

A Phase IIIb open-label study of afatinib in EGFR TKI-naïve patients with EGFRm+ NSCLC: Exploratory biomarker analysis

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Introduction

- The safety and efficacy of afatinib, an irreversible second-generation ErbB family blocker, in patients with EGFRm+ NSCLC has been demonstrated in Phase III clinical studies,^{1,2} and afatinib is now approved for this indication in the majority of countries worldwide
- This Phase IIIb study (NCT01953913) was performed to provide evidence from a near 'real-world' treatment setting on the safety and efficacy of afatinib in EGFR TKI-naïve EGFRm+ Asian patients with locally advanced or metastatic NSCLC³
- An interim analysis found an afatinib-related SAE rate of 6.1%, with 3.8% of patients discontinuing due to afatinib-related SAEs, suggesting that afatinib-related AEs were manageable. Median TTSP was 15.3 months and median PFS was 12.1 months, suggesting that afatinib may be continued beyond radiological progression³
- The final results of this study are presented elsewhere at this conference (Poster #xxxxx)⁴
- Tumour biomarker analysis is increasing in importance as a method of guiding treatment decisions, and has become routine clinical practice. However, more information is needed on how mutations change over the course of treatment in patients with EGFRm+ NSCLC. In addition, the role of non-EGFR mutations in influencing treatment efficacy and outcomes needs to be elucidated

AE, adverse event; EGFRm+, EGFR mutation-positive; NSCLC, non-small cell lung cancer; PFS, progression-free survival; SAE, serious adverse event; TKI, tyrosine kinase inhibitor; TTSP, time to symptomatic progression

Objectives

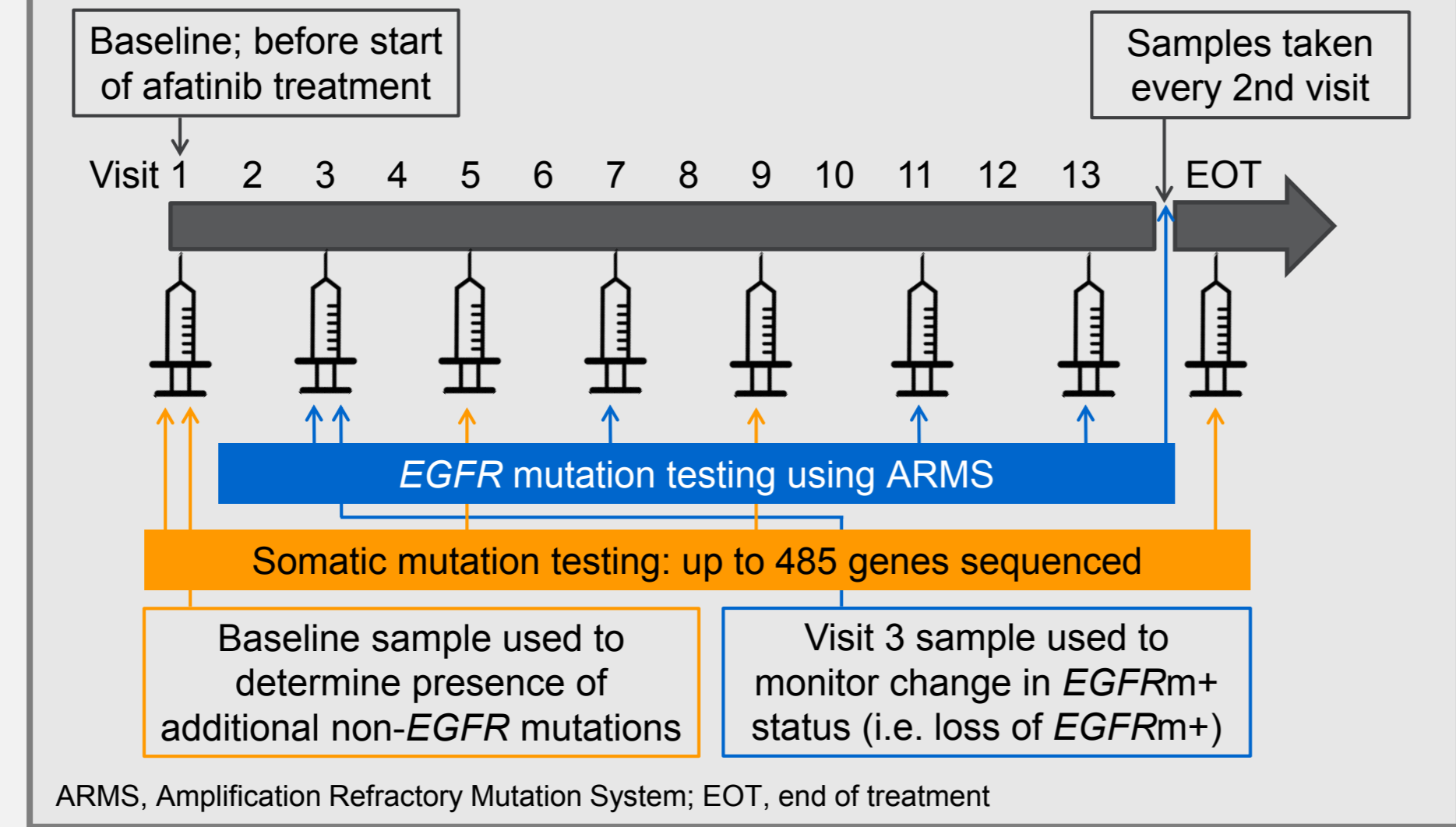
- The aim of this biomarker sub-study was to explore the relationship between tumour mutation type and patients' response to afatinib in terms of efficacy and tolerability

Methods

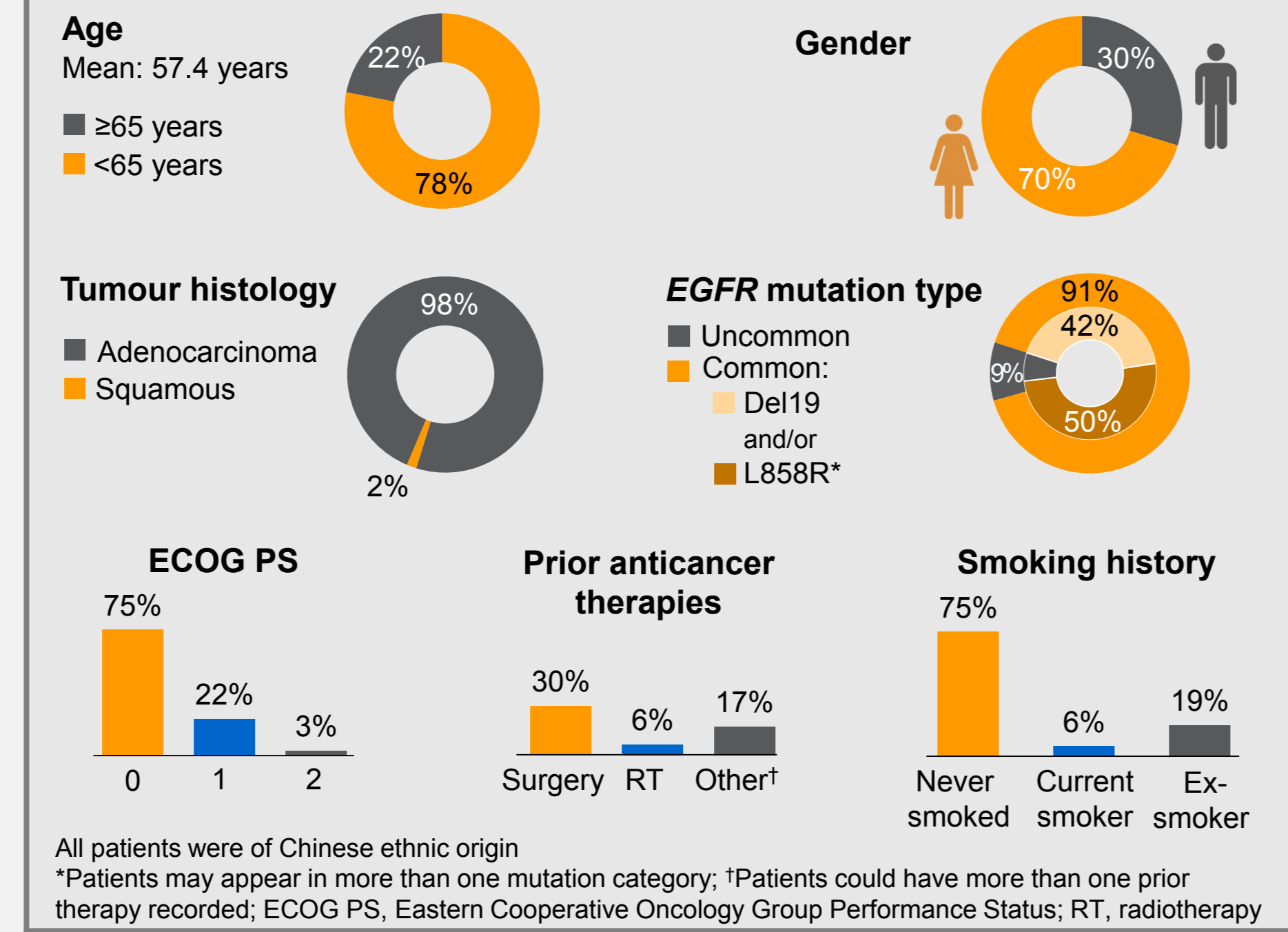
- In this Phase IIIb trial with a similar setting to 'real-world' practice, EGFR TKI-naïve patients with locally advanced/metastatic EGFRm+ NSCLC were recruited from centres in China, Hong Kong, India, Singapore and Taiwan and received afatinib 40mg/day until investigator-assessed progression or lack of tolerability³
- The afatinib dose could be reduced to 30 mg/day or 20 mg/day based on pre-defined criteria to manage tolerability
- This biomarker analysis was conducted on patients entering the study at Beijing Cancer Hospital, China, only
- DNA was extracted from peripheral blood (10 mL) taken during scheduled visits (see Figure)
- Analyses of TTSP and PFS were conducted in subgroups by age, ECOG PS, and EGFR mutation type at study entry
- PFS was analysed by change in mutation status at Visit 3 and the presence of additional, non-EGFR mutations at baseline (see Figure)

ECOG PS, Eastern Cooperative Oncology Group Performance Status

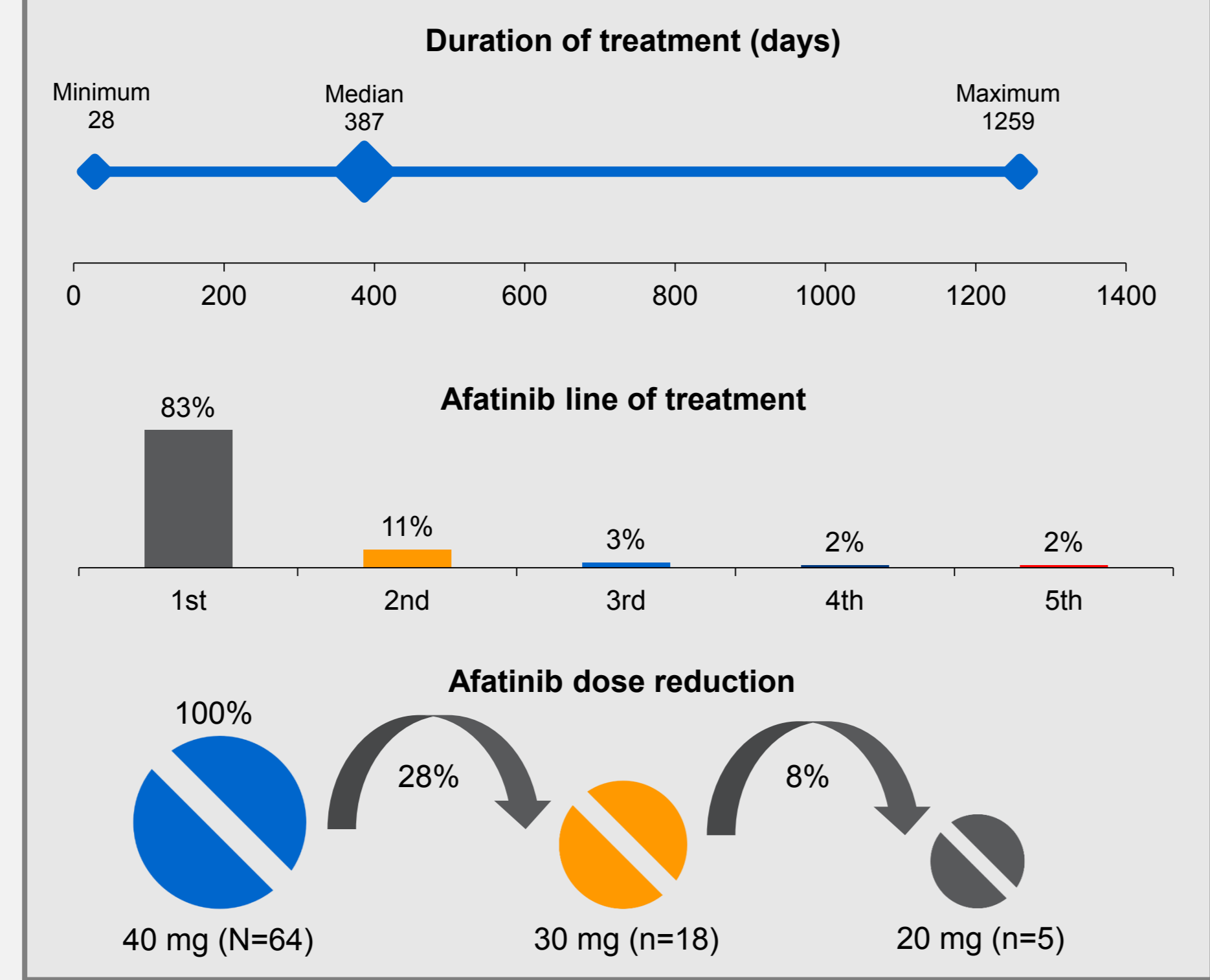
Methods – biomarker analyses



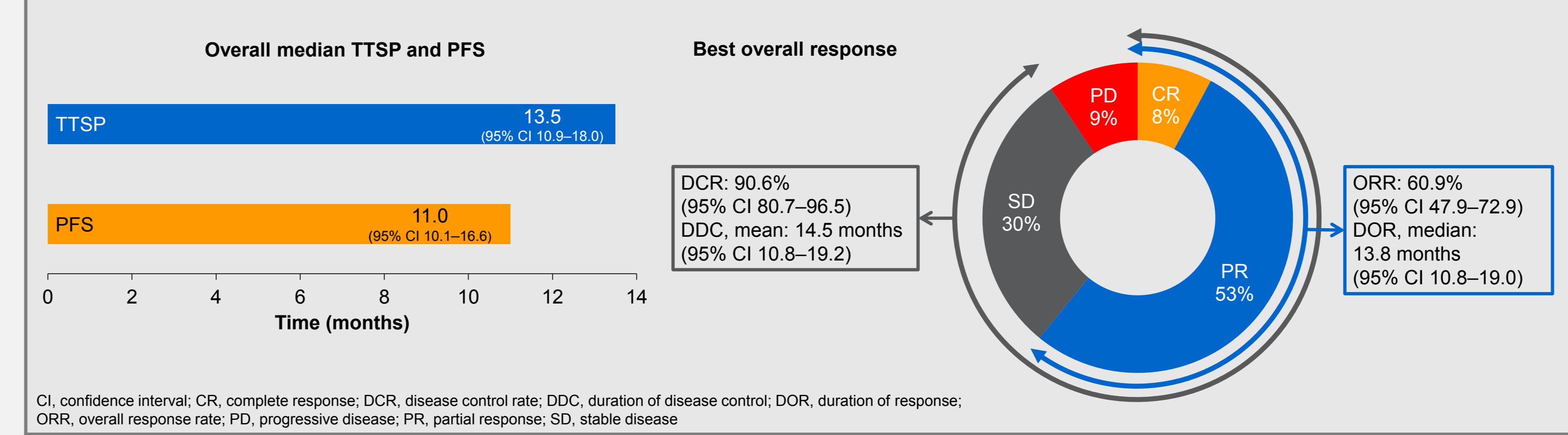
Baseline characteristics (N=64)



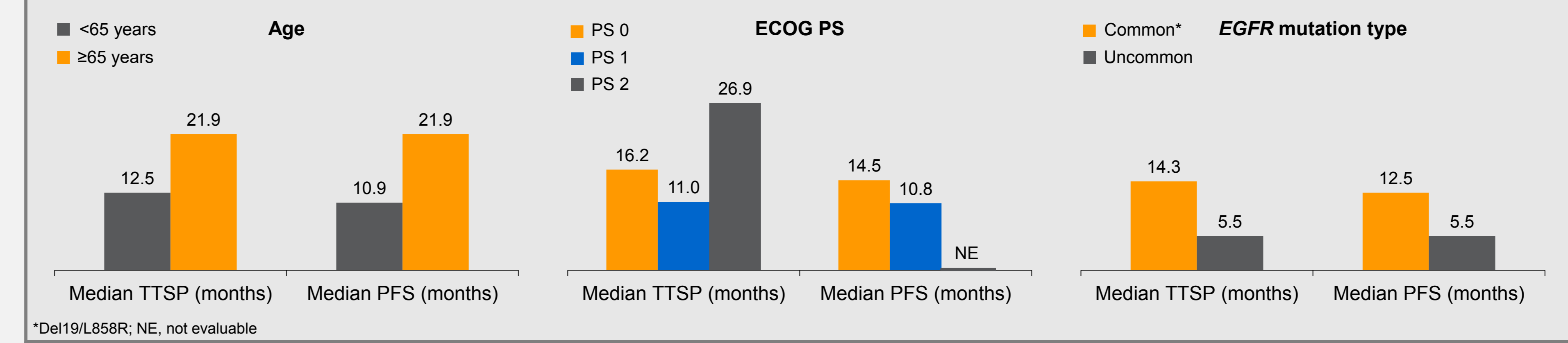
Treatment exposure



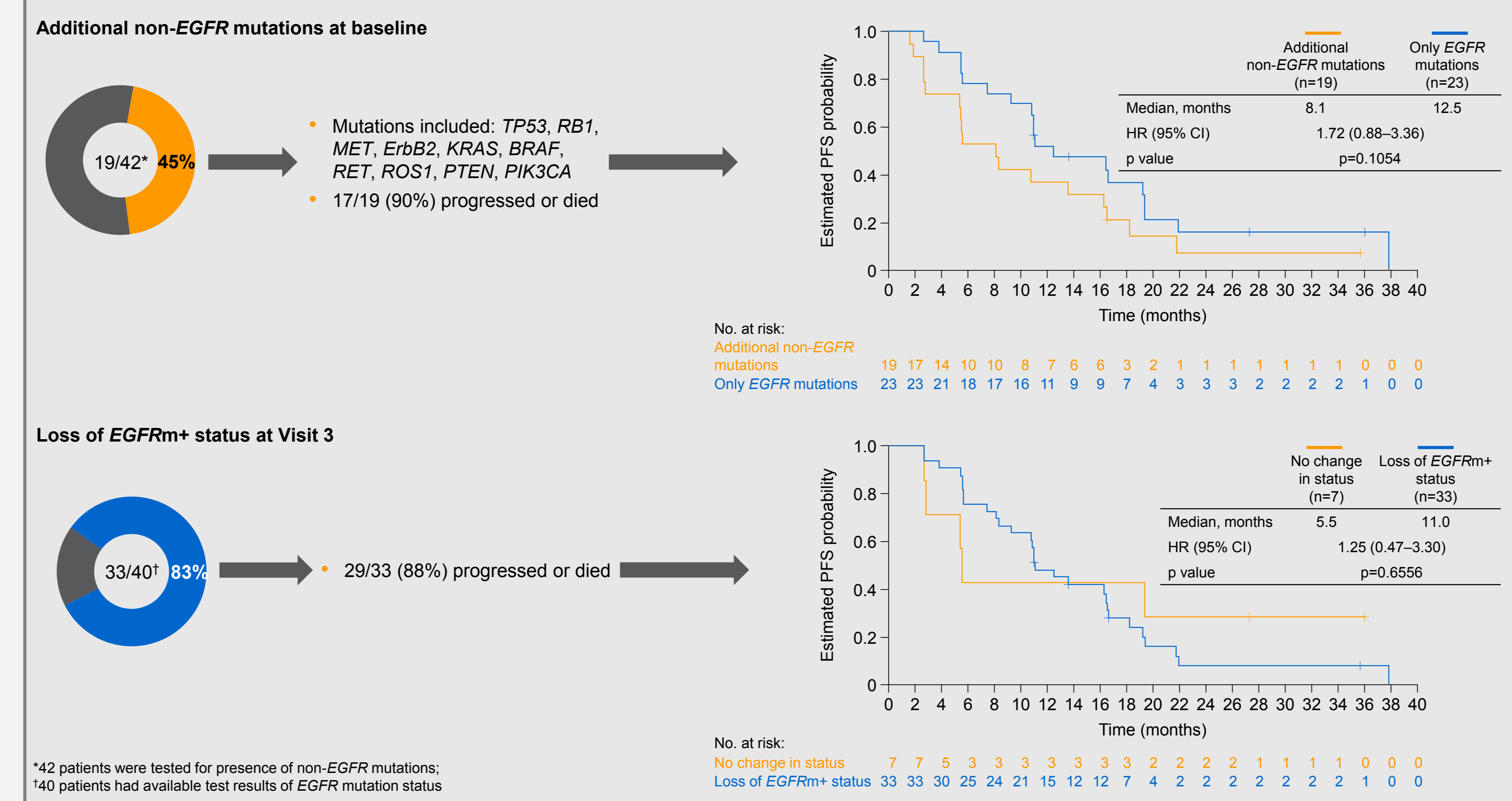
Overall efficacy in biomarker analysis patients (N=64)



Efficacy by subgroup



Biomarker analysis



Safety (N=64)

| n (%) | Afatinib 40 mg/day | | | |
|---|----------------------|---------|---------|---------|
| | All grades | Grade 3 | Grade 4 | Grade 5 |
| Any AE | 64 (100) | 24 (38) | 3 (5) | 4 (6)* |
| AE leading to dose reduction | 16 (25) | - | - | - |
| AE leading to treatment discontinuation | 7 (11) | - | - | - |
| SAE | 15 (23) [†] | - | - | - |
| TRAEs in ≥20% of patients | | | | |
| Total with TRAE | 64 (100) | 19 (30) | 2 (3) | 1 (2) |
| Diarrhoea | 63 (98) | 9 (14) | 0 | 0 |
| Rash/acne [‡] | 52 (81) | 5 (8) | 0 | 0 |
| Stomatitis [‡] | 46 (72) | 1 (2) | 0 | 0 |
| Paronychia [‡] | 32 (50) | 4 (6) | 0 | 0 |
| ALT increased | 19 (30) | 0 | 0 | 0 |
| Nasal dryness | 15 (23) | 0 | 0 | 0 |

*Cancer progression alone (n=1); cancer progression and lung infection (n=1); metastases to CNS (n=1). These were not considered related to afatinib. One death due to decreased appetite was considered treatment related. †Most common SAEs were cerebral infarction (n=3, 5%), malignant neoplasm progression, CNS metastases (both n=2, 3%). The remaining SAEs occurred in single patients only. ‡Grouped terms. ALT, alanine aminotransferase; CNS, central nervous system; TRAE, treatment-related adverse event

Key findings and conclusions

- This exploratory sub-study of a Phase IIIb trial included 64 EGFR TKI-naïve Chinese patients with EGFRm+ NSCLC who received afatinib in a near 'real-world' setting
- 45% of the patients assessed had EGFRm+ NSCLC with additional non-EGFR mutations at baseline. There was no significant difference in PFS in these patients compared with patients who had NSCLC with only EGFR mutations at baseline
- 83% of the patients assessed had a change of NSCLC mutation status at Visit 3, to EGFR mutation-negative. Median PFS was twice as long in these patients compared with patients whose disease remained EGFRm+; however, the difference was not statistically significant
- Overall efficacy and safety findings in this subset of Chinese patients were consistent with results from the total Phase IIIb study population (Poster #TBC)⁴ and pivotal randomised controlled trials of afatinib^{1,2}
- In this sub-study, clinical benefit was also demonstrated across all subgroups assessed

References

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