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Phase IV, open-label, multicentre trial of afatinib in patients aged ≥70 years with NSCLC harbouring common (Del19/L858R) *EGFR* mutations: preliminary results

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Overview

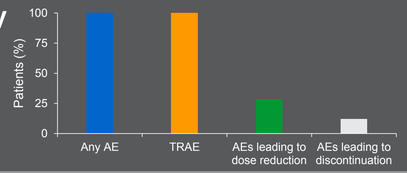
Question

Does afatinib demonstrate an acceptable safety profile in the treatment of patients aged ≥70 years with *EGFR* mutation-positive NSCLC?

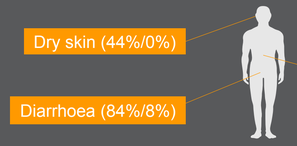
Investigation

Ongoing, multi-centre, single-arm, Phase IV study of afatinib (30 mg/day) in older patients (≥70 years) with recurrent or Stage IV NSCLC harbouring common (Del19 or L858R) *EGFR* mutations (NCT02514174)

Preliminary Data*



- N=25
- Patients experiencing treatment-related AEs (TRAEs; any grade/grade 3): 100%/24%
- Patients experiencing AEs leading to afatinib dose reduction: 28%
- Patients experiencing AEs leading to discontinuation of afatinib: 12%



TRAEs (all grade/grade 3)

- There were no grade >3 AEs
- The most common TRAEs were gastrointestinal and skin disorders

Conclusions

Afatinib is a well-tolerated treatment for patients aged ≥70 years with *EGFR*m+ NSCLC; AEs are usually manageable with supportive care and/or tolerability-guided dose reduction, and the rate of discontinuation due to AEs is comparable to that reported for younger patient populations[1,2]

Background

- Afatinib, an irreversible ErbB family blocker, is approved for first-line treatment of *EGFR*m+ NSCLC[3]
- While afatinib has demonstrated a predictable and manageable safety profile in first-line treatment of patients with *EGFR*m+ NSCLC,[1,2] elderly patients have been under-represented in clinical trials
- In LUX-Lung 3, 6 and 7, 362 (35%) patients were aged ≥65 years and 65 (6%) patients were aged ≥75 years[4]
  - PFS was improved with afatinib versus chemotherapy in patients aged ≥65 years in LUX-Lung 3 and 6[4]
  - Afatinib was generally well-tolerated; predominant TRAEs were diarrhoea, rash/acne and stomatitis[4]
  - AEs were usually manageable in older patients; 14% and 9% of patients aged ≥65 years discontinued afatinib treatment due to AEs in LUX-Lung 3 and 6, respectively, and 16% of patients aged ≥75 years discontinued afatinib treatment in LUX-Lung 7[4]
- In a post-marketing surveillance study of afatinib in Japanese patients with *EGFR*m+ NSCLC, 307 (19%) patients were aged ≥75 years; among 21 (1%) patients aged ≥75 years who received first-line afatinib starting at 30 mg, ORR was 76.2%[5]

Objective

- Determination of the occurrence of AEs leading to dose reduction of afatinib treatment in patients aged ≥70 years with NSCLC with common *EGFR* mutations

This is an ongoing trial; presented data are the result of snapshot analysis*

Methods

- Patients received afatinib 30 mg QD until progression or intolerable AEs
- Dose interruption and subsequent dose reduction to 20 mg QD were required following prolonged or intolerable grade 2 AEs, grade 2 renal dysfunction or any AE of grade ≥3

Figure 1. Study design

- Key inclusion criteria:
  - Age ≥70 years
  - Confirmed diagnosis of recurrent or Stage IV NSCLC not amenable for local radiotherapy
  - Documented *EGFR* mutation (Del 19 and/or L858R)
  - ECOG PS of 0 or 1
  - No prior systemic therapy for metastatic or recurrent NSCLC

Table 1. Endpoints in this study

Primary	• Occurrence of AEs leading to dose reduction of afatinib
Secondary	• Occurrence of grade ≥3 diarrhoea, rash/acne†, stomatitis† and paronychia† • Time to first dose reduction of afatinib caused by AEs
Other	• Progression-free survival • Objective response • Overall survival

Preliminary Data*

Table 2. Disposition of subjects

	n (%)
Enrolled	28‡
Entered	25§
Treated	25 (100.0)
Treated for ≥90 days	22 (88.0)
Median treatment duration	12.1 months
Still on treatment	11 (44.0)
Discontinued	14 (56.0)
Progressive disease	9 (36.0)
AEs	2 (8.0)
Patient refusal	1 (4.0)
Other	2 (8.0)

Figure 2. Patient demographics and baseline characteristics

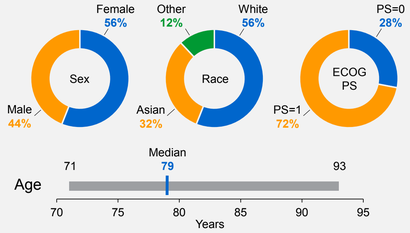


Table 3. Summary of AEs

	Afatinib 30 mg (N=25), n (%)
Patients with any AE	25 (100.0)
Grade 3	14 (56.0)
Grade >3	0 (0.0)
Treatment-related AE	25 (100.0)
Grade 1 or 2	19 (76.0)
Grade 3	6 (24.0)
AEs leading to dose reduction	7 (28.0)
AEs leading to discontinuation	3[¶#] (12.0)
Serious AE	9 (36.0)
Vomiting	2 (8.0)
Dehydration	2 (8.0)
Syncope	2 (8.0)

Serious AEs with occurrence ≥5% are listed

Figure 3. Most common TRAEs

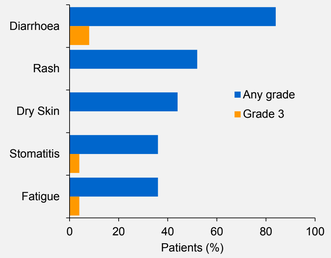
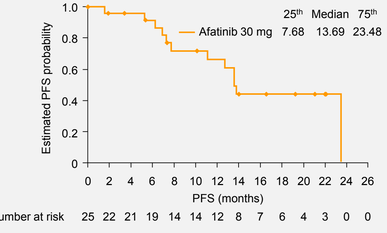
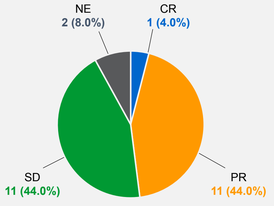


Figure 4. PFS and OS



Median OS was not evaluable at the time of analysis

Figure 5. Best overall response**



ORR: 48%
Disease control rate: 92%

Conclusions

- In this preliminary analysis, there were no unexpected safety findings during afatinib treatment of patients aged ≥70 years with *EGFR*m+ NSCLC
- The rate of afatinib discontinuation due to AEs compared favourably to that previously reported for younger patient populations[1,2]
- AEs could usually be managed with dose reduction and/or supportive care
- Advanced age did not appear to adversely affect the clinical benefits of afatinib
- In this ongoing trial, afatinib treatment resulted in an objective response in nearly a half of the patients, and a median PFS of greater than one year
- Clinicians should use judgement when prescribing afatinib to older adult patients, and should consider physiological age and factors such as functional status and comorbidity

This is an ongoing trial; presented data are preliminary and may differ from final results

Footnotes

*Snapshot analysis performed on 27 Aug 2018; †Grouped terms. AEs reported herein as preliminary data are preferred terms; ‡Enrolment has closed; §Three enrolled patients did not enter the study as they did not meet study criteria; ¶Fatigue (n=1), diarrhoea (n=1) and lower back pain (n=1); #The patient with lower back pain was later found to have progressive disease at discontinuation, and was included in the group that discontinued due to progressive disease (Table 2); **Investigator-assessed confirmed response

AE, adverse event; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *EGFR*m+, *EGFR* mutation-positive; NE, not evaluable; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; QD, once per day; SD, stable disease; TRAE, treatment-related adverse event

References

1. Sequist LV, et al. J Clin Oncol 2013;31:3327–34
2. Wu Y-L, et al. Lancet Oncol 2014;15:213–22
3. Boehringer Ingelheim. Gilotrif Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/201292s014lbl.pdf (Accessed: 11 Oct 2018)
4. Wu Y-L, et al. Clinical Lung Cancer 2018;19:e465–79
5. Yamamoto N, et al. WCLC 2017. Poster P3.01-035

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