. Clin Lung Cancer 2020;21:e216–28
3. Mok TS, et al. N Engl J Med 2017;376:629–40
4. Hochmair MJ, et al. Future Oncol 2020;16:2799–808
5. Clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT04413201 (Accessed: 10 February 2021)

**Disclosure statement**

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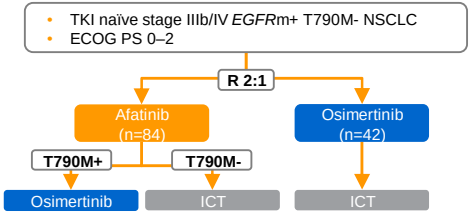
## Key points

- **AFAMOSI (NCT04413201) is a prospective, randomised, multicentre, Phase IV trial assessing sequential afatinib followed by osimertinib in patients who develop T790M, versus osimertinib alone**




Treatment will continue until disease progression per RECIST v1.1, unless the patient continues to show clinical benefit, as assessed by the investigator

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- **AFAMOSI is currently being conducted at eight sites in Germany[5]**
- **The study began in September 2020;[5] recruitment is planned to end in Q2 2022 and 126 patients will be recruited**
- **Observation will end 48 months after randomisation of the last patient‡**

‡Survival data may still be collected after this date. ECOG PS, Eastern Cooperative Oncology Group performance status; Q2, second quarter (Apr–Jun); R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; T790M-, T790M mutation negative

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## Eligibility

| Key inclusion criteria |
|---|
| Age ≥18 years |
| ECOG PS 0–2 |
| Non-squamous *EGFR*m+ NSCLC |
| Unresectable Stage ≥IIIb or metastatic Stage IV disease (UICC) |
| EGFR TKI naïve |
| At least one evaluable lesion according to RECIST v1.1 |
| Adequate bone marrow, kidney, cardiac and liver function |

| Key exclusion criteria |
|---|
| T790M mutation |
| Any investigational drug within 30 days or hormonal anticancer treatment within 2 weeks prior to randomisation |
| Radiotherapy within 2 weeks prior to randomisation (except palliative radiotherapy to target organs other than chest) |
| Major surgery within 2 weeks before starting study treatment, or scheduled during the study |
| History of clinically relevant cardiovascular abnormalities or certain comorbidities |

UICC, Union for International Cancer Control

## Endpoints

| Primary endpoint |
|---|
| Time to EGFR TKI failure within 24 months for afatinib followed by osimertinib in the T790M+ group versus osimertinib |

| Secondary endpoints |
|---|
| Time to EGFR TKI failure (afatinib versus osimertinib) |
| Progression-free survival (afatinib followed by osimertinib or ICT versus osimertinib followed by ICT) |
| Overall survival |
| Response rate at 12 months and 24 months |
| Disease control rate at 12 months and 24 months |
| Safety and tolerability |
| Symptom control, assessed by patient-reported quality of life with EQ-5D, EORTC QLQ-C30, and EORTC QLQ-LC29 |

**Translational research:** detection of clinically relevant *EGFR* mutations

- Deletion 19 (E746_A750del)
- L858R
- T790M
- C797S

EQ-5D, EuroQol-5 Dimension; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Cancer 30; EORTC QLQ-LC29, EORTC QLQ-Lung Cancer 29; ICT, investigator's choice of therapy

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