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A combined analysis of two Phase IIIb studies of afatinib in EGFR TKI-naïve patients with *EGFR* mutation-positive NSCLC

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Introduction

- First-line afatinib significantly improved PFS compared with platinum-doublet chemotherapy in patients with *EGFR*m+ NSCLC, including patients with uncommon mutations, in two Phase III studies:[1,2]
  - LUX-Lung 3[1]: median 11.1 months vs 6.9 months, HR=0.58; p=0.001
  - LUX-Lung 6[2]: median 11.0 vs 5.6 months, HR=0.28; p<0.0001
- First-line afatinib also significantly improved PFS compared with gefitinib in the Phase IIb LUX-Lung 7 study[3] (median 11.0 vs 10.9 months, HR=0.73; p=0.017)
  - TTF was significantly longer with afatinib vs gefitinib (median 13.7 vs 11.5 months, HR=0.73; p=0.0073)
- Here, we report a combined analysis of outcomes from two large Phase IIIb studies (NCT01853826 and NCT01953913) of afatinib in EGFR TKI-naïve patients treated in a setting similar to real-world clinical practice
  - This included patients with brain metastases, poor ECOG PS and uncommon mutations, and those who were treated in second or later lines

ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*m+, *EGFR* mutation positive; HR, hazard ratio; PFS, progression-free survival; TKI, tyrosine kinase inhibitor; TTF, time to treatment failure

Methods

Key inclusion criteria for NCT01853826 and NCT01953913

- Locally advanced/metastatic *EGFR*m+ NSCLC
- EGFR TKI-naïve
- ECOG PS 0–2
- Patients with asymptomatic brain metastases were permitted

Dosing

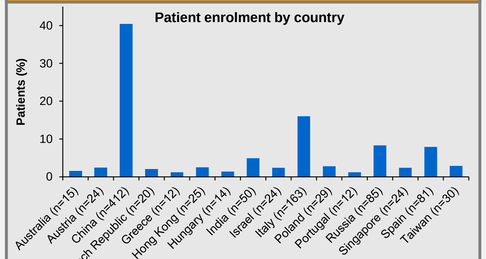
- Patients received afatinib 40 mg/day until PD or lack of tolerability (treatment beyond asymptomatic PD allowed)
- Dose reduction to a minimum of 20 mg/day was permitted

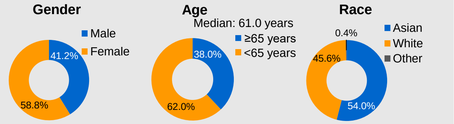
Outcome measures

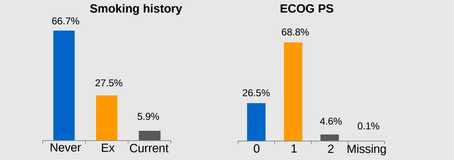
Safety	SAEs, AEs leading to discontinuation, and DRAEs
TTSP	The length of time from the start of treatment until the first documented symptomatic progression
PFS	Time from treatment initiation to disease progression, or death from any cause
ORR	Patients with CR or PR (as a proportion of the total number of patients with a recorded response)

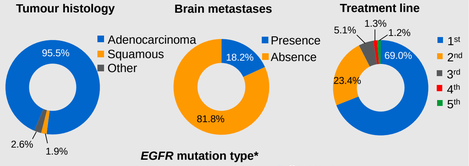
AE, adverse event; CR, complete response; DRAE, drug-related adverse event; ORR, overall response rate; PD, progressive disease; PR, partial response; SAE, serious adverse event; TTSP, time to symptomatic progression

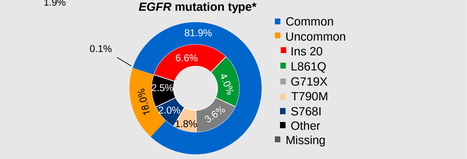
Baseline characteristics (N=1020)











*Patients may appear in more than one mutation category

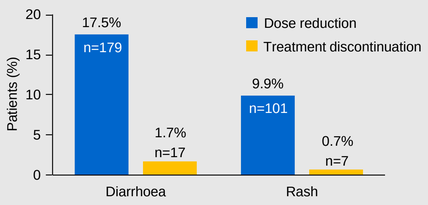
Safety (N=1020)

- Safety data (Table 1) were consistent with previous results seen in the LUX-Lung 3, 6 and 7 trials; AEs were predictable and manageable[1–3]
- AEs of any grade and grade ≥3 occurred in 99% and 55% of patients, respectively

Table 1. Overall summary of AEs

	Afatinib 40 mg/day			
n (%)	**All grades**	**Grade 3**	**Grade 4**	**Grade 5**
Any AE	1012 (99.2)	380 (37.3)	61 (6.0)	115 (11.3)
AE leading to dose reduction	412 (40.4)	270 (26.5)	4 (0.4)	0
AE leading to treatment discontinuation	152 (14.9)	65 (6.4)	24 (2.4)	31 (3.0)
SAE	366 (35.9)	113 (13.0)	51 (5.0)	115 (11.3)
DRAE	990 (97.1)	343 (33.6)	13 (1.3)	5 (0.5)
DRAE in ≥10% of patients				
Diarrhoea	901 (88.3)	131 (12.8)	5 (0.5)	0
Rash	624 (61.2)	94 (9.2)	0	0
Paronychia	407 (39.9)	32 (3.1)	0	0
Stomatitis	204 (20.0)	18 (1.8)	0	0
Mouth ulceration	146 (14.3)	10 (1.0)	0	0
Mucosal inflammation	143 (14.0)	16 (1.6)	0	0
Dry skin	126 (12.4)	2 (0.2)	0	0

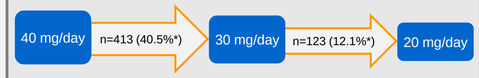
Figure 1. Common AEs leading to dose reduction and treatment discontinuation



152 (14.9%) patients had AEs leading to treatment discontinuation
54 (5.3%) patients had DRAEs leading to treatment discontinuation

Safety (N=1020)

Dose reduction



*Percentage of the overall population who originally received 40 mg

Efficacy (N=1020)

- Median TTSP was 14.6 months (95% CI:13.8–15.8) (Figure 2) and median PFS was 12.9 months (95% CI: 11.6–13.7) (Figure 3)

Figure 2. KM curve of TTSP

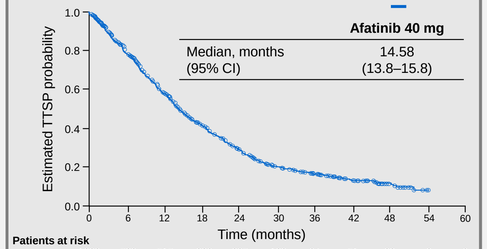
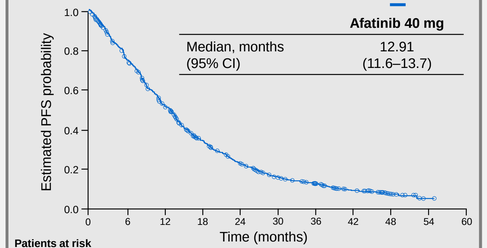


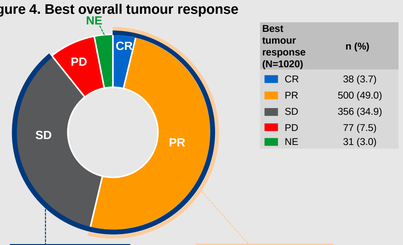
Figure 3. KM curve of PFS



CI, confidence interval; KM, Kaplan–Meier

Efficacy (N=1020)

Figure 4. Best overall tumour response



Best tumour response (N=1020)	n (%)
CR	38 (3.7)
PR	500 (49.0)
SD	356 (34.9)
PD	77 (7.5)
NE	31 (3.0)

DCR: n=894 (87.6%)

ORR: n=538 (52.7%)

Duration of objective response: 12.9 months

Duration of disease control: 13.9 months

DCR, disease control rate; NE, not evaluable; SD, stable disease

Key findings and conclusions

- These were two large, prospective 'real-world' afatinib studies, which included patients treated with afatinib in later lines, patients with ECOG PS 2, patients with brain metastases, and patients with uncommon mutations
- Afatinib had a predictable and manageable safety profile, consistent with previous results seen in LUX-Lung 3, 6 and 7[1–3]
- Efficacy findings were encouraging, with a median TTSP of 14.6 months, median PFS of 12.9 months and median duration of objective response of 12.9 months
- Here, the effectiveness of afatinib in patients with *EGFR*m+ NSCLC, with no prior EGFR TKI treatment, has been demonstrated in a real-world patient population

References

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2. Wu Y-L, et al. Lancet Oncol 2014;15:213–22
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