Afatinib in patients with EGFR mutation-positive NSCLC harbouring uncommon mutations: overview of clinical data

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Background

In patients with adenocarcinoma, the most common types of NSCLC, mutations of EGFR have been reported to:

- Afatinib reduced cell proliferation and inhibited EGFR phosphorylation at L858R.
- The current standard of care for first-line treatment of patients with NSCLC and EGFR mutations includes TKI, tyrosine kinase inhibitor.

Clinical data

Here, we review clinical data for afatinib in people with NSCLC harbouring uncommon EGFR mutations, including data from the clinical trial and real-world clinical settings.

Post-hoc analysis of LUX-Lung 2, 3 and 6

75% of 600 patients (13%) treated with afatinib in the three trials had tumours harbouring uncommon EGFR mutations.

Patients were grouped according to mutation status:

- Group 1: Point mutations or duplications in exons 20, 21 alone, or in combination with other exon
- Group 2: At least one T790M mutation in exon 20, alone or in combination with other mutations
- Group 3: At least two mutations in exons 20, 21

Efficacy outcomes (N=75)

- ORR: partial response + complete response
- Median PFS and OS

Other labels already include non-resistant uncommon mutations: overview of clinical data

Based on data from the post-hoc analysis of LUX-Lung 2, 3 and 6, the label for afatinib was expanded by:

- U.S. label expansion: first-line afatinib for patients with NSCLC with activating EGFR mutations and ECOG PS 0–2; 165 patients with recurrent/metastatic NSCLC were treated with first-line afatinib at a single centre in South Korea

Clinical data (cont’d)

Ongoing Phase Ib open-label, single-arm study: interim analysis16

- Patients (N=75) received afatinib daily at 40 mg, orally
- Median PFS and OS

References

7. Retrospective real-world analysis14,15

- 165 patients with recur/metastatic NSCLC were treated with first-line afatinib at a single centre in South Korea

- EGFR mutation type15


- Summary

- Afatinib has shown pre-clinical and clinical activity in patients with NSCLC harbouring certain uncommon EGFR mutations.

- ORR, PFS and OS outcomes from a post-hoc analysis of LUX-Lung 2, 3 and 6 showed that afatinib was more active in patients with tumours harbouring point mutations or duplications in exons 18–21, compared with do novo T790M mutations or exon 20 insertions

- The activity of afatinib against certain uncommon EGFR mutations is being substantiated by studies outside of the randomised controlled trial setting, including in the real-world clinical setting, demonstrating high ORR and long PFS14,15

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Clinical data (cont’d)

Retrospective real-world analysis14,15

- 165 patients with recurrent/metastatic NSCLC were treated with first-line afatinib at a single centre in South Korea

- EGFR mutation type14

- Median PFS, months

- ORR* by mutation

- Median OS

- U.S. label expansion: first-line afatinib for patients with NSCLC with activating EGFR mutations and ECOG PS 0–2; 165 patients with recurrent/metastatic NSCLC were treated with first-line afatinib at a single centre in South Korea

- The current standard of use for first-line treatment of patients with EGFR-mutant NSCLC is as follows:

- Reversible first-generation EGFR TKI blocker: gefitinib (T正版 & Z版)
- Irreversible second-generation EGFR family blocker: dacomitinib (ARCHER 10509)
- Reversible first-generation EGFR TKIs: gefitinib, erlotinib, lapatinib

- Common, Del19 (n=114) 19.1 -
- Other, uncommon mutations only (not including patients with tumours harbouring both common and uncommon mutations) 6.2 -

- EGFR T790M was detected in 20% of tumours (13 patients).

- In patients with NSCLC harbouring uncommon EGFR mutations, including in the real-world clinical setting, afatinib showed high ORR and long PFS

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