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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Background

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

~25–40% of patients with NSCLC develop brain metastases[1,2] This rises to **~40–60%** in patients with *EGFR* mutations[3,4]

- 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 enrolment of patients with asymptomatic brain metastases

LUX-Lung 3 and 6
- Randomised Phase III studies; first-line afatinib versus platinum-based chemotherapy

LUX-Lung 7
- Randomised Phase IIb study; first-line afatinib versus gefitinib; common *EGFR* mutations

TKI, tyrosine kinase inhibitor

Background (cont'd)

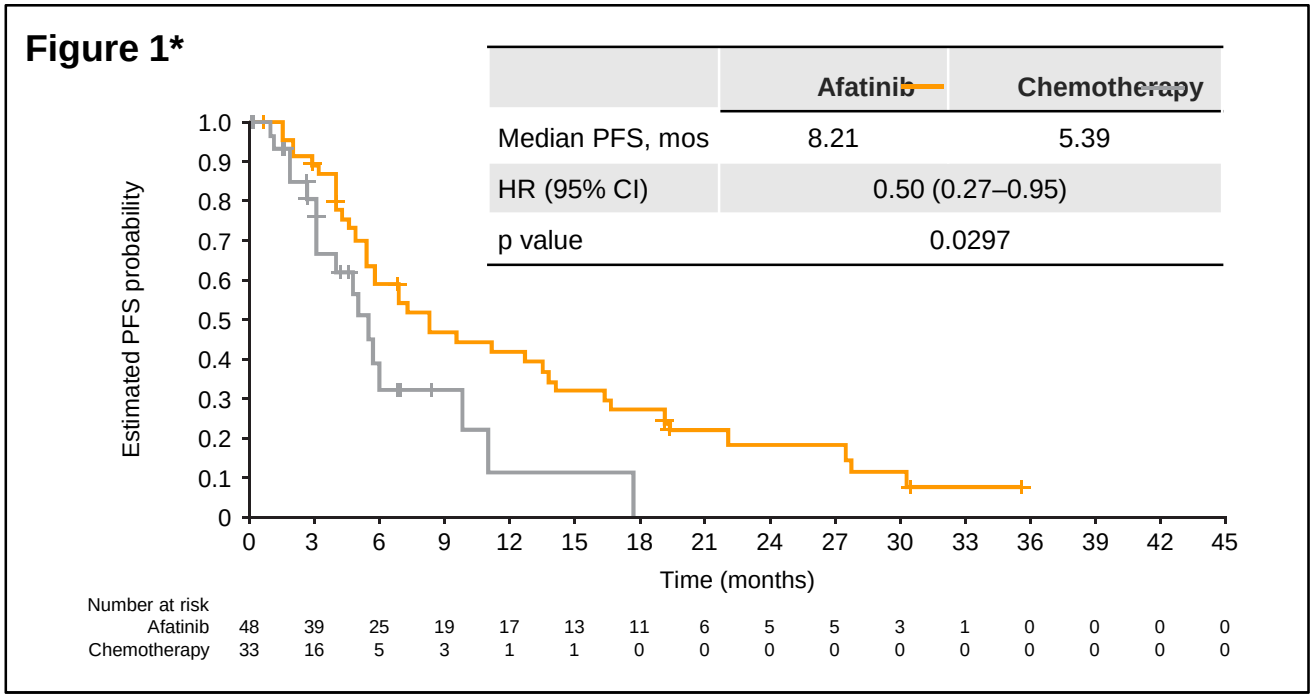
- In all three studies, the magnitude of PFS improvement with afatinib versus chemotherapy or gefitinib in patients with brain metastases was similar to that observed in patients without brain metastases
  - HR 0.54, 0.47, and 0.76 in patients with brain metastases versus 0.48, 0.22, and 0.74 in patients without brain metastases in LUX-Lung 3, 6, and 7, respectively[4,5]

HR, hazard ratio; PFS, progression-free survival

Background (cont'd)

- 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)[4]

Figure 1*



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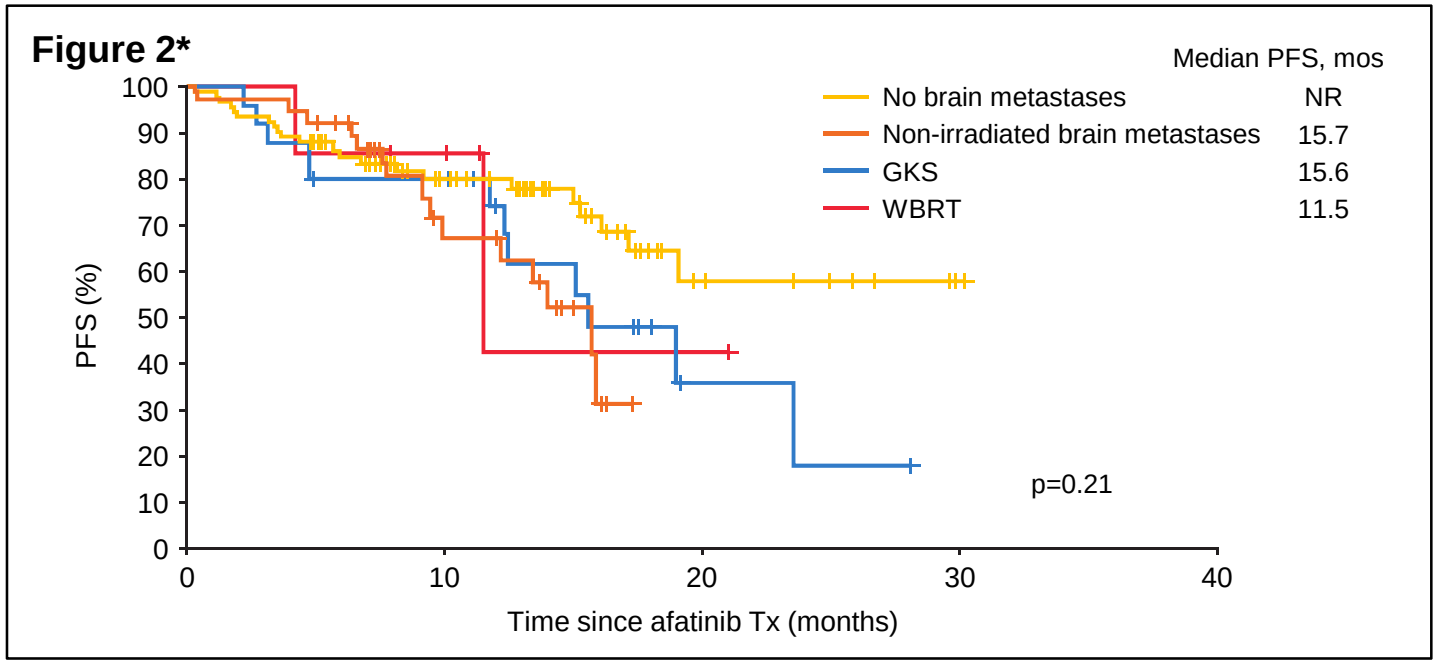
Real-world data

- In a single-centre 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)[6]

Figure 2*



CR, complete response; GKS, gamma knife surgery; ORR, overall response rate; WBRT, whole-brain radiotherapy
*Adapted from Kim Y. et al. J Thorac Oncol 2017;12:S2209 [presented at WCLC] with permission

Real world data (cont’d)

- 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 was numerically higher for patients with afatinib monotherapy[7]

OS, overall survival; TTF, time to treatment failure

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 and 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, and 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

Results

Patients with baseline brain metastases (Figure 3):

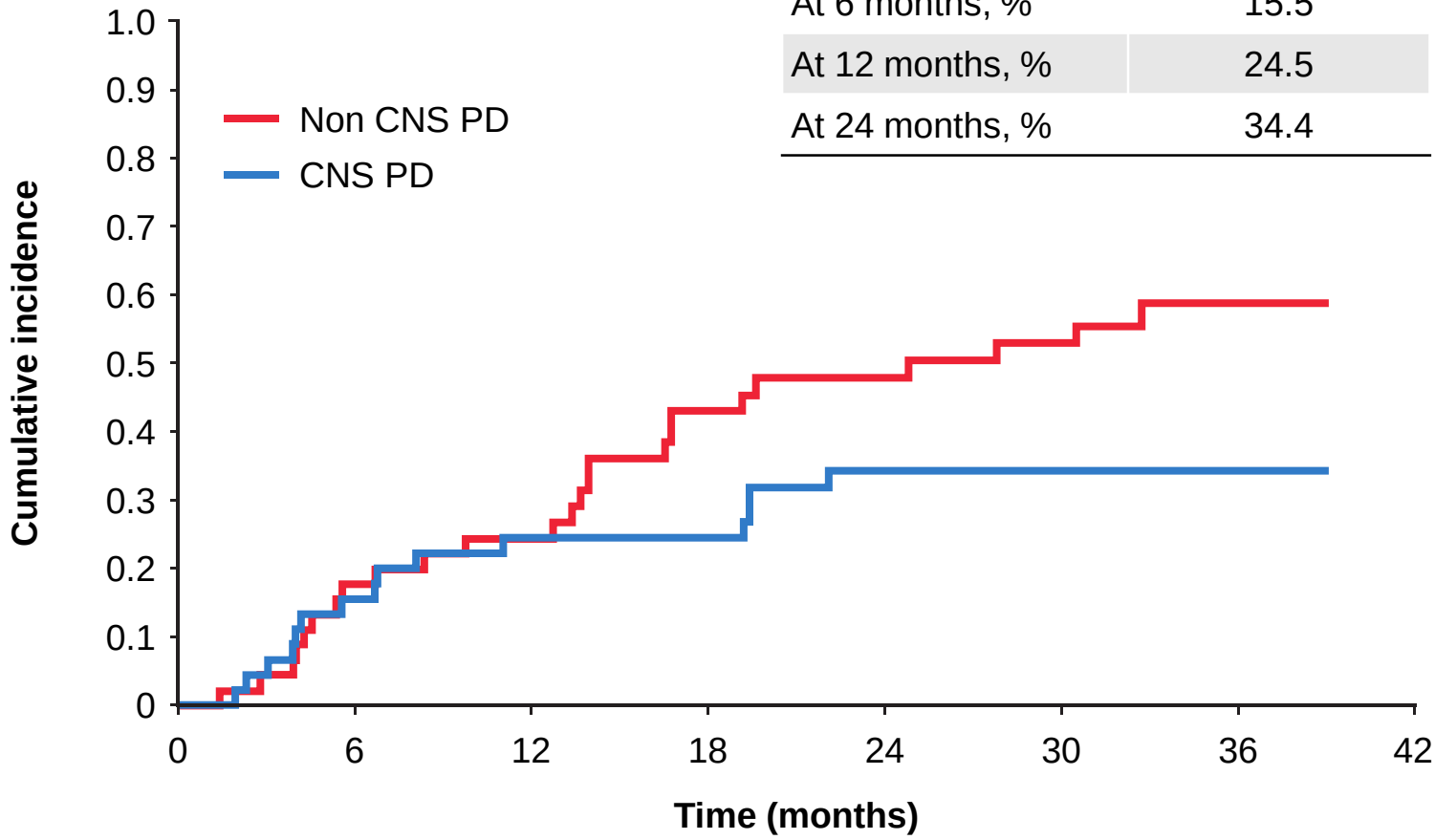
- 48 patients with baseline brain metastases received afatinib in LUX-Lung 3 and 6
- Median follow-up was 10.3 months
- 31.3% had CNS progression versus 52.1% with non-CNS progression
- Best CNS response in patients with baseline brain metastases classified as target lesion (n=5): 2 CRs, 1 PR, and 2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

PD, progressive disease; PR, partial response; SD, stable disease

Results (cont'd)

Figure 3*

Cumulative incidence	CNS progression
At 6 months, %	15.5
At 12 months, %	24.5
At 24 months, %	34.4



PD, progressive disease; PR, partial response; SD, stable disease

*Adapted from Girard N. Future Oncol. (2018) with permission of Future Medicine Ltd.

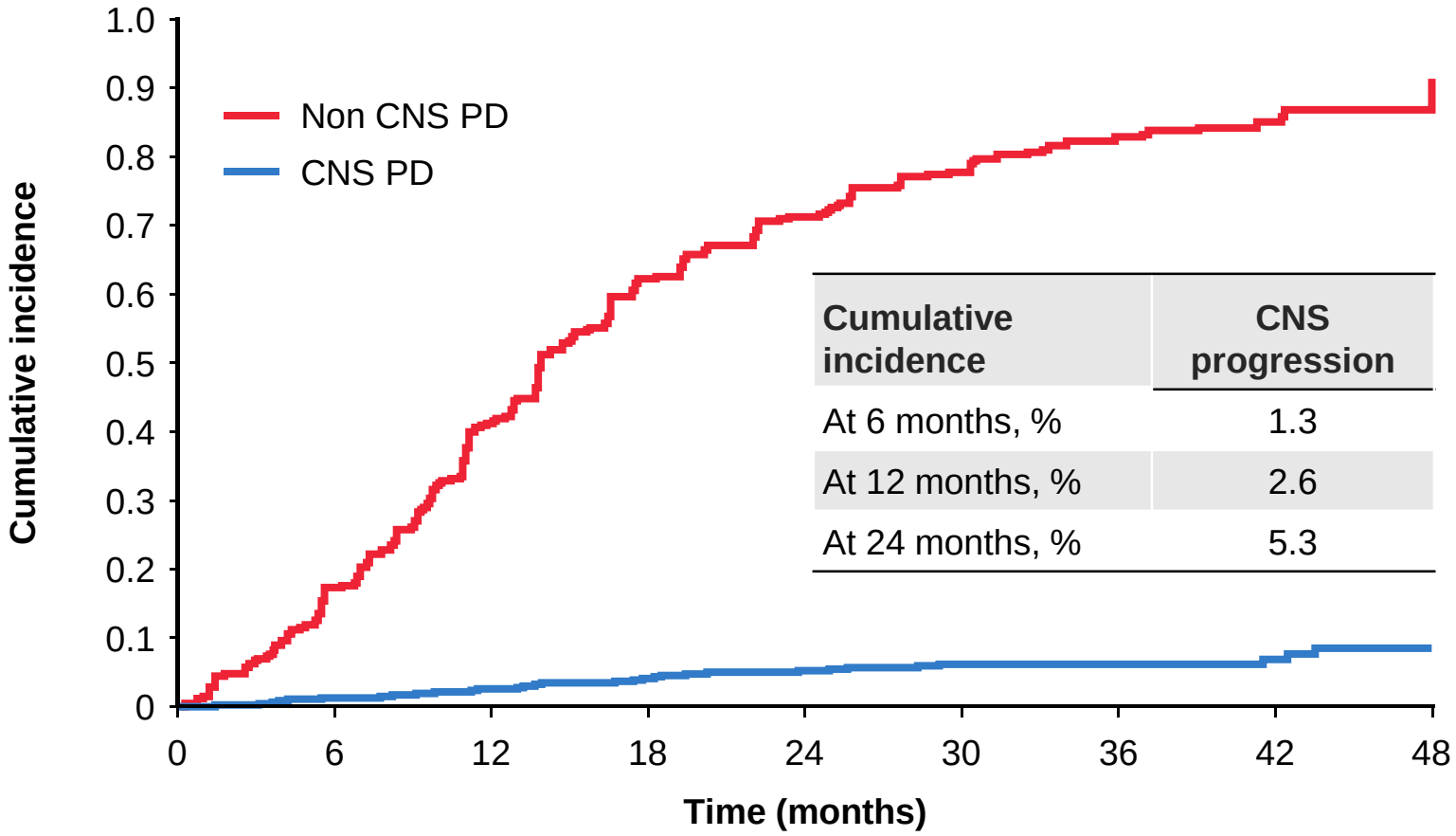
Results (cont'd)

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%)

Results (cont'd)

Figure 4*



Cumulative incidence	CNS progression
At 6 months, %	1.3
At 12 months, %	2.6
At 24 months, %	5.3

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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 suggest afatinib delays the onset/progression of brain metastases**

Summary

- Previous findings from the LUX-Lung trials and real-world practice show 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 *EGFR* mutation-positive NSCLC and baseline brain metastases treated with afatinib in LUX-Lung 3 and 6
- Risk of *de novo* CNS progression in patients with *EGFR* mutation-positive NSCLC treated with afatinib was very low in LUX-Lung 3, 6, and 7

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