

# Competing central nervous system or systemic progression analysis for patients with *EGFR* mutation-positive NSCLC receiving afatinib in LUX-Lung 3, 6, and 7

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## Introduction

- Central nervous system (CNS) metastases are a known complication of advanced *EGFR* mutation-positive NSCLC

**~25–40%** of patients with NSCLC develop brain metastases<sup>1,2</sup>

This rises to **~40–60%** in patients with *EGFR* mutations<sup>3,4</sup>

- The efficacy and optimal integration of *EGFR* TKIs in the treatment concept of brain metastases is less defined; therefore, LUX-Lung trials investigating the ErbB-family blocker afatinib allowed enrollment of patients with asymptomatic brain metastases

### LUX-Lung 3 and 6

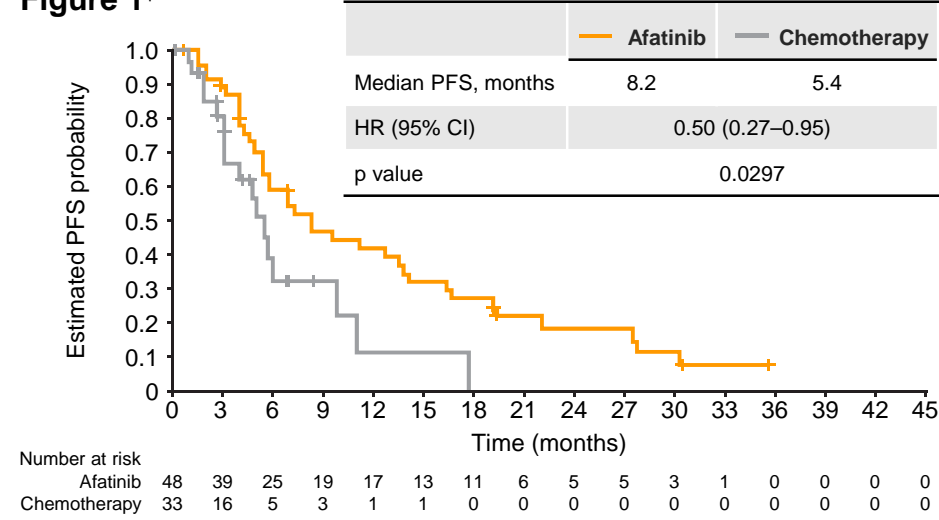
- Randomized Phase III studies; first-line afatinib versus platinum-based chemotherapy

### LUX-Lung 7

- Randomized Phase IIb study; first-line afatinib versus gefitinib; common *EGFR* mutations

- In all three studies, the magnitude of PFS improvement with afatinib versus chemotherapy or gefitinib in patients with brain metastases was similar to that observed in patients without brain metastases
  - HR = 0.54, 0.47, and 0.76 in patients with brain metastases, versus 0.48, 0.22, and 0.74 in patients without brain metastases, in LUX-Lung 3, 6, and 7, respectively<sup>4,5</sup>
- In a combined analysis of patients in LUX-Lung 3 and 6, PFS was significantly improved with afatinib versus chemotherapy in patients with asymptomatic brain metastases (Figure 1)<sup>4</sup>

Figure 1<sup>†</sup>

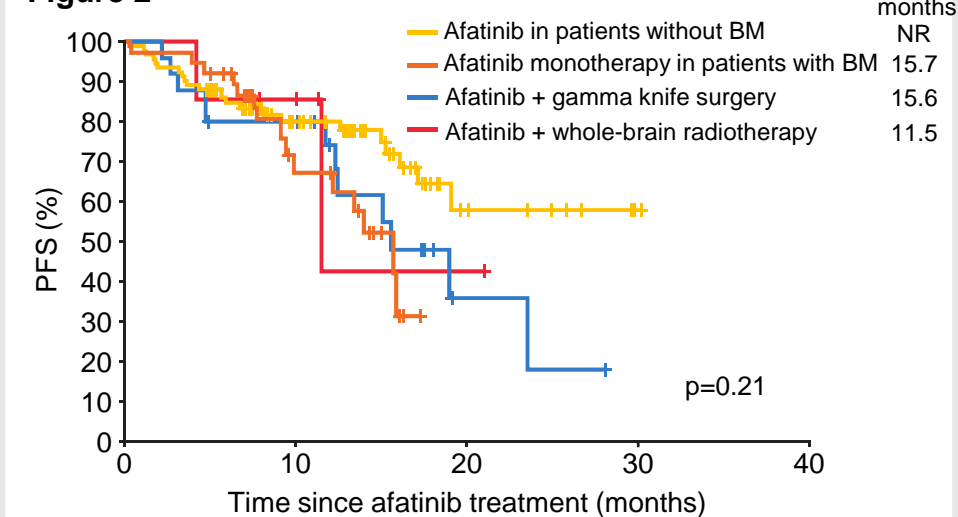


HR, hazard ratio; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.  
<sup>†</sup>Adapted from Schuler, J Thorac Oncol 2016 (ref. 4) under the terms of the Creative Commons Attribution License (CC BY).

## Real-world data

- In a single-center retrospective analysis in Korea (n=165), ORR for afatinib monotherapy was 76%, with 21% CR. PFS data were not significantly different between patients receiving afatinib monotherapy, or afatinib plus surgery or WBRT (Figure 2)<sup>6</sup>

Figure 2<sup>†</sup>



- In another retrospective review, ORR was similar for patients receiving afatinib monotherapy (82%; n=11) and patients receiving afatinib in combination with WBRT (88%; n=17); TTF and OS were numerically higher for patients on afatinib monotherapy<sup>7</sup>

BM, brain metastases; CR, complete response; NR, not reached; ORR, overall response rate; OS, overall survival; TTF, time to treatment failure; WBRT, whole-brain radiotherapy; <sup>†</sup>Adapted from Kim Y, et al. J Thorac Oncol 2017;12:S2209 [presented at WCLC] (ref. 6) with permission.

## Objective

- To investigate whether afatinib can prevent CNS progression or metastasis, we performed competing risk analyses for the progression and metastasis pattern in the CNS or non-CNS region in patients with or without brain metastases in LUX-Lung 3, 6, and 7

## Methods

- Competing risk analyses were performed in patients with stage IIIB/IV *EGFR* mutation-positive NSCLC who received afatinib 40 mg/day in LUX-Lung 3, 6, or 7
- Analyses were performed separately for patients with baseline brain metastases and without baseline brain metastases
- Risk of CNS progression versus non-CNS progression or death was calculated based on the cumulative frequency of the event of interest versus the competing risk event

## Summary

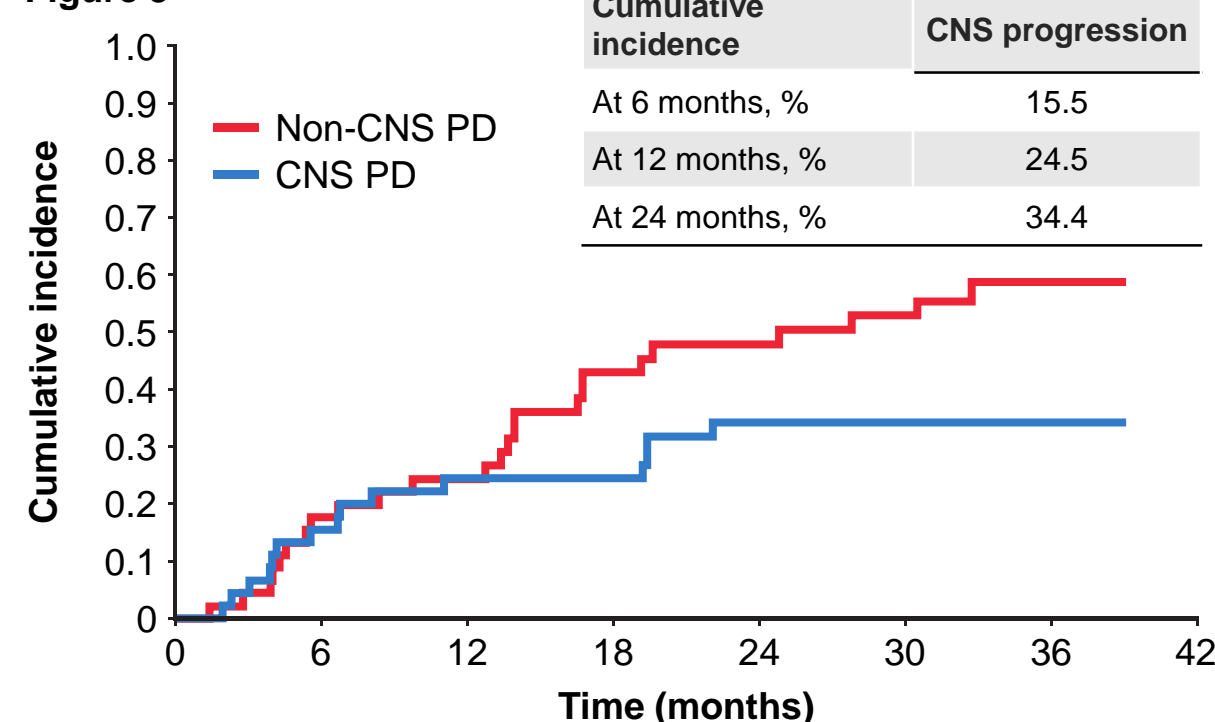
- Previous findings from the LUX-Lung trials and real-world practice show that afatinib has clinical activity against brain metastases in *EGFR* mutation-positive NSCLC
- Cumulative incidence of CNS progression was lower than that of non-CNS progression in patients with baseline brain metastases treated with afatinib
- Risk of *de novo* CNS progression in patients with *EGFR* mutation-positive NSCLC treated with afatinib was very low

## Results

### Patients with baseline brain metastases (Figure 3):

- 48 patients with baseline brain metastases received afatinib in LUX-Lung 3 and 6
- Median follow-up was 10.3 months
- Cumulative incidence of CNS progression was 40% lower than that of non-CNS progression (31.3% versus 52.1%)
- Best CNS response in patients with baseline brain metastases classified as target lesion (n=5): 2 CRs, 1 PR, and 2 SDs
  - PR/CR was achieved by visits 1–2

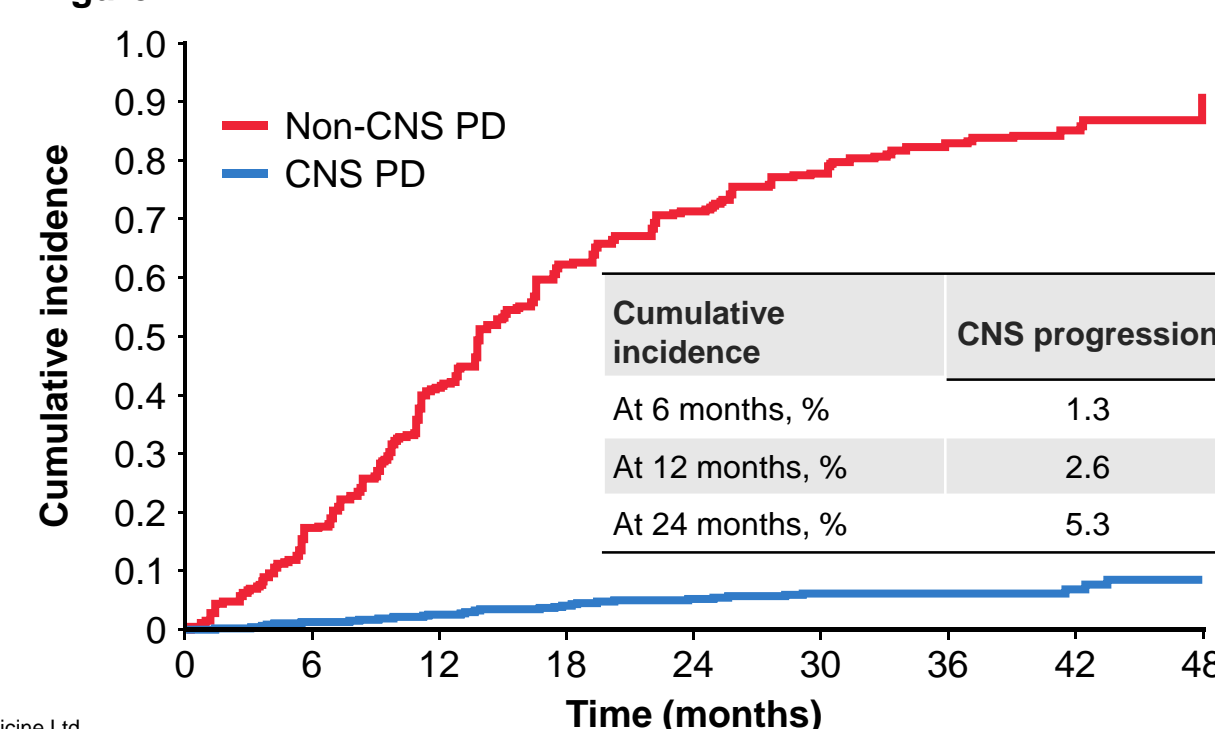
Figure 3<sup>§</sup>



### Patients without baseline brain metastases (Figure 4):

- 485 patients without baseline brain metastases received afatinib in LUX-Lung 3, 6, and 7
- Median follow-up was 13.0 months
- Risk of *de novo* CNS progression was very low (6.4%) compared with non-CNS progression (78.4%)

Figure 4<sup>§</sup>



PD, progressive disease; PR, partial response; SD, stable disease.  
<sup>§</sup>Adapted from Girard N. Future Oncol 2018 (ref. 8) with permission of Future Medicine Ltd.

## Conclusions

- These results add to the existing evidence supporting afatinib use in patients with *EGFR* mutation-positive NSCLC and CNS metastases**
- Taken together, these results show afatinib delays the onset/progression of brain metastases**

## References

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