

**Lorlatinib for previously treated ALK-positive advanced
non-small-cell lung cancer [ID1338]**

Second addendum to the main ERG report

Produced by Aberdeen HTA Group

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Following submission of the ERG report for this appraisal, the NICE technical team asked the ERG to replicate the results of the ERGs exploratory analysis (contained in Table 17 and Table 18 of the main ERG report), using list prices for comparators and subsequent treatments, rather than the company-estimated cPAS prices which the ERG used in the original tables for comparability with the company's base case results. These results are provide below as requested.

Table 17 Summary sensitivity analyses undertaken by the ERG

	Description		Incremental costs	Incremental LYs	Incremental QALYs	ICER (£/QALY)
Company Base-case			██████	████	████	£46,033
1	Alternative PDC PFS and OS survival cure methods	a) Method 1: MAIC HR EXP-2:3A	██████	████	████	£42,416
		b) Method 2: MAIC HR EXP-3B:5	██████	████	████	£53,915
		c) Method 3: Unadjusted HR EXP-2:3A	██████	████	████	£40,728
		d) Method 4: Unadjusted HR EXP-3B:5	██████	████	████	£46,184
		e) Method 6: Independent curves & population adjustment	██████	████	████	£40,520
2	Hazard ratios for upward adjustments to PFS and OS in the PDC arm	a) 0.9	██████	████	████	£46,615
		b) 0.8	██████	████	████	£47,338
		c) 0.7	██████	████	████	£48,290
		d) 0.6	██████	████	████	£49,710
3	Treatment waning	a) Hazard of death on lorlatinib equal to PCD from three years	██████	████	████	£50,863
		b) Hazard of death on lorlatinib equal to PCD from five years	██████	████	████	£46,948
4	Mean time on lorlatinib following progression	a) ██████	██████	████	████	£49,819
		b) ██████	██████	████	████	£55,378
5	Lorlatinib time on treatment	Generalised gamma	██████	████	████	£52,758

6	Utilities	a) PF utility on lorlatinib = PF utility on PDC (0.72) + 0.02	██████	████	████	£48,319
		b) PF utility on lorlatinib = PF utility on PDC (0.72) + 0.08	██████	████	████	£45,327
		c) PD utility is 0.59 (Chouaid et al)	██████	████	████	£47,633
		d) PD utility is 0.46 (Chouaid et al)	██████	████	████	£51,511
		e) a and d combined	██████	████	████	£54,390
7	Subsequent therapies	a) Fixed dose regimen for pembrolizumab	██████	████	████	£43,371
		b) proportion of treated patients receiving atezolizumab and pembrolizumab following progression on PDC (████ and █████ respectively)	██████	████	████	£43,264
		c) a and b combined	██████	████	████	£42,068
		d) Proportion of subsequently treated patients who receive PDC and pemetrexed alone following progression on lorlatinib (80% and 20%)	██████	████	████	£46,102
		e) 50% receive subsequent therapy following PDC	██████	████	████	£48,424
8	Combination	Combines 2b), 5), 6c), 7a), and 7e)	██████	████	████	£57,114
		Probabilistic ICER for scenario 8	██████	████	████	£55,057

Abbreviations: ERG = Evidence Review Group; EXP = expansion; HR = hazard ratio; ICER = incremental cost-effectiveness ratio; LY = life year; MAIC = match adjusted indirect comparison; NHS = National Health Service; OS = overall survival; PDC = platinum doublet chemotherapy; PFS = progression free survival; QALY = quality-adjusted life year; ToT = time on treatment

Table 18 Summary sensitivity analyses undertaken by the ERG

	Description		Incremental costs	Incremental LYs	Incremental QALYs	ICER (£/QALY)
	Company Base-case		██████	████	████	£8,955
1	Reducing population adjustment hazard ratios (on log scale)	a) By 25% (HR for PFS = 1.53; HR for OS = 2.86)	██████	████	████	£1,197
		b) By 50% (HR for PFS = 1.33; HR for OS = 2.01)	██████	████	████	Dominant
2	Treatment waning	a) Hazard of death on lorlatinib equal to ABCP from three years	██████	████	████	Dominant
		b) Hazard of death on lorlatinib equal to ABCP from five years	██████	████	████	Dominant
3	Mean time on lorlatinib following progression	a) ██████	██████	████	████	£13,091
		b) ██████	██████	████	████	£19,163
4	Lorlatinib time on treatment	Generalised gamma curve	██████	████	████	£16,301
5	Utilities	a) PF utility on lorlatinib = PF utility on PDC (0.72) + 0.02	██████	████	████	£9,443
		b) PF utility on lorlatinib = PF utility on PDC (0.72) + 0.08	██████	████	████	£8,806
		c) PD utility is 0.59 (Chouaid et al)	██████	████	████	£9,388
		d) PD utility is 0.46 (Chouaid et al)	██████	████	████	£10,485
		e) a and d combined	██████	████	████	£11,160

6	Subsequent therapies	a) 80% of subsequently treated patients who progress on lorlatinib receive PDC	██████	██████	██████	£9,031
		b) 40% receive subsequent treatment with docetaxel following progression on ABCP	██████	██████	██████	£9,147
7	Combination	Combines 1b), 4), 5c), and 6b),	██████	██████	██████	£30

Abbreviations: ERG = Evidence Review Group; EXP = expansion; HR = hazard ratio; ICER = incremental cost-effectiveness ratio; LY = life year; MAIC = match adjusted indirect comparison; NHS = National Health Service; OS = overall survival; PDC = platinum doublet chemotherapy; PFS = progression free survival; QALY = quality-adjusted life year; ToT = time on treatment