Scan the QR code to get a PDF and interactive copy of the poster

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

1456P

Karen L. Reckamp,[1] Paul Gilman,[2] Balazs Halmos,[3] Mohammad Jahanzeb,[4] John McCann,[5] Harshita Paripati,[6] Lasika Seneviratne,[7] James A. Wallace,[8] Bjoern Rueter,[9] Anne Esler,[10] Elizabeth Dowling,[11] Marianna Koczywas[12]

[1]Department of Medical Oncology, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [2]Cancer Center, Lankenau Medical Center, Wynnewood, PA, USA; [3]Department of Oncology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA; [4]Sylvester Comprehensive Cancer Center, University of Miami, Deerfield Beach, FL, USA; [5]D'Amour Center for Cancer Care, Baystate Regional Cancer Program, Springfield, MA, USA; [6]Division of Hematology/Oncology, Mayo Clinic, Phoenix, AZ, USA; [7]Los Angeles Hematology/Oncology Medical Group, Los Angeles Cancer Network, Los Angeles, CA, USA; [8]Department of Hematology/Oncology and Geriatrics; UChicago Medicine: Ingalls, Harvey, IL, USA; [9]CMDA Oncology, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [10]Statistics, Syneos Health, Raleigh, NC, USA; [11]Study Management and Conduct, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [12]Department of Medical Oncology and Therapeutic Research, City of Hope Comprehensive Cancer Center, Duarte, CA, USA

Overview

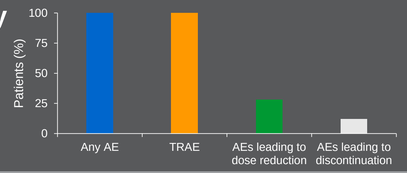
Question

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

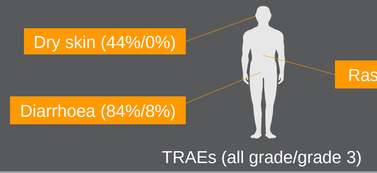
Investigation

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

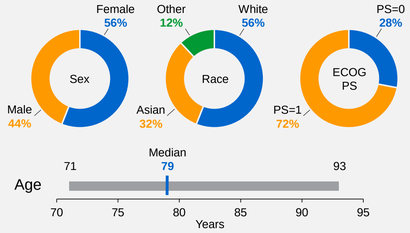


Table 3. Summary of AEs

	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

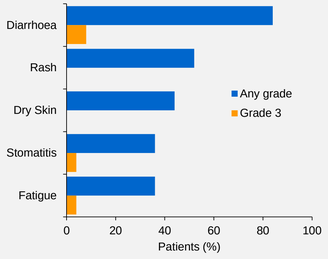
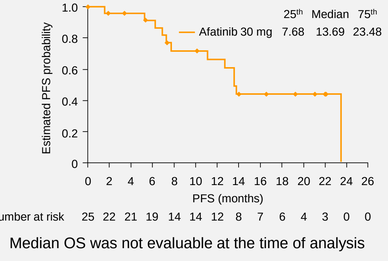
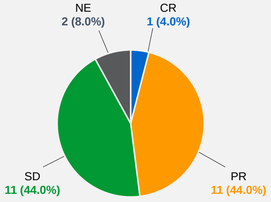


Figure 4. PFS and OS



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

Acknowledgements

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors received no direct compensation related to the development of the poster. Writing, editorial support, and formatting assistance for this poster was provided by Victoria Steele, PhD of GeoMed, an Ashfield company, part of UDG Healthcare plc, which was contracted and compensated by Boehringer Ingelheim Pharmaceuticals Inc. (BIPI), for these services. BIPI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations

Disclosures

This study was funded by Boehringer Ingelheim

Prof. Reckamp has held consulting roles with Boehringer Ingelheim, Exelixis, Genentech, Guardant, Loxo, Seattle Genetics, Takeda and Tesaro, and has received grants/research support to her institution from AbbVie, Acea, Adaptimmune, Boehringer Ingelheim, Bristol-Myers Squibb, Genentech, Guardant, Janssen, Loxo Oncology, Novartis, Pfizer, Seattle Genetics, Takeda, Xcovery and Zeno

Presented at the European Society for Medical Oncology Congress, 19–23 October 2018, Munich, Germany

Corresponding author email address: KReckamp@coh.org