

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

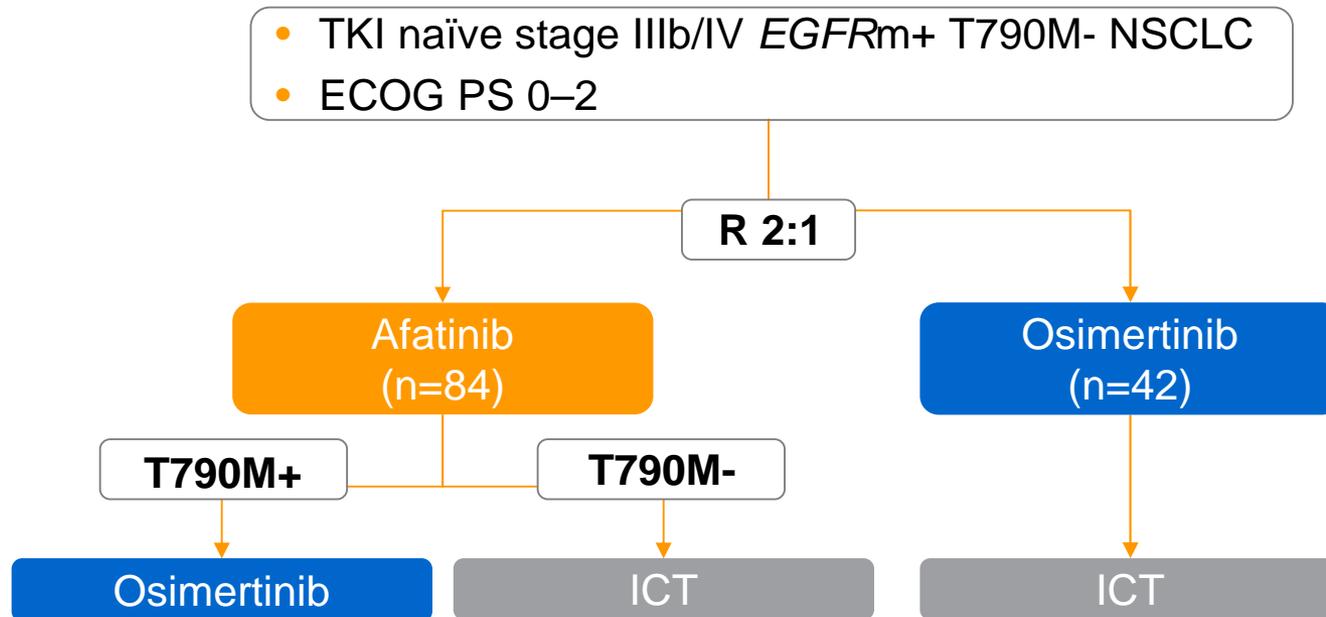
- EGFR TKIs are the standard first-line treatment for patients with advanced *EGFR*_{m+} NSCLC¹
- The T790M mutation is the most common resistance mechanism to the second-generation TKI afatinib²
- The third-generation TKI osimertinib has shown efficacy in patients with T790M+ NSCLC³
- Consequently, a sequential treatment strategy of afatinib followed by osimertinib has been proposed for patients who develop T790M⁴
- This sequential approach was associated with a median time on EGFR TKI treatment of 27.7 months in the observational GioTag study⁴ but has not been assessed in a prospective clinical trial

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
- AFAMOSI is currently being conducted at eight sites in Germany⁵
- 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

Key points (cont'd)



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

‡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

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

Eligibility

Key inclusion criteria
Age ≥18 years
ECOG PS 0–2
Non-squamous <i>EGFR</i> 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

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 <i>EGFR</i> mutations
<ul style="list-style-type: none">• 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

References

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Disclosure statement

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