Effectiveness of afatinib in clinical practice - first results of the GIDEON trial: a prospective non-interventional study in EGFR-mutated NSCLC in Germany

Introduction

• Afatinib irreversibly inhibits all homo- and heterodimers formed by members of the ErbB family.
• Afatinib is approved for the treatment of EGFR tyrosine kinase inhibitor (TKI) naïve patients with advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutations.1,2
• Numerous randomized clinical trials (RCTs) have shown significant improvement effects on survival with afatinib compared with chemotherapy or other EGFR TKIs, and a manageable safety profile.3–6

Methods

• Recruitment into the GIDEON NSCLC was initiated following launch of afatinib in Germany in February 2014:
  – First patient in: April 2014
  – Last patient in: December 2016
  • 160 patients were recruited at 49 centres across Germany (Fig. 1)
• Patient inclusion criteria:
  – ≥18 years
  – Diagnosed with advanced or metastatic NSCLC
  – Confirmed EGFR mutations
  – First patient in: April 2014
  – Last patient in: December 2016
• Disease characteristics:
  – NO induction chemotherapy
• Exclusion criteria:
  – History of brain metastasis

Patient demographics and baseline characteristics

• 160 patients were included in the analysis. 101 of whom received the study drug and were included in the analysis (Table 1) [Fig. 2].
• Median PFS was 13.9 months in the overall population; the median for Del19 patients has not been reached (Fig. 3).

• ORR and DCR were similar to the values reported for afatinib in the LUX-Lung 3, 6, and 7 studies

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Endpoints

Primary

• Progression-free survival at 12 months

Key Secondary

• PFS
• OS
• Objective response rate (ORR)
• Disease control rate (DCR)
• Time to progression
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• Time to progression

Results

• ORR and DCR were similar to the values reported for afatinib in the LUX-Lung 3, 6, and 7 studies

Progression-free survival

• The PFS rate at 12 months was 54.8% in the overall population

OS by mutation subtype

• OS data matured in 23.8 months; 1-year mortality rate: 79.7% for a median survival of over 23 months in the overall population

Key findings and conclusions

• The efficacy and safety of afatinib in the real-world setting is similar to that observed in clinical trials

• The results of this prospective NSCLC confirm the robust clinical data for afatinib in the routine clinical setting, especially in the elderly population, which is underrepresented in clinical trials

• Although a high number of patients with brain metastases (≥50%) and uncommon EGFR mutations (≤1%) were included in GIDEON, afatinib showed robust response rates across all patient subgroups and with a median PFS of 12.9 months

• In selected patients, a starting dose of >40 mg afatinib does not seem associated with an inferior PFS compared with <40 mg afatinib and were similar for all reported adverse events in the LUX-Lung 3, 6, and 7 studies

• The safety profile of afatinib was consistent with that determined in the LUX-Lung 3, 6, and 7 studies

• Preliminary OS analyses showed a median OS of 33.3 months in the overall population

• Final results are expected in 2019 including multivariate analyses and data for the 10-year sequence of outcomes followed by censoring

References


Figure 1. Patient recruitment centres.

Figure 2. Afatinib starting dose and dose modification (starting dose ≥40 mg).

Figure 3. Best response to afatinib, by investigator assessment.

Figure 4. ORR and DCR in patient subgroups.

Figure 5. Progression-specific survival (PFS) by (A) mutation subtype, (B) starting dose, (C) age, and (D) baseline brain metastases.

Figure 6. OS, by mutation subtype.

Figure 7. OS, by (A) mutation subtype, (B) starting dose, (C) age, and (D) baseline brain metastases.

Figure 8. OS, by (A) mutation subtype, (B) starting dose, (C) age, and (D) baseline brain metastases.

Figure 9. OS, by (A) mutation subtype, (B) starting dose, (C) age, and (D) baseline brain metastases.

Table 1. Patient demographics and baseline characteristics.