A Phase IIb open-label, single-arm study of afatinib in EGFR TKI-naïve patients with EGFRm+ NSCLC: An interim analysis

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Introduction

- Afatinib, an irreversible second-generation EGFR family blocker, is approved in many countries for the first-line treatment of patients with advanced EGFR-mutation-positive (EGFRm+) NSCLC from the Phase III B LUX-Lung 3 (LL3) and LUX-Lung 7 (LL7) trials that suggest afatinib may offer more favorable clinical outcomes over standard platinum-based chemotherapy in EGFRm+ NSCLC.
- In a pre-specified analysis of Del19+L858R patients from LL3 and LL7, afatinib significantly prolonged overall survival (OS) versus chemotherapy.
- Here, we present an interim analysis of a large Phase IIb open label study of afatinib in a broad Asian population of EGFR TKI-naïve patients with EGFRm+ NSCLC, in a setting similar to real-world practice.

Methods

- Study objective: To evaluate the safety of afatinib in patients with locally advanced or metastatic NSCLC harboring EGFR mutation(s) and who have never been treated for NSCLC.
- Patients 18-75 years old with advanced NSCLC and one of the following EGFR mutations: Del19, L858R, Del19+L858R, L858R+T790M (Del19 and/or L858R).
- Three single-arm cohort studies: LL3 (250 patients evaluable), LL6 (200 patients evaluable), and LL7 (250 patients evaluable).

Baseline characteristics

- As of 13 February 2017, data were available for 479 patients.
- Median age: 64.0 years (range, 21.0-85.0 years).
- Gender: Male, 54.4% (259 patients); Female, 45.6% (220 patients).
- Smoking history: Smoking, 66.2% (317 patients); Never-smoked, 33.8% (162 patients).

Safety and tolerability

- Dose modifications: The reduction in 30 mg afatinib was required for 24.9% of patients - 6.1% had further reductions to 20 mg afatinib.
- Safety and tolerability: No afatinib-induced deaths in all trials. Treatment discontinuation due to AEs was rare (1.0% in LL3, 0.6% in LL6, 0.4% in LL7).
- Median PFS of afatinib in EGFR TKI naïve patients with EGFRm+ NSCLC was 15.3 months (95% CI: 12.8-17.3) from this interim analysis of a clinical study.

Key findings and conclusions

- Safety and tolerability: The study data of afatinib from this interim analysis of a large-scale Asian population of EGFR TKI naïve, EGFRm+ NSCLC patients are consistent with those of the LL3, 6, and 7 studies.
- Dose reductions were lower in this interim analysis (25%) versus 52%, 28% and 39% in the LL3, 6, and 7 trials, respectively, suggesting that in real-world practice most treatment modifications are manageable and result in few treatment discontinuations.

Efficacy

- Median TTSP was longer in median PFS of afatinib in EGFR TKI naïve patients with EGFRm+ NSCLC, which suggests that afatinib treatment may be continued beyond progression.
- Afatinib demonstrated encouraging TTSP and PFS in patients with common and/or uncommon EGFR mutations. TTSP and PFS were longer in patients with uncommon EGFR mutations compared to those with common EGFR mutations.
- Data from this interim analysis will be updated in a full analysis of the trial.

References

- National Cancer Institute: Common Terminology Criteria for Adverse Events (CTCAE), version 4.03.
- World Health Organization: The 2010 International Classification of Functioning, Disability and Health (ICF).