Overall survival with afatinib versus chemotherapy in patients with NSCLC harboring common *EGFR* mutations: subgroup analyses by race/ethnicity in LUX-Lung 3 and LUX-Lung 6

#445P

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INTRODUCTION

- Afatinib, an irreversible ErbB family blocker, demonstrated superior progression-free survival (PFS) as first-line therapy versus standard platinum-doublet chemotherapy in *EGFR* mutation-positive NSCLC patients in two large Phase III trials (LUX-Lung [LL] 3 and 6)[1,2]
- A more pronounced treatment effect with afatinib was observed in the ~89% of patients with NSCLC harboring the two most frequently reported *EGFR* mutations (Del19 or L858R)[1–3]
  - Median PFS with afatinib versus chemotherapy in patients with common mutations was 13.6 vs 6.9 months in LL3 (hazard ratio [HR]=0.47, p<0.0001) and 11.0 vs 5.6 months in LL6 (HR=0.25, p<0.0001)
  - Median overall survival (OS) with afatinib versus chemotherapy in patients with common mutations was 31.6 vs 28.2 months in LL3 (HR=0.78, p=0.109) and 23.6 vs 23.5 months in LL6 (HR=0.83, p=0.176)
- In both trials, afatinib significantly improved OS versus chemotherapy in patients with Del19 mutations (LL3: HR=0.54, p=0.0015; LL6: HR=0.64, p=0.023); no significant difference was observed for the L858R mutation subgroup (LL3: HR=1.30, p=0.292; LL6: HR=1.22, p=0.343)[3]

METHODS

Patients and study design

- Randomized, open-label, Phase III studies conducted globally (LL3; NCT00949650) and in China, South Korea and Thailand (LL6; NCT01121393)[1,2]
- Treatment-naïve patients with *EGFR* mutation-positive Stage IIIB/IV lung adenocarcinoma were randomized (2:1) to afatinib (40 mg/day) or up to 6 cycles of standard-of-care, platinum-doublet chemotherapy, selected based on the regulatory requirements of the different regions (LL3: cisplatin + pemetrexed; LL6: cisplatin + gemcitabine)
- The primary endpoint for each study was PFS; OS was a key secondary endpoint

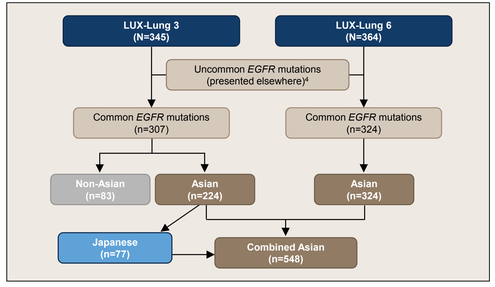
Statistical analyses

- OS analyses were conducted via a log-rank test and Cox proportional hazards models stratified by *EGFR* mutation type (Del19/L859R/Other) and race/ethnicity (Asian/non-Asian; LL3 only)[3]
- Preplanned subgroup analyses included
  - *EGFR* mutation type (Del19/L858R/Other) in each trial
  - Patients with common *EGFR* mutations (Del19 or L858R) in each trial
  - Asian, non-Asian (LL3) and Japanese patients (LL3)

OBJECTIVE

- To investigate whether the OS findings with afatinib versus standard platinum-doublet chemotherapy in NSCLC patients harboring common *EGFR* mutations (Del19 or L858R) enrolled in the LL3 and LL6 trials are consistent across different preplanned race/ethnic subgroups

Figure 1. Race/ethnic subgroups analyzed in LUX-Lung 3 and LUX-Lung 6



RESULTS

- OS by race/ethnicity in patients with NSCLC harboring common *EGFR* mutations (Del19 or L858R) treated with afatinib versus chemotherapy is displayed in Table 1

Table 1. OS by race/ethnicity in NSCLC patients harboring common *EGFR* mutations (Del19 or L858R)

	Median OS for afatinib vs CT (mo)	HR (95% CI)	p value
Non-Asian	28.1 vs 20.7	0.68 (0.39–1.20)	0.179
Asian	27.3 vs 24.7	0.82 (0.66–1.03)	0.083
Japanese	46.9 vs 35.0	0.57 (0.29–1.11)	0.097

CI, confidence interval; CT, chemotherapy; mo, months

- Among patients with common *EGFR* mutations, significant OS improvements with afatinib versus chemotherapy were observed in those with *EGFR* Del19 mutation-positive disease in all race subgroups analyzed (Figures 2–4)

Figure 2. OS in non-Asian patients with *EGFR* Del19 mutation-positive NSCLC

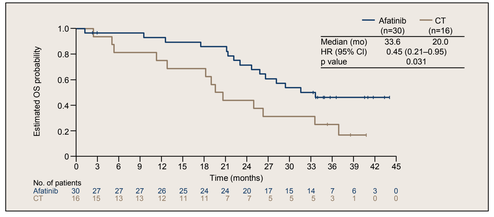


Figure 3. OS in Asian patients with *EGFR* Del19 mutation-positive NSCLC

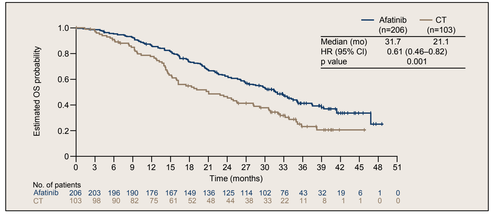
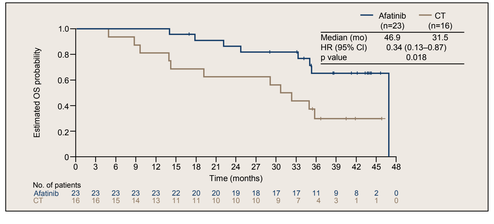


Figure 4. OS in Japanese patients with *EGFR* Del19 mutation-positive NSCLC



- No significant differences in OS with afatinib versus chemotherapy were observed for patients with *EGFR* L858R mutation-positive disease in any of the race/ethnic subgroups analyzed (Table 2)

Table 2. OS by race/ethnicity in patients with *EGFR* L858R mutation-positive NSCLC

	Median OS for afatinib vs CT (mo)	HR (95% CI)	p value
Non-Asian (n=37)	19.8 vs 21.2	1.22 (0.50–2.99)	0.668
Asian (n=239)	22.1 vs 27.0	1.25 (0.89–1.74)	0.191
Japanese (n=38)	41.7 vs 40.3	1.13 (0.40–3.21)	0.821

- In patients harboring common *EGFR* mutations, treatment beyond first-line therapy was balanced across study treatment arms in each race/ethnic subgroup (Table 3); no notable differences were observed in the Del19 or L858R subgroups

Table 3. Treatment beyond first-line therapy by race/ethnicity in NSCLC patients harboring common *EGFR* mutations

	Afatinib	CT
Non-Asian, n	54	29
Discontinued study treatment, n (%)	46 (100)	29 (100)
Subsequent systemic therapy	32 (70)	24 (83)
Chemotherapy	29 (63)	9 (31)
EGFR TKI therapy	21 (46)	20 (69)
Asian, n	365	183
Discontinued study treatment, n (%)	332 (100)	183 (100)
Subsequent systemic therapy	235 (71)	134 (73)
Chemotherapy	216 (65)	69 (38)
EGFR TKI therapy	110 (33)	119 (65)
Japanese, n	50	27
Discontinued study treatment, n (%)	44 (100)	27 (100)
Subsequent systemic therapy	39 (89)	27 (100)
Chemotherapy	35 (80)	21 (78)
EGFR TKI therapy	24 (55)	27 (100)

TKI, tyrosine kinase inhibitor

- The safety profile of afatinib was consistent across race/ethnic subgroups and with that observed in the LL3 and LL6 total populations[1,2]

CONCLUSIONS

- OS findings were consistent across preplanned subgroup analyses of Asian, non-Asian and Japanese patients with NSCLC harboring common *EGFR* mutations, with numerical improvements in median OS observed with afatinib versus standard platinum-doublet chemotherapy
- Significant improvements in OS were observed with afatinib versus chemotherapy in patients with NSCLC harboring *EGFR* Del19 mutations in all race/ethnic subgroups analyzed, with 10- to 15-month improvements in median OS observed between treatment arms
  - Median OS was not significantly different between treatment arms in NSCLC patients harboring *EGFR* L858R mutations in any of the race/ethnic subgroups
- The OS benefit observed with afatinib was independent of subsequent anticancer therapies received following first-line study treatment
- These OS findings are consistent with the analysis of the total LL3 and LL6 populations,[3] and further support the use of afatinib as first-line therapy for patients with NSCLC harboring common *EGFR* mutations independent of race/ethnicity, particularly those with Del19 mutation-positive disease

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