

Afatinib versus erlotinib as second-line treatment of patients with advanced squamous cell carcinoma of the lung: final analysis of the randomised phase 3 Lux-Lung 8 trial

Supplementary appendix

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Supplementary Tables

Adverse event	Afatinib (n=392)				Erlotinib (n=395)			
	All grades	Grade 3	Grade 4	Grade 5	All grades	Grade 3	Grade 4	Grade 5
Total	174 (44.4%)	58 (14.8%)	19 (4.8%)	77 (19.6%)	175 (44.3%)	66 (16.7%)	15 (3.8%)	71 (18.0%)
Pneumonia	26 (6.6%)	7 (1.8%)	2 (<1%)	9 (2.3%)	16 (4.1%)	8 (2.0%)	3 (<1%)	3 (<1%)
Malignant neoplasm progression	23 (5.9%)		3 (<1%)	20 (5.1%)	16 (4.1%)			16 (4.1%)
Diarrhoea	18 (4.6%)	12 (3.1%)	3 (<1%)		7 (1.8%)	4 (1.0%)		
Dehydration	12 (3.1%)	6 (1.5%)	4 (1.0%)		4 (1.0%)	3 (<1%)		
Dyspnoea	12 (3.1%)	4 (1.0%)	3 (<1%)	3 (<1%)	30 (7.6%)	11 (2.8%)	3 (<1%)	10 (2.5%)
General physical health deterioration	11 (2.8%)	4 (1.0%)	1 (<1%)	5 (1.3%)	6 (1.5%)	4 (1.0%)		
Pulmonary embolism	10 (2.6%)	4 (1.0%)		4 (1.0%)	5 (1.3%)	1 (<1%)	2 (<1%)	
Sepsis	9 (2.3%)	1 (<1%)	3 (0.8%)	4 (1.0%)	2 (<1%)		1 (<1%)	1 (<1%)
Acute renal failure	9 (2.3%)	4 (1.0%)	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)		
Asthenia	6 (1.5%)	4 (1.0%)		1 (<1%)	3 (<1%)	2 (<1%)	1 (<1%)	
Anaemia	5 (1.3%)	3 (<1%)	1 (<1%)		2 (<1%)	1 (<1%)		
COPD	5 (1.3%)	3 (<1%)			4 (1.0%)	1 (<1%)	1 (<1%)	1 (<1%)
Haemoptysis	5 (1.3%)	2 (<1%)		2 (<1%)	10 (2.5%)	2 (<1%)	1 (<1%)	
Abdominal pain	5 (1.3%)	3 (<1%)	1 (<1%)		5 (1.3%)	3 (<1%)	1 (<1%)	
Convulsion	4 (1.0%)	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)			
Atrial fibrillation	4 (1.0%)	3 (<1%)			2 (<1%)			
Interstitial lung disease	4 (1.0%)	1 (<1%)	1 (<1%)	2 (<1%)	1 (<1%)			1 (<1%)
Vomiting	4 (1.0%)	2 (<1%)			5 (1.3%)	3 (<1%)	1 (<1%)	
Death	4 (1.0%)			4 (1.0%)	2 (<1%)			
Pyrexia	3 (<1%)	2 (<1%)			4 (1.0%)			

Pleural effusion	3 (<1%)		1 (<1%)	6 (1.5%)	4 (1.0%)		
Dizziness	2 (<1%)	2 (<1%)		4 (1.0%)	1 (<1%)		
Pneumothorax	2 (<1%)			4 (1.0%)			
Bronchitis	2 (<1%)			6 (1.5%)	6 (1.5%)		
Lung infection	2 (<1%)	1 (<1%)	1 (<1%)	5 (1.3%)	2 (<1%)	1 (<1%)	1 (<1%)
Metastases to CNS	2 (<1%)		1 (<1%)	1 (<1%)	6 (1.5%)	2 (<1%)	1 (<1%)
Respiratory failure	2 (<1%)	1 (<1%)	1 (<1%)	12 (3.0%)	1 (<1%)	3 (<1%)	8 (2.0%)
Hypercalcaemia	1 (<1%)		1 (<1%)	6 (1.5%)	2 (<1%)	2 (<1%)	
Chest pain				6 (1.5%)	4 (1.0%)		
Myocardial infarction				4 (1.0%)	1 (<1%)		3 (<1%)

Data shown n (%) are serious adverse events in $\geq 1\%$ of patients with serious adverse events (all grades), or $\geq 1\%$ of patients with grade 3–5 serious adverse events in any treatment group.

Table S1: Serious adverse events

Adverse event	Afatinib (n=392)				Erlotinib (n=395)			
	All grades	Grade 3	Grade 4	Grade 5	All grades	Grade 3	Grade 4	Grade 5
Total	390 (100%)	124 (32%)	23 (6%)	77 (20%)	385 (98%)	138 (35%)	18 (5%)	71 (18%)
Diarrhoea	293 (75%)	39 (10%)	3 (<1%)		164 (42%)	12 (3%)	1 (<1%)	
Rash or acne*	272 (69%)	26 (7%)			277 (70%)	42 (11%)		
Fatigue*	132 (34%)	18 (5%)	1 (<1%)	1 (<1%)	120 (30%)	23 (6%)	3 (<1%)	
Stomatitis*	115 (29%)	16 (4%)			39 (10%)	2 (<1%)		
Decreased appetite	97 (25%)	12 (3%)			103 (26%)	8 (2%)		
Nausea	81 (21%)	6 (2%)			65 (17%)	4 (1%)	1 (<1%)	
Dyspnoea	79 (20%)	12 (3%)	3 (<1%)	3 (<1%)	94 (24%)	18 (5%)	4 (1%)	10 (3%)
Cough	67 (17%)	2 (<1%)			69 (18%)	2 (<1%)		
Vomiting	51 (13%)	3 (<1%)			41 (10%)	4 (1%)	1 (<1%)	
Haemoptysis	49 (13%)	2 (<1%)		2 (<1%)	49 (12%)	2 (<1%)	1 (<1%)	
Constipation	43 (11%)				43 (11%)	1 (<1%)		
Paronychia*	43 (11%)	2 (<1%)			20 (5%)	1 (<1%)		
Pruritus	38 (10%)	1 (<1%)			52 (13%)			
Weight decreased	38 (10%)	2 (<1%)			52 (13%)	2 (<1%)		
Dry skin	36 (9%)	2 (<1%)			47 (12%)			
Anaemia	34 (9%)	8 (2%)	2 (<1%)		43 (11%)	7 (2%)		

Data shown n (%) are adverse events in >10% of patients with adverse events (all grades). *Grouped terms.

Table S2: All-cause adverse events

Adverse event	Afatinib (n=392)				Erlotinib (n=395)			
	All grades	Grade 3	Grade 4	Grade 5	All grades	Grade 3	Grade 4	Grade 5
Total	104 (26.5%)	60 (15.3%)	2 (0.5%)		56 (14.2%)	37 (9.4%)		
Diarrhoea	58 (14.8%)	22 (5.6%)	2 (0.5%)		14 (3.5%)	5 (1.3%)		
Rash or acne*	23 (5.9%)	15 (3.8%)			37 (9.4%)	28 (7.1%)		
Stomatitis*	12 (3.1%)	11 (2.8%)						
Fatigue*	5 (1.3%)	4 (1.0%)			3 (<1.0%)	2 (<1.0%)		

Data shown n (%) are adverse events in >1% of patients (all grades). *Grouped terms.

Table S3: Adverse events leading to dose reduction

Adverse event	Afatinib (n=392)				Erlotinib (n=395)			
	All grades	Grade 3	Grade 4	Grade 5	All grades	Grade 3	Grade 4	Grade 5
Total	80 (20.4%)	33 (8.4%)	16 (4.1%)	2 (<1%)	66 (16.7%)	35 (8.9%)	8 (2.0%)	7 (1.8%)
Diarrhoea	16 (4.1%)	9 (2.3%)			6 (1.5%)	4 (1.0%)		
Malignant neoplasm progression	7 (1.8%)	2 (<1%)	3 (<1%)	1 (<1%)	2 (<1%)		1 (<1%)	1 (<1%)
Rash	6 (1.5%)	4 (1.0%)			4 (1.0%)	3 (<1%)		
Pneumonia	6 (1.5%)	2 (<1%)	3 (<1%)		1 (<1%)			
Dyspnoea	5 (1.3%)	3 (<1%)			6 (1.5%)	4 (1.0%)		1 (<1%)

Data shown n (%) are adverse events in ≥1% of patients (all grades) resulting in treatment discontinuation, or ≥1% of patients with grade 3–5 adverse events resulting in treatment discontinuation in any treatment group.

Table S4: Adverse events leading to treatment discontinuation

Supplementary Figure

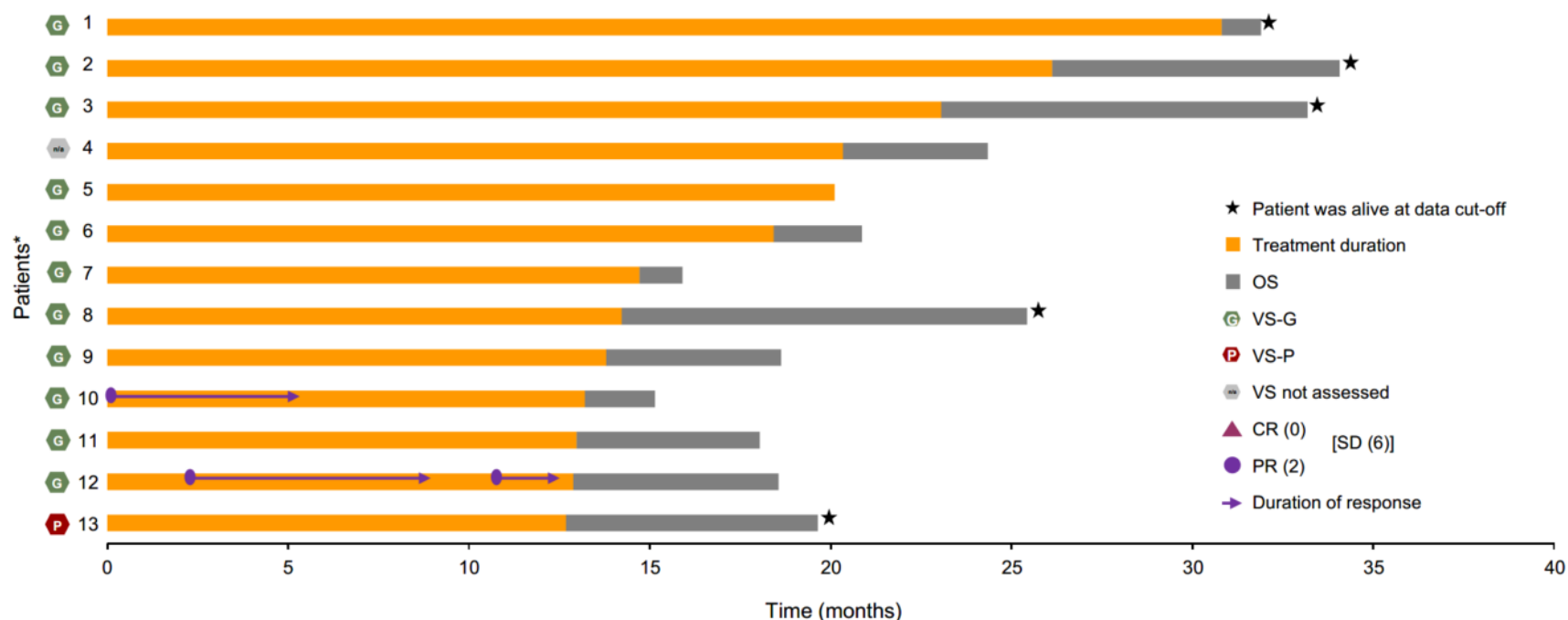


Figure S1: Efficacy outcomes and biomarkers in patients who received long-term benefit on erlotinib

*Patients were ordered and numbered by treatment duration (at data cut-off). Next-generation sequencing was undertaken in 3/13 patients with long-term benefit. Mutation data was available for only 1 patient (not annotated in figure).

CR=complete response; PR=partial response; OS=overall survival; SD=stable disease; VS-G=VeriStrat-Good; VS-P=VeriStrat poor; WT=wild-type.