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Real-World Experience with Afatinib after Failure of First-Generation Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor

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Methodology

- A retrospective observational study of patients with *EGFR* mutant advanced NSCLC receiving afatinib after failure of first-generation *EGFR*-TKI in University Malaya Medical Center from 1st December 2014 to 30th April 2018

Table 1. Demographic and clinical characteristics of 27 patients on afatinib after first generation EGFR-TKI failure

Demographic and clinical characteristics		
Age, years	Means ± SD	63.4 ± 9.6
Gender, No. (%)	Male	15 (55.6)
	Female	12 (44.4)
Smoking status, No. (%)	Never smoker	20 (74.1)
	Ex/current smoker	7 (25.9)
ECOG performance status, No. (%)	0-1	23 (85.2)
	2-4	4 (14.8)
Stage, No. (%)	IIIB	2 (7.5)
	IV	25 (92.5)
Symptomatic brain metastases, No. (%)	No	24 (88.9)
	Yes	3 (11.1)
EGFR mutation subtype, No. (%)	Exon 19 del	13 (48.1)
	Exon 21 L858R	11 (40.7)
	Rare/complex mutation	2 (7.4)
	Not tested*	1 (3.7)

First-line EGFR-TKI of patients that subsequently received afatinib

- 23 patients received first-line gefitinib
- 4 patients received first-line erlotinib
- Median progression-free survival (mPFS) with first-line first generation EGFR-TKI was 11.9 months
- 15 (55.6%) patients had disease progression (PD) while on second-line afatinib

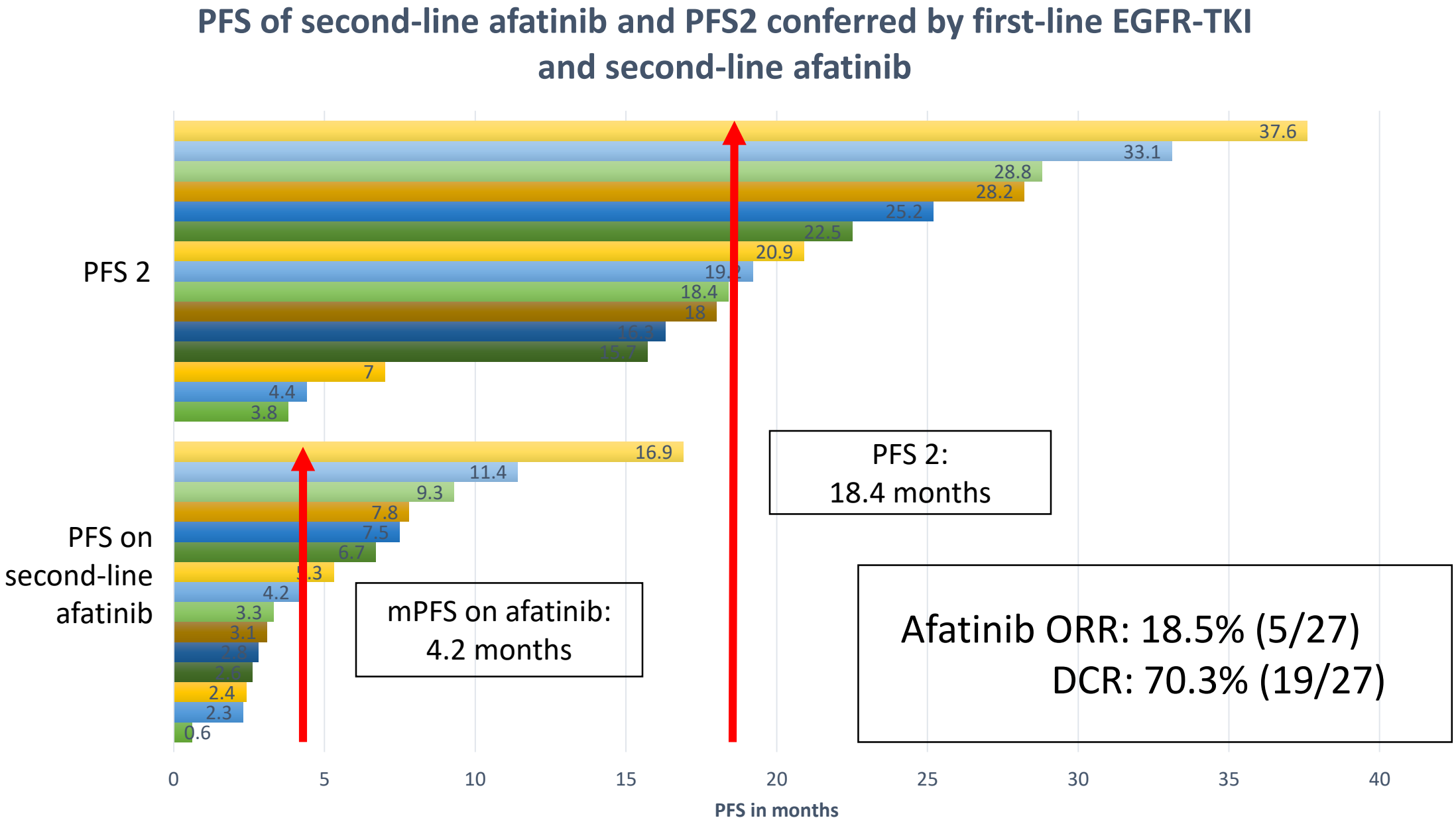

Figure 1. 15 out of 27 (55.6%) patients had progression of disease after afatinib. The mPFS of second-line afatinib was 4.2 months; while median time-to-treatment failure (mTTF) was 5.7 months. The mPFS2 conferred by first-line first-generation *EGFR*-TKI followed by second-line afatinib was 18.4 months. The overall response rate to afatinib was 18.5% (5/27), while the disease control rate was 70.3% (19/27).

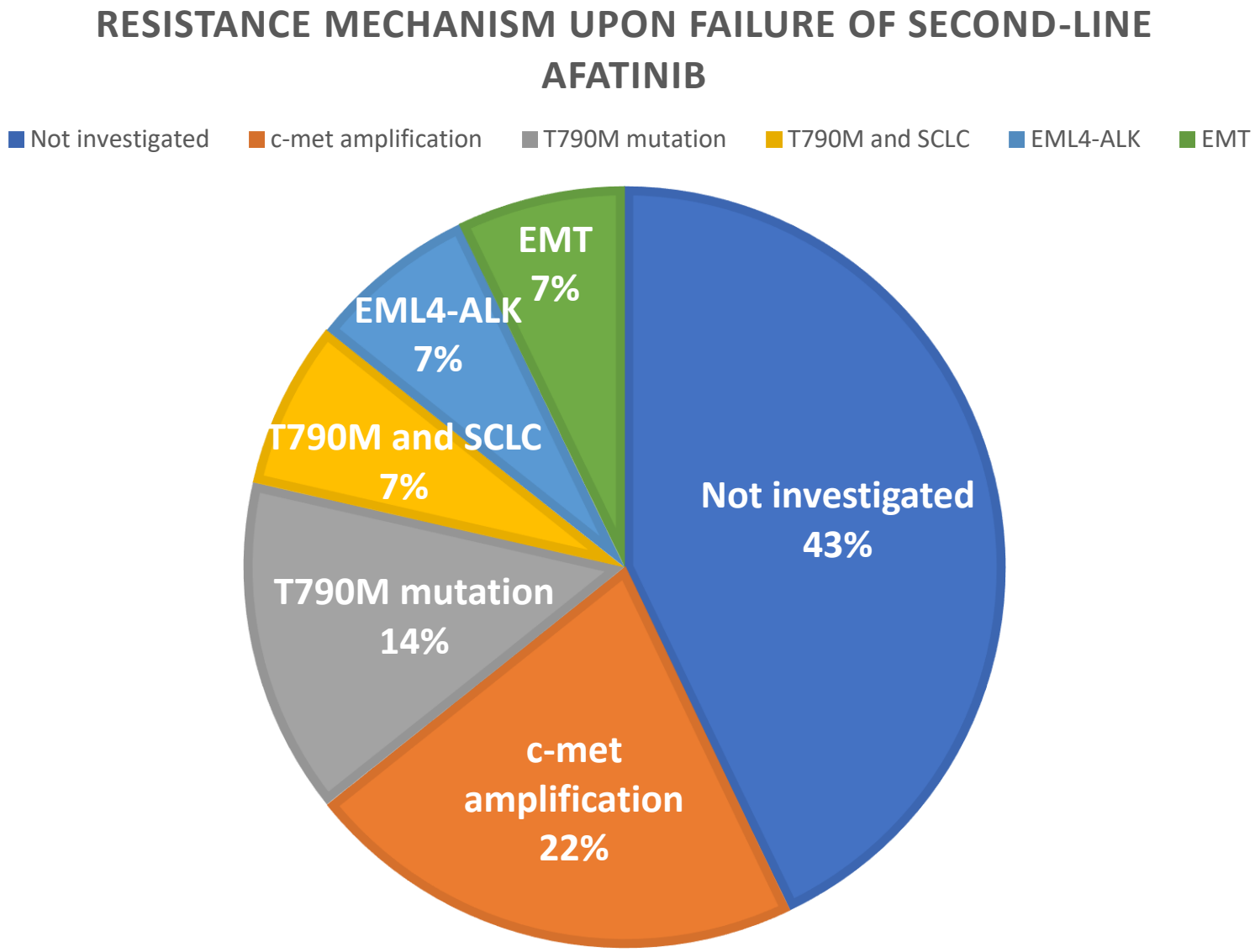

Figure 2. 9 of the 15 patients (69.2%) with PD on afatinib were investigated for resistance mechanisms, 3 had *T790M* mutation with one of them also having small cell lung cancer (SCLC) transformation, 3 had *c-MET* amplification, and one each had *EML4-ALK* rearrangement and epithelial mesenchymal transition (EMT).

Conclusions

- After failure of first-generation *EGFR*-TKI, afatinib provides additional few months of disease control
- The mPFS of sequential treatment with first-generation *EGFR*-TKI followed by afatinib was longer than the mPFS of first-line afatinib alone
- Other than *T790M mutation,* other less resistance mechanisms were also observed when afatinib was used after first-generation EGFR-TKI failure