Analysis of long-term response to first-line afatinib in the LUX-Lung 3, 6 and 7 trials in advanced EGFRm+ NSCLC

Martin Schuler,1 James Chih-Hsin Yang,2 Lecia V. Sequist,3 Yi-Long Wu,4 Caicun Zhou,5 Sarayut L. Geater,6 Tony Mok,7 Eng-Huat Tan,8 Cheng-Ping Hu,9 Nobuyuki Yamamoto,10 Jifeng Feng,11 Kenneth O’Byrne,12 Shun Lu,13 Vera Hirsh,14 Yunchao Huang,15 Stuart Ellis,16 Carl Samuelsen,17 Angela Märten,17 Jean Fan,18 Keunchil Park,19 Luis Paz-Ares20

1West German Cancer Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany; 2National Taiwan University Hospital and National Taiwan University, Taipei, Taiwan; 3Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; 4Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China; 5Shanghai Pulmonary Hospital, Tongji University, Shanghai, China; 6Prince of Songkla University, Songkhla, Thailand; 7State Key Laboratory of South China, Hong Kong Cancer Institute, The Chinese University of Hong Kong, Hong Kong, China; 8Division of Medical Oncology, National Cancer Centre Singapore, Singapore; 9Xiangya Hospital, Central South University, Changsha, China; 10Wakayama Medical University, Wakayama, Japan; 11Jiangsu Province Cancer Hospital, Nanjing, Jiangsu, China; 12Princess Alexandra Hospital, Woolloongabba, and Queensland University of Technology, Brisbane, Queensland, Australia; 13Shanghai Lung Tumor Clinical Medical Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; 14McGill University, Montreal, Canada; 15Yunnan Tumor Hospital (The Third Affiliated Hospital of Kunming Medical University), Kunming, Yunnan Province, China; 16Independent Statistical Consultant, Cheshire, UK; 17Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; 18Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; 19Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; 20Hospital Universitario Doce de Octubre and CNIO, Madrid, Spain

Presented at the IASLC 18th World Conference on Lung Cancer (WCLC), Yokohama, Japan, October 15–18, 2017
Introduction

• Afatinib, an irreversible ErbB family blocker, is approved in many countries for the first-line treatment of patients with advanced \( \text{EGFR} \) mutation-positive (\( \text{EGFR}_{m+} \)) non-small cell lung cancer (NSCLC)

Studies LUX-Lung 3 (LL3) and LL6 (Phase III)
• First-line afatinib significantly improved progression-free survival (PFS) and objective response (OR) versus platinum-doublet chemotherapy in patients with \( \text{EGFR}_{m+} \) NSCLC\(^{1,2} \)
• Afatinib significantly prolonged overall survival (OS) vs chemotherapy in Del19+ patients\(^3 \)

Study LL7 (Phase IIb)
• Afatinib significantly improved PFS, time to treatment failure (TTF), and OR vs gefitinib in the same setting\(^4 \)
• Non-significant trend towards improved OS with afatinib versus gefitinib\(^5 \)
Introduction (cont’d)

LL3, LL6 and LL7 studies\textsuperscript{1,2,4}

- Treatment-naïve patients with stage IIIB/IV \textit{EGFR}m+ NSCLC were randomised as follows:

\begin{itemize}
  \item LL3: Cisplatin + pemetrexed (n=115) 
  \hspace{2cm} Up to 6 cycles
  \item LL6: Cisplatin + gemcitabine (n=122) 
  \hspace{2cm} Up to 6 cycles
  \item LL7: Gefitinib (n=159) 
  \hspace{2cm} 250 mg QD
\end{itemize}

- PFS (LL3 and LL6) and TTF (LL7) curves indicated that some patients showed long-term responses to afatinib treatment\textsuperscript{5,6}

QD, once daily
Methods

• We performed a *post-hoc* analysis of afatinib long-term responders (LTRs; patients treated with afatinib ≥3 years) in LL3, LL6 and LL7
• All patients randomized to afatinib 40 mg QD were included
• We assessed efficacy and safety outcomes, as well as patient reported outcomes (PROs) measured using the European Organization for Research and Treatment of Cancer (EORTC) quality of life (QoL) questionnaire and the EQ-5D™ health status self-assessment questionnaire
Results

LTRs in LL3, LL6 and LL7

• 24 (10%), 23 (10%) and 19 (12%) afatinib-treated patients in LL3, LL6 and LL7 were LTRs
  – Median (range) treatment duration was 50 months (41–73), 56 months (37–68), and 42 months (37–50), for LL3, LL6 and LL7, respectively
  – Six, nine and 14 LTRs were on treatment at the time of analysis
  – Seven (4%) gefitinib-treated patients in LL7 were LTRs
Results (cont’d)

Baseline characteristics

• Baseline characteristics were generally consistent with the overall study populations, with the exception of greater proportions of women and Del19+ patients among LTRs.

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*At enrolment; †Unknown for one LTR; ‡One patient had L858R and uncommon mutation.
Results (cont’d)

Treatment outcomes
• Tolerability-guided dose adjustment and OS are shown in Figure 1 for LL3 (A), LL6 (B), and LL7 (C)

Figure 1. (A) Tolerability-guided dose adjustment and OS in LL3

*Patients were ordered and numbered by treatment duration, with Patient 1 being on treatment longest; †At the time of enrolment.
D, Del19; EGFRm, EGFR mutation; L, L858R; U, uncommon
Results (cont’d)

Figure 1. (B) Tolerability-guided dose adjustment and OS in LL6

*Patients were ordered and numbered by treatment duration, with Patient 1 being on treatment longest; †At the time of enrolment.
Results (cont’d)

*Patients were ordered and numbered by treatment duration, with Patient 1 being on treatment longest; †At the time of enrolment.
Results (cont’d)

- Median OS could not be estimated due to few deaths; median follow-up time for OS was 64.6, 57.0 and 42.1 months in LL3, LL6 and LL7, respectively.
- The frequency of afatinib dose reductions due to AEs was broadly consistent with the overall LL3, LL6 and LL7 populations\(^1,2,4\).
- Tumour volume change among LTRs is shown in Figure 2.
Results (cont’d)

Figure 2. Tumour volume change in LL3, LL6 and LL7

*Patients were ordered by maximum percentage decrease in tumour volume from baseline; †N numbers include all LTRs; tumour volume change not available for seven patients (two patients with NN in LL3, one patient with a CR and three patients with NN in LL6, and one patient with SD in LL7)

CR, complete response; PR partial response; SD, stable disease; NN, non-CR, non-progressive disease
Results (cont’d)

• Objective response rates (ORRs) among LTRs were higher than in the overall populations\textsuperscript{1,2,4}

Subsequent therapies
• The frequency and duration of subsequent therapy among LTRs was similar to that in the overall LL3, LL6 and LL7 populations
Subsequent therapies

- The frequency and duration of subsequent therapy among LTRs was similar to that in the overall LL3, LL6 and LL7 populations

<table>
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<tr>
<th>Any subsequent therapy</th>
<th>2nd line, n</th>
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<th>3rd line, n</th>
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<td>10</td>
<td>222 (62–885); 2</td>
<td>6</td>
<td>32 (7–84)</td>
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<td>5</td>
<td>149 (121–354); 1</td>
<td>3</td>
<td>21 (7–84)</td>
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<tr>
<td>EGFR tyrosine kinase inhibitor (TKI)</td>
<td>4</td>
<td>27 (20–33); 2</td>
<td>3</td>
<td>293 (62–885)</td>
<td>3</td>
<td>42; 2</td>
</tr>
</tbody>
</table>
Patient reported outcomes (PROs)

- In afatinib-treated LTRs in LL3, LL6 and LL7, PROs appeared stable between ~Week 24 to ~Week 160, with slight improvements after ~3 years of afatinib treatment versus the start of treatment.
Key findings and conclusions

- In LL3, LL6 and LL7, 10–12% of afatinib-treated patients were LTRs
- Afatinib was well tolerated in LTRs
- Long-term treatment was independent of tolerability-guided dose adjustment, or baseline brain metastases, and had no detrimental impact on subsequent treatment
- In afatinib-treated LTRs, PROs were not negatively affected by long-term treatment, and were slightly improved after ~3 years of treatment versus scores at treatment initiation
References


Acknowledgments

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 Christina Jennings of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster.

Corresponding author email address: Martin.Schuler@uk-essen.de. Data were previously presented: Schuler, et al. ELCC 2017, poster #92PD.

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