Scan the QR code for an electronic copy of the poster and supplementary material

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

474P

Sumitra Thongprasert[1]*, Sarayut L. Geater[2], Dana Clement[3], Amr Abdelaziz[4], Jasmin Reyes-Igama[5], Dragana Jovanovic[6], Aurelia Alexandru[7], Michael Schenker[8], Virote Sriuranpong[9], Piotr Serwatowski[10], Sheethal Suresh[11], Agnieszka Cseh[12], Rabab Gaafar[13]

[1]Medical Oncology Unit, Wattanosoth Hospital and Bangkok Hospital Chiang Mai (BDMS), Chiang Mai, Thailand; [2]Department of Internal Medicine, Songklanagarind Hospital, Prince of Songkla University, Songkhla, Thailand; [3]Medical Oncology Department, Regional Oncology Institute of Iasi, Iasi, Romania; [4]Clinical Oncology Department, Alexandria Clinical Research Centre, Alexandria University, Alexandria, Egypt; [5]Department of Internal Medicine, Hematology and Oncology, Baguio General Hospital and Medical Center, Baguio City, Philippines; [6]Clinic for Pulmonology, Clinical Center Serbia, Belgrade, Serbia; [7]Medical Oncology II Department, Oncology Institute of Bucharest, Bucharest, Romania; [8]Department of Oncology, Oncology Center Sf Nectarie Ltd., Craiova, Romania; [9]Department of Medicine, Faculty of Medicine, Chulalongkorn University & The King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [10]Department of Clinical Oncology and Chemotherapy, Specialist Hospital, Szczecin-Zdunowo, Poland; [11]Oncology Department, Boehringer Ingelheim Pharmaceuticals, Inc., Singapore, Republic of Singapore; [12]Oncology Department, Boehringer Ingelheim RCV GmbH & Co. KG, Vienna, Austria; [13]Medical Oncology Department, National Cancer Institute, Cairo University, Cairo, Egypt

Introduction

- The oral, irreversible ErbB family blocker afatinib is approved in the US and the EU for first-line treatment of *EGFR* mutation-positive (*EGFR*m+) locally advanced or metastatic NSCLC[1,2]
  - Afatinib improved PFS versus chemotherapy in the LUX-Lung 3 and 6 trials,[3,4] and versus gefitinib in LUX-Lung 7[5] in patients with *EGFR*m+ NSCLC receiving first-line afatinib 40 mg/day
- While the benefits of first-line afatinib have been shown, chemotherapy is still commonly used as first-line therapy
- In the EU, afatinib is also approved as a second-line treatment option for EGFR TKI-naïve patients with *EGFR*m+ NSCLC that has progressed on or after platinum-based chemotherapy[2]
- Results from the LUX-Lung 2 study[6] support the use of second-line afatinib in patients with *EGFR*m+ NSCLC progressing following first-line platinum-based chemotherapy, but only 10% of patients in this study received the recommended afatinib dose of 40 mg/day

EU, European Union; NSCLC, non-small-cell lung cancer; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

Objectives

- The aim of this trial was to assess the efficacy and safety of afatinib 40 mg/day as second-line therapy in patients with advanced/metastatic NSCLC harboring *EGFR* common mutations (Del19 and/or L858R), who had progressed following first-line platinum-based chemotherapy and were EGFR TKI-naïve

Methods

- Multicenter, open-label, single-arm Phase IV study conducted across 24 sites in 7 countries (Egypt, Malaysia, Philippines, Poland, Romania, Serbia, and Thailand)

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 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 prior to the start of the trial†
- Major surgery within 4 weeks before starting trial

*Not counting radiotherapy, radiosensitizers, and/or intrapleural administration of anti-cancer agents; †Hormonal therapy was allowed up to 2 weeks prior to treatment
ECOG PS, Eastern Cooperative Oncology Group performance status

Methods (Cont'd)

- Eligible patients received afatinib 40 mg/day
- If patients developed grade ≥3 drug-related AEs, grade 2 diarrhea for more than 2 days, or rash for more than 7 days, treatment was interrupted until recovery to grade ≤1, followed by dose reduction in 10 mg decrements
- Patients were treated with afatinib until disease progression or discontinuation for other reasons

Endpoints

Primary	• OR* (RECIST v1.1)
Secondary	• PFS • Disease control†
Safety	• Intensity and incidence of AEs‡

*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 Tumours; SD, stable disease

- Efficacy and safety were evaluated in a descriptive manner, and there were no formal statistical hypotheses

Results

Patients and treatment

- 60 patients received at least one dose of afatinib 40 mg/day
- 87% of patients were treated for at least 90 days; mean treatment duration was 336.7 days

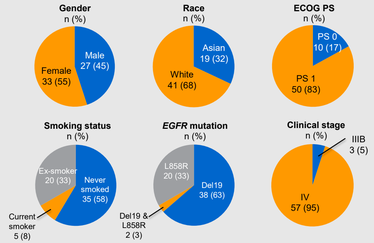
Patient disposition

	Afatinib 40 mg/day	
	n	%
Enrolled	70	
Treated	60	
Patients discontinued afatinib treatment	60	100.0
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
Lost to follow-up	0	0.0
Refused to continue afatinib	1	1.7
Switched to commercially available afatinib at end of trial	20	33.3

Results (Cont'd)

Patient demographics and baseline characteristics

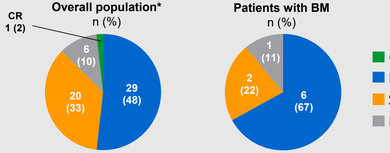
- Patients were mostly white (68%) and had a mean age (std dev) of 59.9 (9.8) years
- The most frequent sites of distant metastases were the ipsilateral lung (48%) and contralateral lung (45%), while 15% of patients had brain metastases (BM) at screening
- All patients had prior chemotherapy; 17 (28%) and 18 (30%) had also undergone surgery and radiotherapy, respectively
- Among patients with baseline BM (n=9), 7 had whole brain irradiation and 1 had stereotactic radiation



Efficacy

Objective response

- The primary study endpoint of OR by investigator assessment was achieved by 30 (50%) patients
- 1 (2%) patient had a CR, 29 (48%) patients achieved PR, and 20 (33%) had SD
- Of the 9 patients with BM, 6 (67%) had PR and 2 (22%) had SD

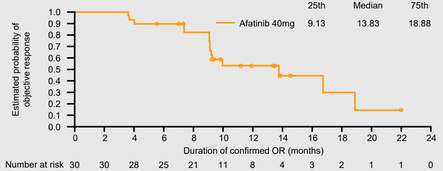


*4 patients who were classified as non-evaluable were exposed to study drug for up to 4 weeks or less and did not have a visit to check tumor response due to death prior to the scheduled visit
PD, progressive disease

Efficacy (Cont'd)

- Median duration of OR was 13.8 months (95% CI: 9.16, 18.88)

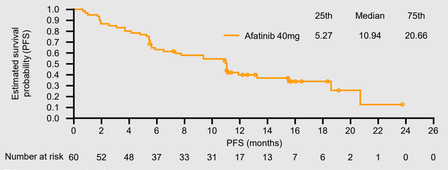
Kaplan–Meier curve of duration of OR



Progression-free survival

- 39 patients (65.0%) experienced an event contributing to PFS analysis (i.e. disease progression as determined by investigator assessment or death)
- Median PFS was 10.9 months (95% CI: 6.4, 13.2)

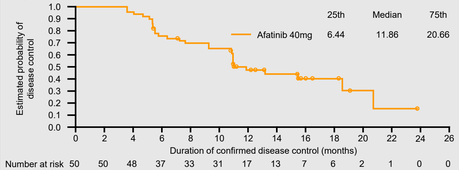
Kaplan–Meier curve of PFS



Disease control

- 50 patients (83.3%) showed confirmed disease control; 8 (88.9%) of patients with BM had disease control
- In the overall population, median duration of disease control was 11.9 months (95% CI: 10.8, 20.7)

Kaplan–Meier curve of duration of disease control



CI, confidence interval

Safety

- The most commonly occurring drug-related AEs of any grade/grade 3 were diarrhea (72%/10%), rash (28%/2%), paronychia (23%/0%), mucosal inflammation (18%/7%), and dermatitis acneiform (17%/0%)
- 25 patients (42%) had dose reduction to 30 mg/day, with six patients (10%) having a further dose reduction to 20 mg/day

Summary of AEs

	Afatinib 40 mg/day	
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
Highest CTCAE grade of any AEs		
Grade 1 or 2	32	53.3
Grade ≥3	25	41.7

*Guideline from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) on the structure and content of clinical study reports

Summary and conclusions

- 50% of patients achieved a confirmed OR, with a median duration greater than 1 year; more than 80% of patients had disease control, with a median duration of 11.9 months
- The majority of patients with BM at baseline achieved disease control, with 67% achieving systemic PR
- Median PFS was 10.9 months
- The safety and tolerability profile of afatinib was consistent with the known safety profile of afatinib, with the most common afatinib-related AEs observed being diarrhea and rash
- The current study supports the use of afatinib at the recommended 40 mg/day starting dose as second-line therapy in EGFR TKI-naïve patients with locally advanced/metastatic NSCLC harboring common *EGFR* mutations (Del19 or L858R), after failure of first-line chemotherapy

References

1. Boehringer Ingelheim Pharmaceuticals, Inc. Gilotrif® Prescribing Information. January 2018
2. Boehringer Ingelheim Pharmaceuticals, Inc. Giotrif® Summary of Product Characteristics. May 2018
3. Sequist LV, et al. J Clin Oncol 2013;31:3327–34
4. Wu Y-L, et al. Lancet Oncol 2014;15:213–22
5. Park K, et al. Lancet Oncol 2016;17:577–89
6. Yang JC-H, et al. Lancet Oncol 2012;13:539–48

Scan the QR code for an electronic copy of the poster and supplementary content†

https://tinyurl.com/yldzy4hl

†These materials are for personal use only and may not be reproduced without written permission of the authors and the appropriate copyright permissions.

Presented at the European Society for Medical Oncology (ESMO) Asia 2018 Congress, Singapore, November 23–25, 2018

This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version.
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 poster.
*Corresponding author email address: sumitra95@gmail.com