115O Afatinib in EGFR TKI-naïve patients (pts) with locally advanced/metastatic NSCLC harbouring EGFR mutations: An interim analysis of a phase IIIB trial

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Background: First-line afatinib significantly improved progression-free survival (PFS) in pts with EGFR mutation-positive (EGFRm+) NSCLC (including uncommon mutations) vs chemotherapy (CT) in the LUX-Lung (LL) 3/6 trials (median 11.1 vs 6.9 mos; HR 0.58/11.0 vs 5.6 mos; HR 0.28) and vs gefitinib in LL7 (median 11.0 vs 10.9 mos; HR 0.73). However, in real-world (RW) practice CT remains a first-line choice. Here, we report an interim analysis of a Phase IIIb study of afatinib in treatment-naïve or CT pre-treated pts with EGFRm+ NSCLC, similar to RW practice.

Methods: EGFR TKI-naïve pts with locally advanced/metastatic EGFRm+ NSCLC and ECOG PS 0–2 received 40 mg/day afatinib (starting dose). Dose reduction was permitted (to minimum 20 mg/day). Primary endpoint: adverse events (AEs) in a descriptive fashion. Efficacy was also assessed.

Results: At data cut-off (30 April 2018), 479 pts were enrolled and treated with afatinib (Caucasian/Asian/other: 97%/2%/<1%; male/female: 34%/66%; $1^{st}/2^{nd}/\geq 3^{rd}$-line therapy: 78%/17%/5%; ECOG PS 0/1/2: 36%/57%/8%; brain metastases: 17%; common/uncommon mutations: 87%/13%). Median time on afatinib was 359 days. The most common grade ≥3 afatinib-related AEs were diarrhoea (16%) and rash (11%). AEs led to dose reduction in 258 (54%) pts (most frequently diarrhoea 25%; rash 11%) and to afatinib discontinuation in 105 (22%) pts (most frequently diarrhoea 3% [rash 0.8%]). Afatinib-related serious AEs occurred in 39 (8%) pts. Time to symptomatic progression (TTSP) and PFS are shown in the table. Objective response rate and disease control rate were 46% and 86%, respectively.

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	Median TTSP, months (95% CI)	Median PFS, months (95% CI)
All pts (n = 479)	14.9 (13.8–17.6)	13.4 (11.8–14.5)
Line of therapy		
1st (n = 374)	15.6 (14.1–18.5)	13.8 (12.6–15.1)
2nd (n = 81)	14.7 (11.3–20.6)	13.2 (8.3–17.7)
≥3rd (n = 24)	8.1 (3.7–14.4)	6.6 (3.2–12.6)
Baseline ECOG PS*		
0 (n = 171)	17.2 (14.8–19.8)	15.4 (13.4–18.8)
1 (n = 271)	14.7 (13.0–18.7)	12.9 (10.3–14.4)
2 (n = 36)	8.9 (5.7–13.2)	6.2 (2.5–11.6)
Baseline brain metastases		
No (n = 395)	15.8 (14.1–18.8)	13.9 (12.7–15.5)
Yes (n = 83)	13.7 (9.7–17.2)	10.1 (8.2–13.9)
Baseline mutation type*		
Common† (n = 416)	15.9 (14.5–19.1)	14.1 (13.0–15.7)
Uncommon‡ (n = 62)	7.4 (5.7–9.0)	6.0 (4.2–8.1)

*Missing (n = 1);
†Del 19 and/or L858R with or without uncommon mutation;
‡Includes ex 20 ins, T790M, S768I, G719S/A/C, L861Q

Conclusions: Interim analysis of this study, which included pts treated with afatinib in later lines, and pts with ECOG PS 2, brain metastases and/or uncommon mutations, indicates a predictable and manageable safety profile for afatinib, consistent with the pivotal LL trials. Interim efficacy findings are encouraging, with a median TTSP of 14.9 months.

Clinical trial identification: NCT01853826.

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