LUX-Lung 5

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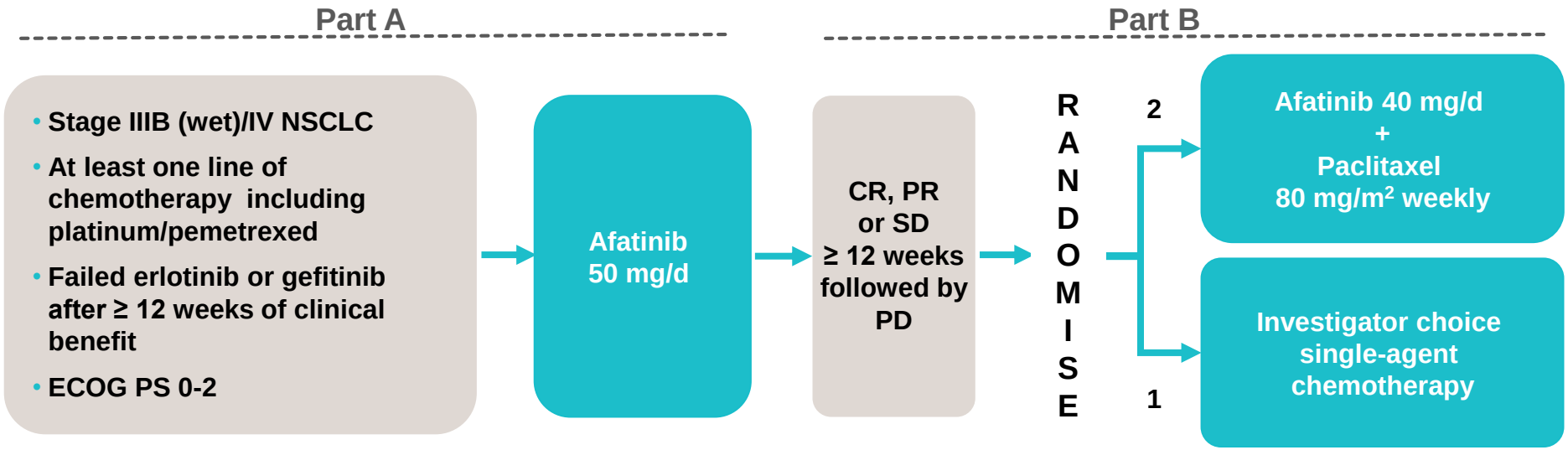
LUX-Lung 5: Background and Aim

- Patients with NSCLC who initially respond to an EGFR-TKI eventually **develop resistance** with subsequent disease progression[1,2]
- Retrospective/non-randomised studies suggest that continued EGFR **inhibition beyond progression improves disease control**; this has not been prospectively evaluated in a randomised trial
- Combination of afatinib + paclitaxel has demonstrated preclinical synergy[5] and promising activity/manageable tolerability in a phase I study[6]
- **LUX-Lung 5**: To investigate the **efficacy and safety of afatinib plus weekly paclitaxel vs investigator's choice of chemotherapy** in patients with **Stage III B or IV NSCLC experiencing a benefit from afatinib** monotherapy **after failing** at least one line of **chemotherapy and** prior treatment with **erlotinib or gefitinib for at least 12 weeks**

1. Paz-Ares L, et al. *J Cell Mol Med 2010*;14:51–69; 2. Jackman D, et al. *J Clin Oncol* 2010;28:357–60;
3. Li D, et al. *Oncogene* 2008;27:4702–11; 4. Solca F, et al. *J Pharmacol Exp Ther* 2012;343:342–50;
5. Solca F, et al *EORTC-NCI-AACR* 2006; 6. Spicer JF, et al. *Ann Oncol* 2008;19(suppl 8): Abstract 474P.

LUX-Lung 5: Study Design

- Open label, global trial across 115 centers in 23 countries
- Recruited Part A: April 2010 – May 2011
- Primary Analysis: Randomised Part B is presented (Data base lock Nov 2013)
- Non-randomised Part A reported previously (Schuler et al ASCO 2012)



Primary End point: PFS in Part B (investigator review)
Secondary End points: OS in Part B, PFS in Part A, ORR in Parts A & B

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; PR, partial response; SD, stable disease

1. Schuler et al. ASCO 2012. Abstract 7557; 2. Schuler et al. ASCO 2014. Abstract 8019.

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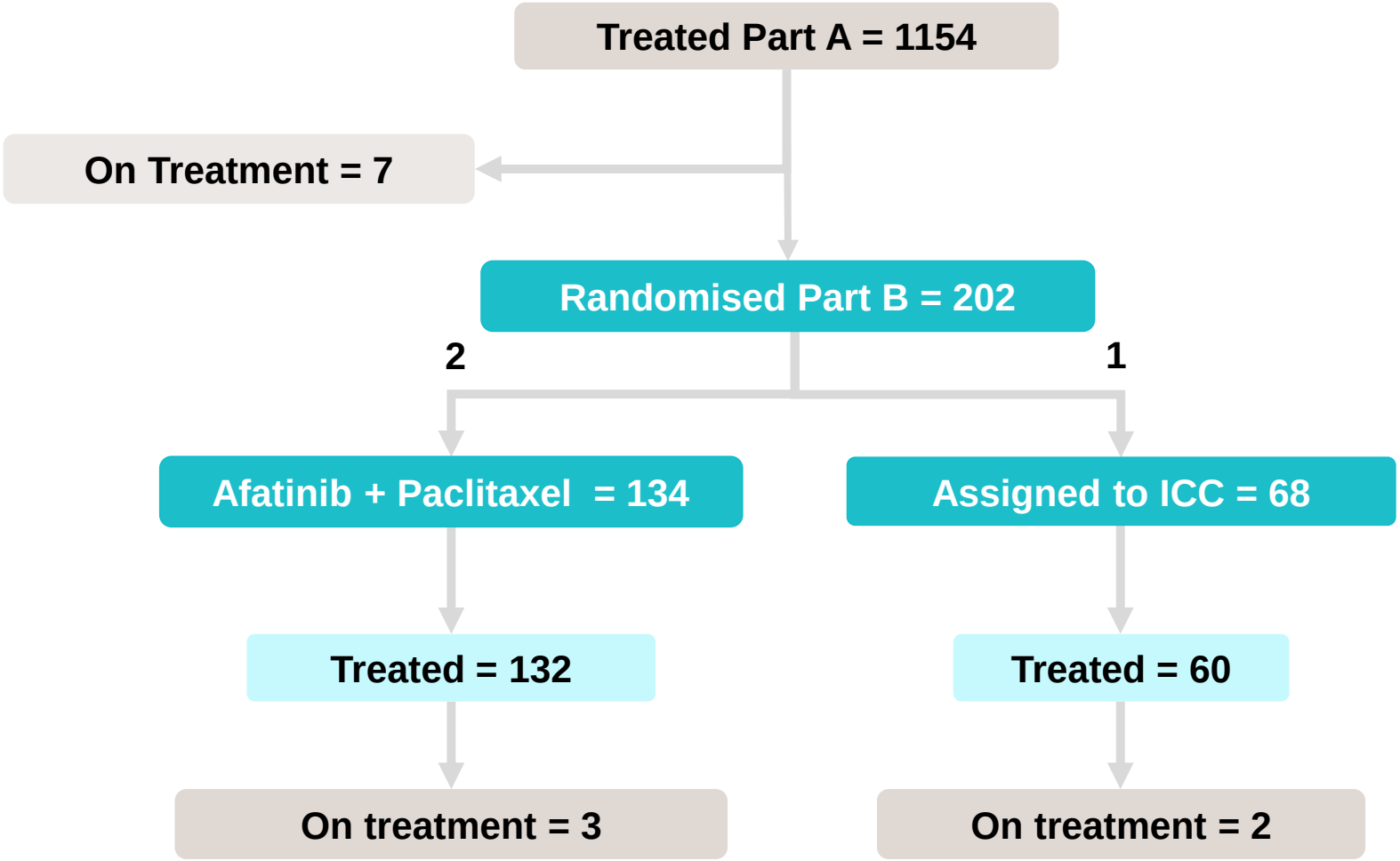
Patient Disposition



Schuler et al. ASCO 2014. Abstract 8019.

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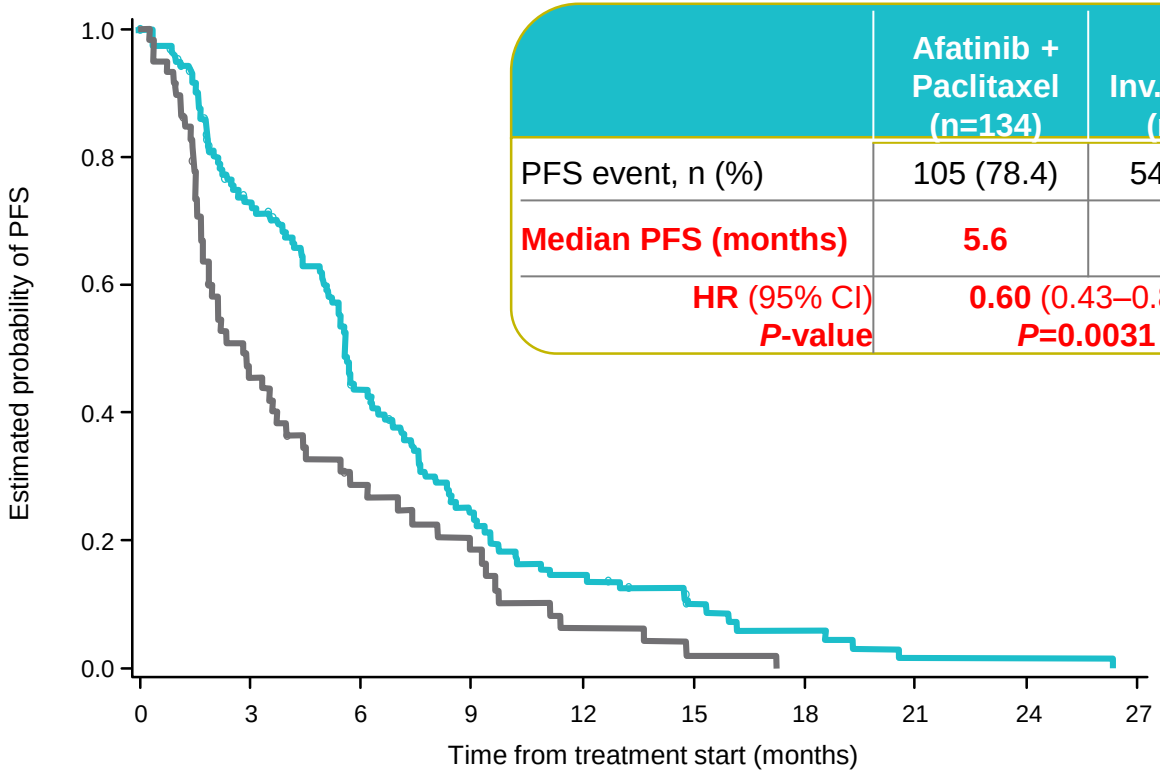
Primary End Point: PFS by Investigator Review



	Afatinib + Paclitaxel (n=134)	Inv. Choice (n=68)
PFS event, n (%)	105 (78.4)	54 (79.4)
Median PFS (months)	**5.6**	**2.8**
HR (95% CI)	**0.60** (0.43–0.85)	
***P*-value**	***P*=0.0031**	

No. at risk:										
Afa + Pac	134	82	46	25	15	7	4	1	1	0
Inv. Choice	68	25	14	9	3	1	0	0	0	0

Schuler et al. ASCO 2014. Abstract 8019.

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Part B: Best Overall Response

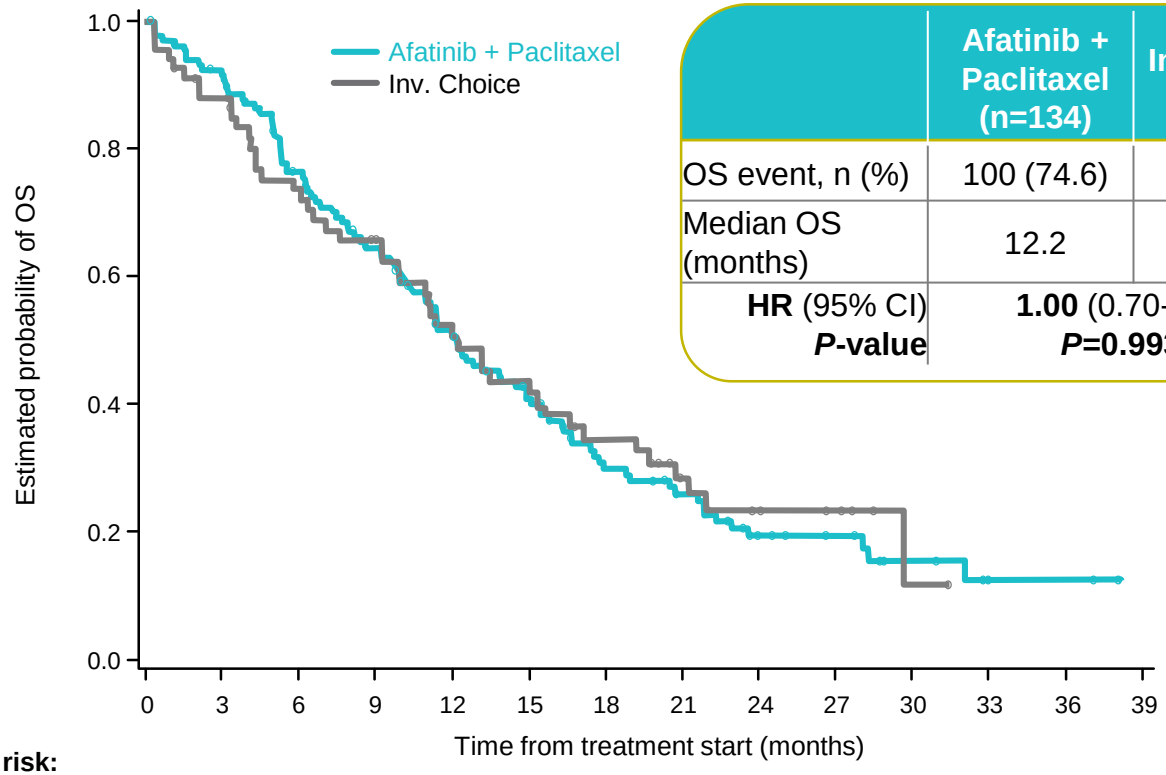
	Afatinib + Paclitaxel (n=134)	Inv. Choice Chemo (n=68)
Total randomised [N (%)]	134 (100.0)	68 (100.0)
Disease control [N (%)]	**100 (74.6)**	**31 (45.6)**
Objective response [N (%)]	**43 (32.1)[a]**	**9 (13.2)**
Complete response	1 (0.7)	0 (0.0)
Partial response	42 (31.3)	9 (13.2)
Stable disease	57 (42.5)	22 (32.4)
Duration of response Median in months (Range)	**4.2** (1.1-26.9)	**3.3** (0.3-11.9)
Duration of Disease Control Median in months (Range)	**7.0** (0.9-28.3)	**5.7** (1.4-21.3)
Maximum **decrease in tumour size** from baseline: [%]	15.1	1.2

[a]Odds ratio for response: 3.1, *P*=0.0049.

Data on file. Boehringer Ingelheim.

Part B: Overall Survival

OS



	Afatinib + Paclitaxel (n=134)	Inv. Choice (n=68)
OS event, n (%)	100 (74.6)	46 (67.6)
Median OS (months)	12.2	12.2
HR (95% CI)	**1.00** (0.70-1.43)	
***P*-value**	***P*=0.9936**	

No. at risk:

Afa + Pac	134	121	98	82	61	47	31	24	14	11	6	2	2	0
Inv. Choice	68	57	46	40	31	25	18	11	7	5	1	0	0	0

Schuler et al. ASCO 2014. Abstract 8019.

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Part B: Summary of Adverse Events

	Afatinib + Paclitaxel (n=132) (%)	Inv. Choice Chemo (n=68) (%)
Median time on treatment (days), range	**132.5 (2-910)**	**50.5 (1-517)**
Any AEs	127 (96.2)	51 (85)
Drug-related AEs	117 (88.6)	42 (70)
Any AEs grade ≥3	86 (65.1)	31 (51.7)
Drug-related AEs ≥3	64 (48.5)	18 (30)
AEs leading to dose reduction	57 (43.2)	7 (11.7)
AE leading to discontinuation	43 (32.6)	6 (10.0)
Drug-related AEs leading to discontinuation	25 (18.9)	4 (6.7)
SAE	53 (40.2)	19 (31.7)
Drug-related SAE	15 (11.4)	2 (3.3)
AEs leading to death	18 (13.6)	4 (6.7)
Drug-related AEs leading to death	1 (0.8)[a]	0 (0)

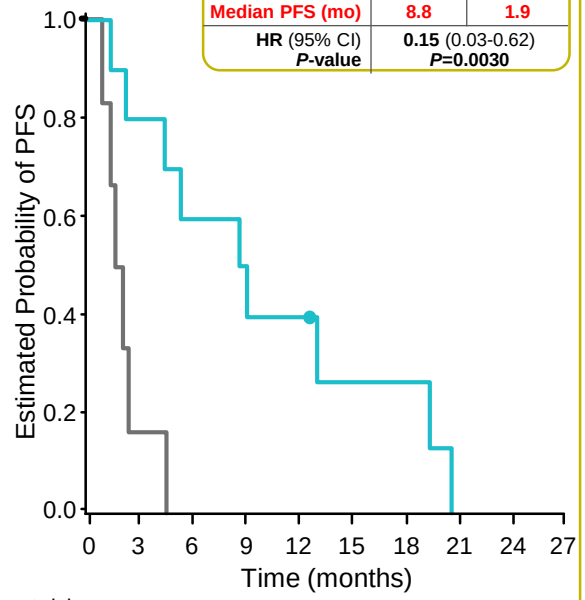
[a]Pneumonia (related to paclitaxel).

Data on file. Boehringer Ingelheim.

Part B: Exploratory Analysis of Squamous Cell Subset

PFS

	A+P (n=11)	ICC (n=6)
PFS events, n (%)	9 (81.8)	6 (100)
Median PFS (mo)	**8.8**	**1.9**
HR (95% CI) ***P*-value**	**0.15** (0.03-0.62) ***P*=0.0030**	

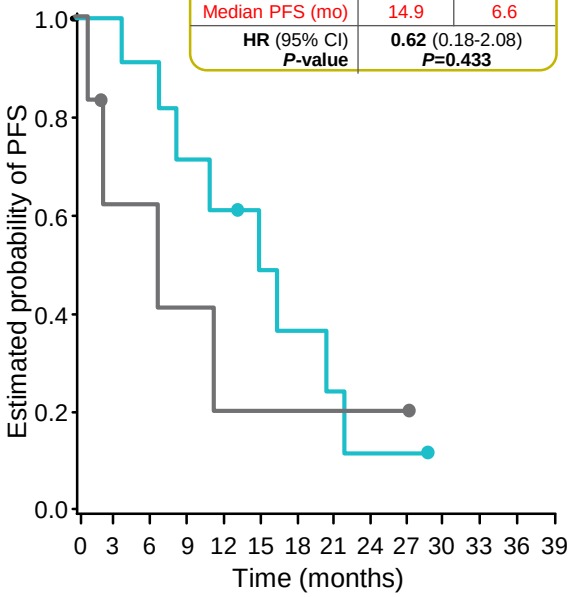


No. at risk:

A+P	11	8	6	5	4	2	2	0	0	0

OS

	A+P (n=11)	ICC (n=6)
OS events, n (%)	8 (72.7)	4 (66.7)
Median PFS (mo)	14.9	6.6
HR (95% CI) ***P*-value**	**0.62** (0.18-2.08) ***P*=0.433**	

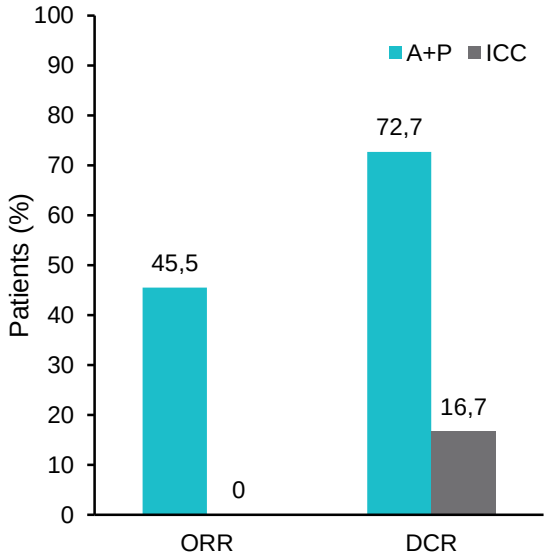


No. at risk:

A+P	11	11	10	7	6	4	3	2	1	1	0	0	0	0
ICC	6	3	3	2	1	1	1	1	1	1	0	0	0	0

ORR and DCR (regardless of confirmation)

	A+P (n=11)	ICC (n=6)
ORR, % *P*-value	45.5 *P*=0.1023*	0
DCR, % *P*-value	**72.7 *P*<0.0207**	**16.7**

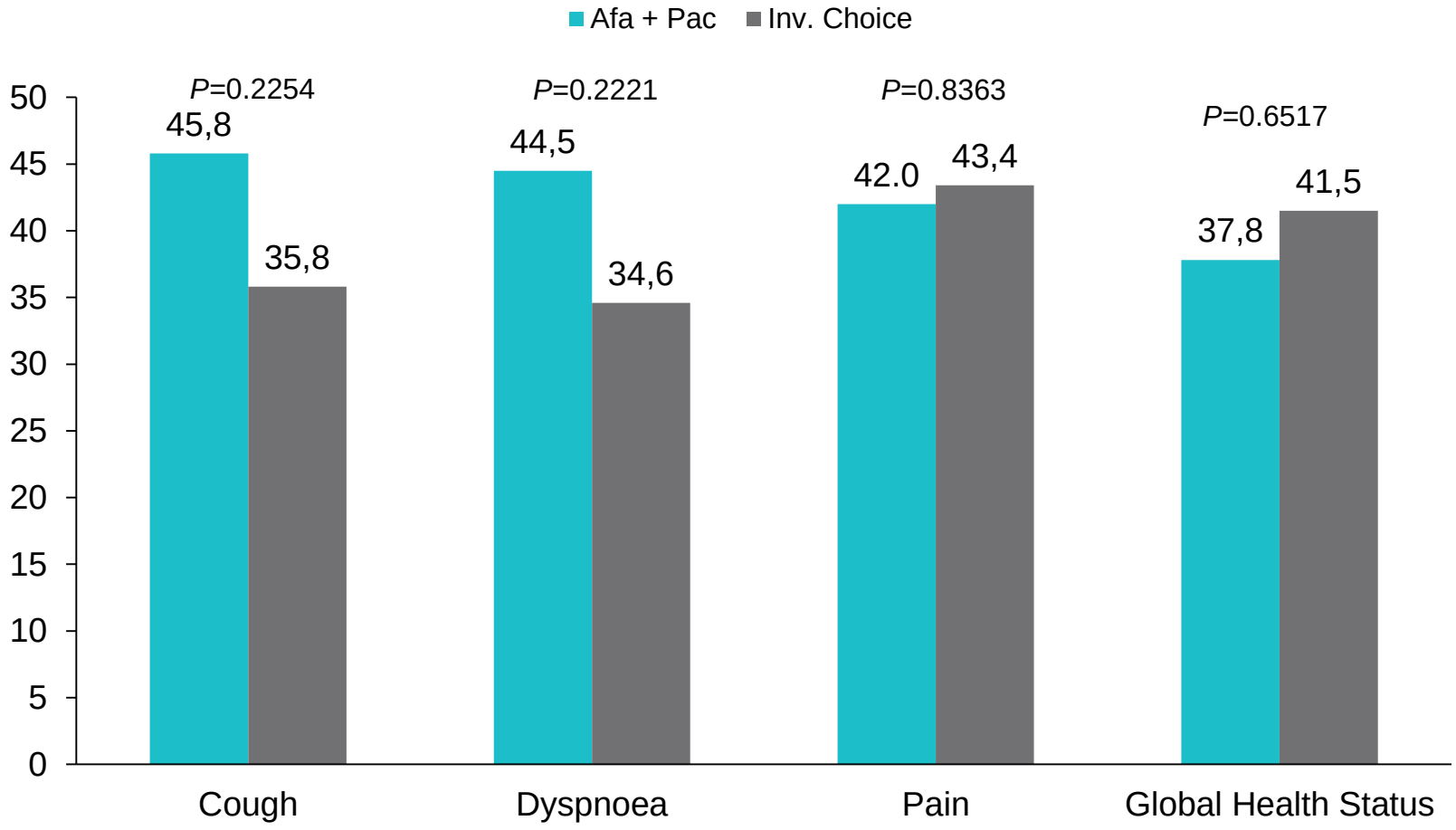


*Fisher exact test two-sided.

A+P, afatinib + paclitaxel; CI, confidence interval; HR, hazard ratio; ICC, investigator's choice of chemotherapy; OS, overall survival; PFS, progression-free survival; ORR, overall response rate; DCR, disease control rate.

Park et al. ESMO 2014. Abstract 1263P.

Percentage of Patients Improved[a] Cough, Dyspnoea, and Pain Scores



[a]EORTC scores improved by ≥10 points.
All scores were from the QLQ-LC13 except for "Short of Breath," which was used from the QLQ-C30.
Planchard et al. ESMO 2014. Abstract 1265P.

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LUX-Lung 5 Part B: Conclusions

- **LUX-Lung 5** met its primary endpoint of **demonstrating superior PFS of continued afatinib (+ paclitaxel) vs investigator choice of chemotherapy in patients with prior benefit from EGFR TKI and afatinib**
  - **mPFS 5.6 vs. 2.8, HR=0.60, *P*=0.0031**
  - **ORR 32% vs. 13%, OR=3.1, *P*=0.0049**
- Afatinib + paclitaxel had a **manageable safety profile**; diarrhoea, rash/acne, alopecia, nail disorders and stomatitis were more frequent in the combination arm vs single-agent chemotherapy
- Global health status/QoL was **maintained over time** in patients treated with afatinib + paclitaxel
- **LUX-Lung 5 is the first and the largest** prospectively designed randomised **trial demonstrating the benefit of continuous EGFR blockade ('treatment beyond progression') with afatinib in patients with NSCLC previously treated with EGFR TKIs**

Schuler et al. ASCO 2014. Abstract 8019.

The End

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