Afatinib in chemotherapy pre-treated *EGFR* mutation-positive NSCLC

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Introduction

- The oral, irreversible ErbB family blocker, afatinib, is approved for the treatment of tyrosine kinase inhibitor-naïve patients with *EGFR* mutation-positive (*EGFR*m+) NSCLC, both as first-line therapy, and following progression on or after platinum-based chemotherapy[1]

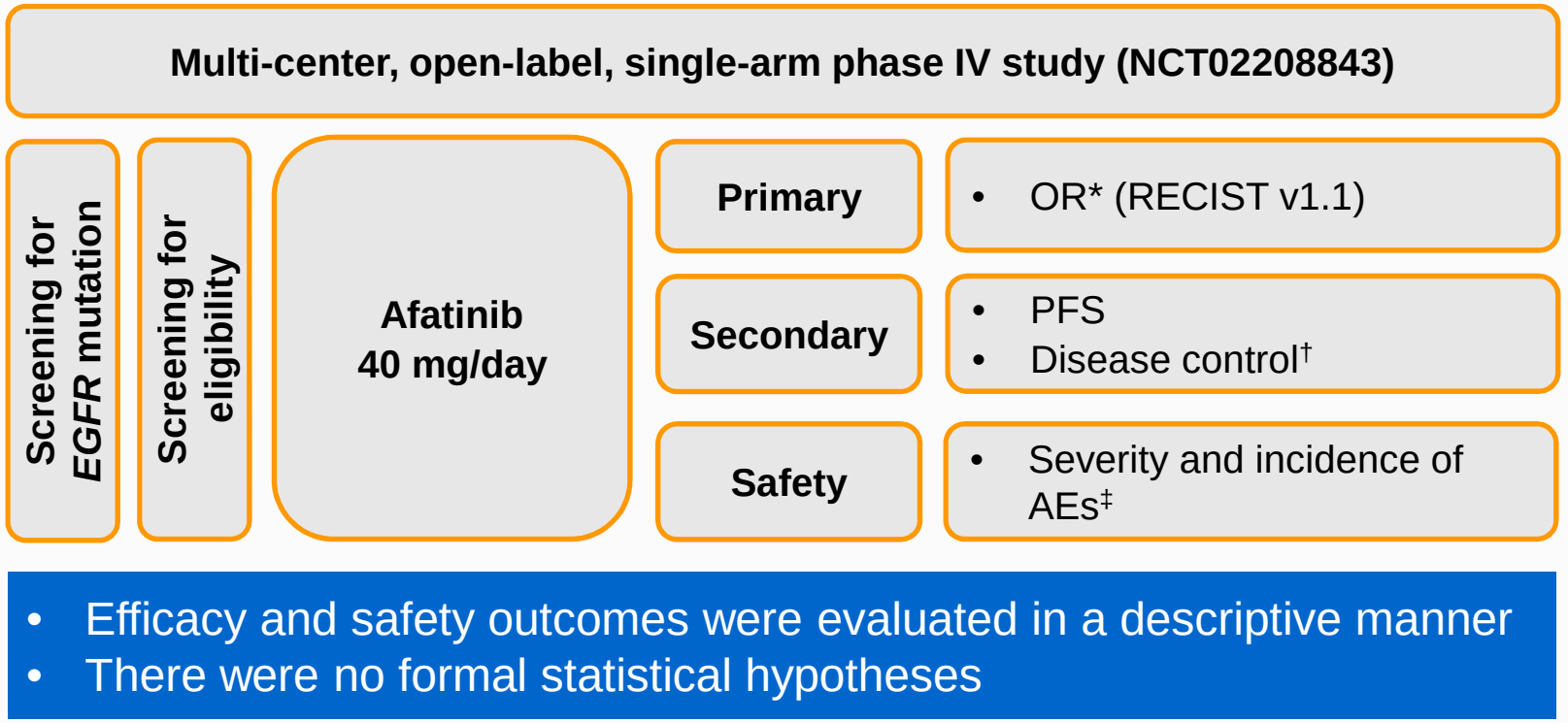
- In the LUX-Lung 2 study,[2] second-line afatinib demonstrated clinical activity and an acceptable safety profile in patients with advanced NSCLC harboring *EGFR* mutations following chemotherapy
  - However, the starting dose was 50 mg/day for most patients

Here, we report efficacy and safety of second-line afatinib at the recommended dose of 40 mg/day in patients with NSCLC harboring common *EGFR* mutations

EGFRm+, EGFR mutation-positive; TKI, tyrosine kinase inhibitor.

1. Boehringer Ingelheim Pharmaceuticals, Inc. Giotrif® Summary of Product Characteristics. May 2018.
2. Yang JC-H, et al. Lancet Oncol 2012;13:539–48.

Study design



- Efficacy and safety outcomes were evaluated in a descriptive manner
- There were no formal statistical hypotheses

*Defined as CR or PR; †Defined as CR, PR, or SD; ‡Graded according to US National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 3.0.
AE, adverse event; CR, complete response; OR, objective response; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors.

Patient eligibility criteria

Key inclusion criteria

- Aged ≥18 years
- Del19 and/or L858R
- ECOG PS 0 or 1
- Confirmed stage IIIB or IV lung adenocarcinoma
- Radiologically confirmed progression or recurrence during or following first-line chemotherapy

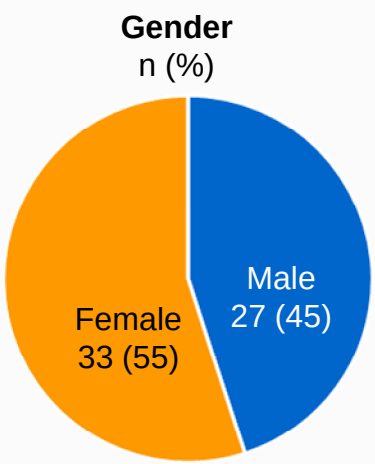
Key exclusion criteria

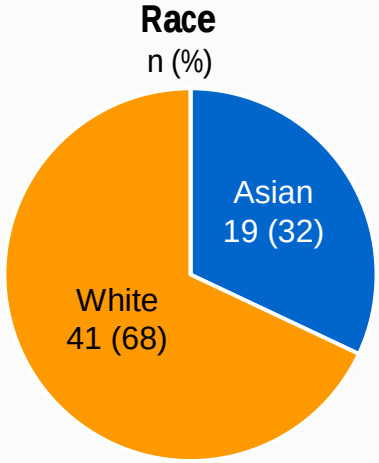
Previous treatment with:

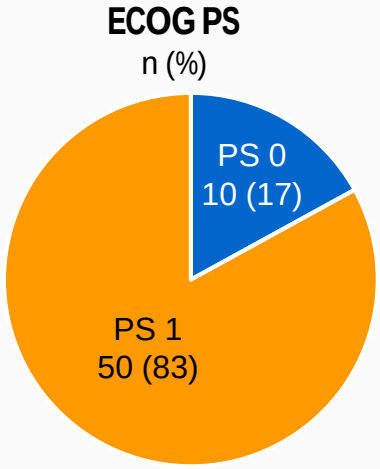
- More than 1 prior line of therapy*
- Less than 3 cycles of platinum-based chemotherapy
- Any EGFR-targeting TKI or antibody
- Any treatment within 3 weeks of the trial
- Major surgery within 4 weeks of the trial

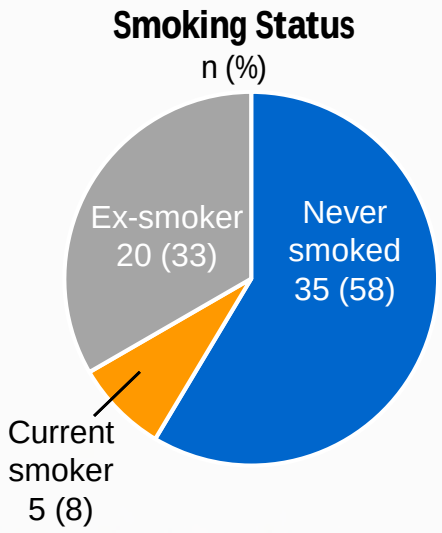
*Not including radiotherapy, radiosensitizers, and/or intrapleural administration of anti-cancer agents.
ECOG PS, Eastern Cooperative Oncology Group Performance Status.

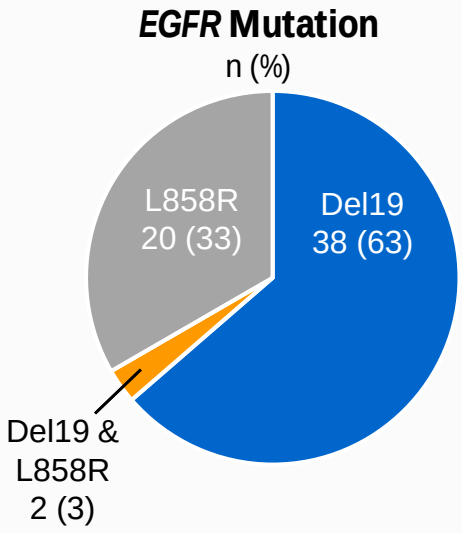
Baseline demographics and clinical characteristics

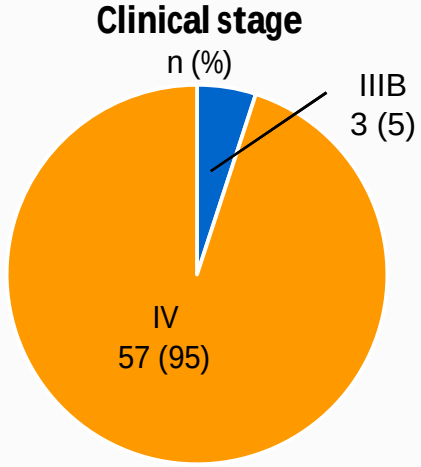












Patient disposition

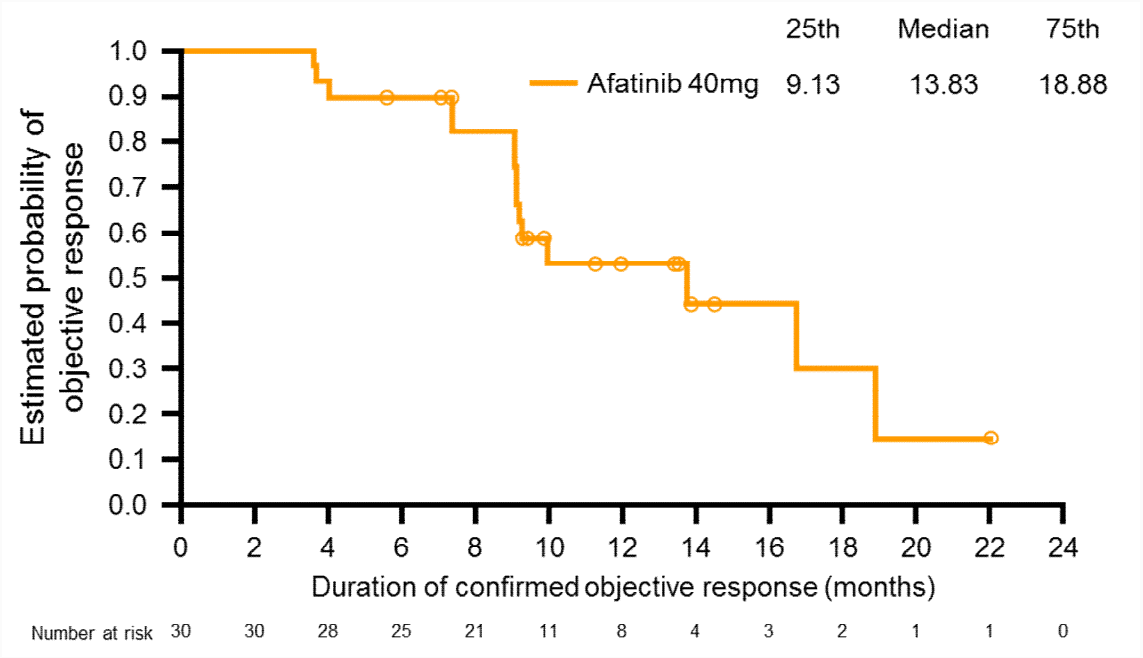
	Afatinib 40 mg/day	
	n	%
Enrolled	70	
Treated	60	
Reasons for discontinuation*		
Progressive disease according to RECIST	24	40.0
Clinical signs and symptoms of progression	2	3.3
AEs	12	20.0
Non-compliant with protocol	1	1.7
Refused to continue afatinib	1	1.7
Switched to commercially-available afatinib	20	33.3

*Due to trial completion, all patients are reported as having discontinued afatinib. However, 20 patients were still benefitting from second-line afatinib and continued to receive afatinib per label outside of clinical trial.

Objective response

- The primary study endpoint of OR by investigator assessment was achieved by 30 patients (50%)
  - PR: 29 (48.3%)
  - CR: 1 (1.7%)
- 20 patients (33.3%) had stable disease

Kaplan–Meier curve of duration of response in 30 patients with an OR

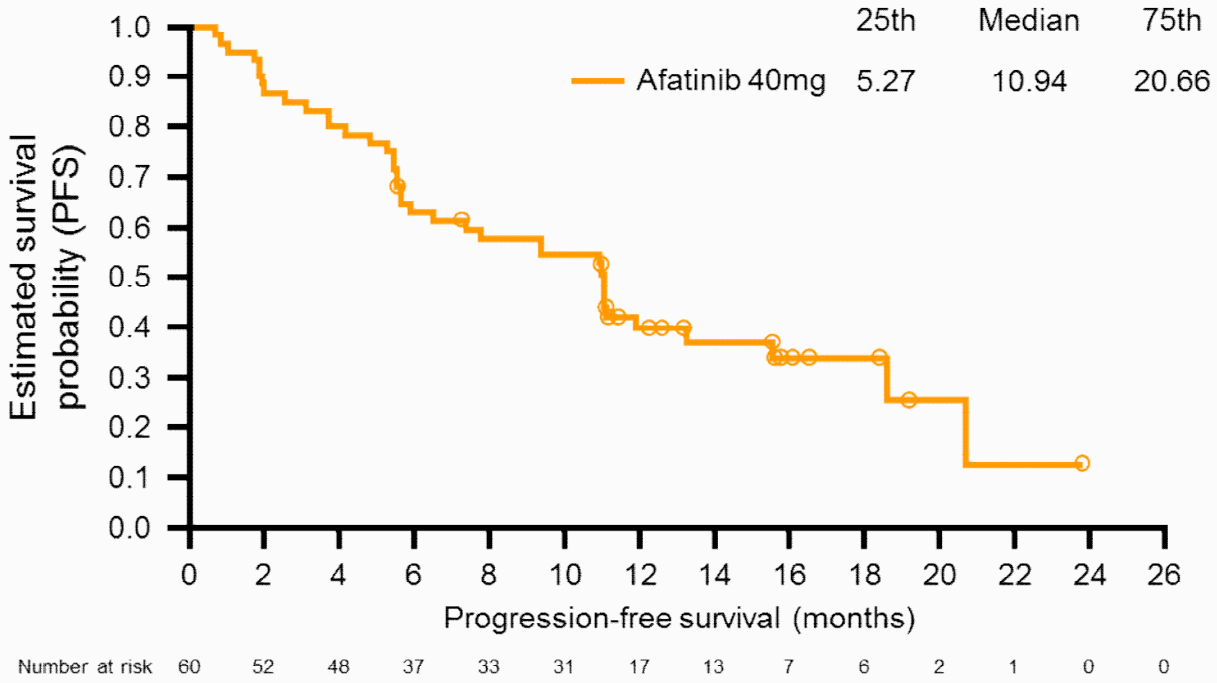


Median duration of response was 13.8 months (95% CI: 9.2, 18.9)

CI, confidence interval; SD, stable disease.

Progression-free survival

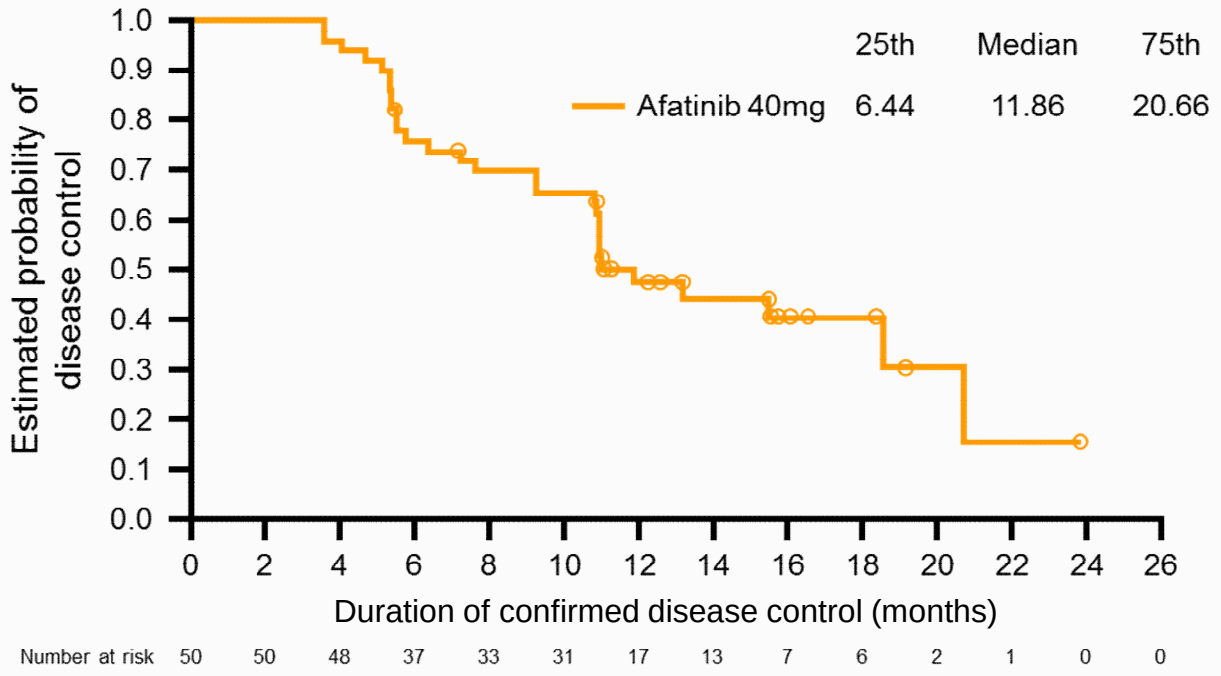
- 39 patients (65.0%) experienced an event contributing to PFS analysis (disease progression or death)



Median PFS was 10.9 months (95% CI: 6.4, 13.2)

Disease control

- 50 patients (83.3%) showed confirmed disease control (CR, PR, or SD)



Median duration of disease control was 11.9 months (95% CI: 10.8, 20.7)

Safety outcomes

	Afatinib 40 mg/day N=60	
Patients	**n**	**%**
Any AE	57	95.0
Afatinib-related AEs*	55	91.7
AEs leading to afatinib dose reduction	25	41.7
AEs leading to afatinib discontinuation†	12	20.0
Other significant AEs (according to ICH E3‡)	25	41.7
Serious AEs¶	21	35.0
AEs by highest CTCAE grade		
Grade 1 or 2	32	53.3
Grade ≥3	25	41.7

The most common afatinib-related AEs were diarrhea and rash/acne

*As defined by the investigator; †Four additional patients discontinued treatment due to AEs; however, these 4 patients were reclassified as having symptoms of disease progression, rather than AEs, and are therefore not included here; ‡Guideline from the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) on the structure and content of clinical study reports; ¶Patients could be counted in more than one category of serious AE

Summary and conclusions

- 50% of patients who received afatinib in second-line after progression on chemotherapy achieved a confirmed OR, with a median duration of response >12 months; median PFS was 10.9 months
- More than 80% of patients achieved 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 being diarrhea and rash

The current study supports the use of afatinib as second-line therapy at the recommended 40 mg/day starting dose in EGFR TKI-naïve patients with locally advanced/metastatic NSCLC harboring common *EGFR* mutations (Del19 or L858R), after failure of first-line platinum-based chemotherapy

Acknowledgments

- We thank all patients and their families, and investigators and staff at all clinical sites for their valuable participation in this study
- This study was funded by Boehringer Ingelheim
- Medical writing assistance, supported financially by Boehringer Ingelheim, was provided by Hashem Dbouk of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this oral presentation

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