Second-line afatinib for patients with locally advanced or metastatic NSCLC harbouring common EGFR mutations: a Phase IV study

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Introduction

• The oral, irreversible EGFR family blocker afatinib is approved in many countries for the treatment of EGFR mutation-positive (EGFR+)-locally advanced or metastatic NSCLC.
• The recommended starting dose of afatinib is 40 mg/day.
• Afatinib improved PFS versus chemotherapy in the LUX-Lung 3 and 6 trials,1,2 and versus gefitinib in LUX-Lung 73 in patients with EGFR mutation-positive (EGFR+) lung cancer.
• Alfatinib improved PFS versus chemotherapy in the LUX-Lung 3 and 6 trials,1,2 and versus gefitinib in LUX-Lung 73 in patients with EGFR mutation-positive (EGFR+) lung cancer.
• Afatinib improved PFS versus chemotherapy in the LUX-Lung 3 and 6 trials,1,2 and versus gefitinib in LUX-Lung 73 in patients with EGFR mutation-positive (EGFR+) lung cancer.

Methods

• Multicenter, open-label, single-arm Phase IV study conducted across 24 sites in 7 countries (Egypt, Malaysia, Philippines, Poland, Romania, Serbia, and Thailand).
• The LUX-Lung 2 study supports the use of second-line afatinib in patients with EGFR+ NSCLC harbouring EGFR exon 19 deletion (Del19) and/or L858R mutation.
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Objectives

• Key inclusion criteria

1. Aged ≥18 years
2. Presence of locally advanced or metastatic NSCLC with progression or recurrence following first-line platinum-based chemotherapy and were on EGFR TKI naïve.

Methods (Cont’d)

• More than 1 prior line of platinum-based chemotherapy, but only 7/68 (10%) patients received ≥3 prior lines of chemotherapy.

Results

• Patients were mostly white (68.3%) and had a mean age (Std dev) of 59.9 (9.8) years.
• 50% of patients achieved a confirmed OR, with a median duration of response was 10.8 months.

Table 1. Patient disposition. 

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<thead>
<tr>
<th>AE</th>
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<th>%</th>
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<tbody>
<tr>
<td>Afatinib-related AEs</td>
<td>113</td>
<td>95.0</td>
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<tr>
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Efficacy

• Objectives response

1. The primary study endpoint of OR by investigator assessment was achieved to 30 (57%) patients.
• 50% of patients achieved a confirmed OR, with a median duration of response was 10.8 months.
• Median duration of disease control was 19.9 months (95% CI: 11.8, 30.7)

Kaplan-Meier curve of duration of OR

Disease control

Expressed levels of afatinib at 20 mg

Kaplan-Meier curve of duration of disease control

Endpoints

• More than 1 prior line of platinum-based chemotherapy, but only 7/68 (10%) patients received ≥3 prior lines of chemotherapy.

Key inclusion criteria

• Aged ≥18 years
• Presence of locally advanced or metastatic NSCLC with progression or recurrence following first-line platinum-based chemotherapy and were on EGFR TKI naïve.

Endpoints

• More than 1 prior line of platinum-based chemotherapy, but only 7/68 (10%) patients received ≥3 prior lines of chemotherapy.

Key exclusion criteria

• Aged <18 years
• Current smoker
• Del19 & L858R
• EGFR wild-type
• Patient had received prior EGFR TKI therapy
• Y79F mutation

Results (Cont’d)

• Median PFS was 10.9 months (95% CI: 6.4, 13.2).
• 39 patients (65.0%) experienced an event contributing to PFS analysis (i.e. disease progression as determined by investigator, death).

Safety

• Summary of AEs

1. The most commonly occurring drug-related AEs of any grade were gastrointestinal (GI) toxicities and rash.
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References


Results

• Median PFS was 10.9 months (95% CI: 6.4, 13.2).
• 39 patients (65.0%) experienced an event contributing to PFS analysis (i.e. disease progression as determined by investigator, death).

Conclusions

• This study supports the use of afatinib 40 mg/day as second-line therapy in patients with EGFR+ NSCLC who had progressing disease following first-line platinum-based chemotherapy and were on EGFR TKI naïve.
• The safety and tolerability profile of afatinib was consistent with previous clinical trials, and the current study supports the use of afatinib as second-line therapy in patients with EGFR mutation-positive (EGFR+) lung cancer.

Summary

• 55% of patients achieved a confirmed OR, with a median duration greater than 1 year: median PFS was 10.9 months.
• >60% of patients had disease control, with a median duration of 11.9 months.
• The safety and tolerability profile of afatinib was consistent with the known safety profile of afatinib, with the most common afatinib-related AEs observed being diarrhoea and rash.
• The current study supports the use of afatinib as second-line therapy at the recommended 40 mg/day starting dose in EGFR mutation-positive patients with locally advanced/metastatic NSCLC harbouring common EGFR mutations (Del19 & L858R), after failure of first-line chemotherapy.