

CONFIDENTIAL

Evidence Review Group Report commissioned by the NIHR HTA Programme on behalf of NICE

Atezolizumab in combination for treating advanced non-squamous non-small-cell lung cancer

Addendum to the ERG report: Results with list prices for all treatments

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This is an addendum to the ERG report dated 8th November 2018. In this addendum we present the company’s base case results, ERG corrected company base case results, ERG corrected company scenario analyses, ERG base case analyses and ERG scenario analyses, all of which are based on available list prices. In addition to the above, this addendum contains an additional ERG scenario analysis in which one of the subsequent treatment options for patients progressing on first line treatment is nintedanib in combination with docetaxel (based on PAS discount prices for atezolizumab and bevacizumab).

Analyses based on all available PAS analyses are available in a separate confidential addendum (dated 8th November 2018).

1.1 Cost-effectiveness results at list prices

1.1.1 Company base case results (from clarification response)

The company base results for the three populations at list price for all treatments are shown in Table 1-Table 3.

Table 1 Company base-case results ITT population – list price, deterministic (Clarification response Table 31)

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+plat	██████	██████		██████
Pem+plat+pem maint	██████	██████	██████	██████
Atezo+Bev+CP	██████	██████	██████	-

Table 2 Company base-case results PD-L1 negative/low population – list price, deterministic (Clarification response Table 32)

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+plat	██████	██████		██████
Pem+plat+pem maint	██████	██████	██████	██████
Atezo+Bev+CP	██████	██████	██████	-

Table 3 Company base-case results EGFR/ ALK positive population – list price, deterministic (Clarification response Table 33)

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+plat	██████	██████		██████
Pem+plat+pem maint	██████	██████	██████	██████
Atezo+Bev+CP	██████	██████	██████	-

1.1.2 Company base case results (with ERG corrections)

The company base case results for the three populations with ERG corrections are shown in Table 4-Table 6 with list price for all treatments.

Table 4 Company base case results with ERG corrections for ITT population – list price

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+platinum	██████	██████	██████	██████
Pem+platinum w Pem maint	██████	██████	██████	██████
Atezo+Bev+CP	██████	██████	██████	

Table 5 Company base case results with ERG corrections for PD-L1 population – list price

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+platinum	██████	██████	██████	██████
Pem+platinum w Pem maint	██████	██████	██████	██████
Atezo+Bev+CP	██████	██████	██████	

Table 6 Company base case results with ERG corrections for EGFR/ALK+ population – list price

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+platinum	██████	██████	██████	██████
Pem+platinum w Pem maint	██████	██████	██████	██████
Atezo+Bev+CP	██████	██████	██████	

1.2 Company scenarios with ERG corrections at list price

Table 7 and Table 8 show the scenario analyses with ERG corrections for the ITT population with list price for all treatments.

Table 7 Scenario analysis results- ITT population vs. Pemetrexed plus platinum plus pemetrexed maintenance – list price

	Description	Atezo+Bev+CP			Pem+platinum w Pem maint			ICER (£/QALY)
		Total LYs	Total QALYs	Total costs	Total LYs	Total QAL Ys	Total costs	
OS distribution	Exponential (base case)	████	████	████████	████	████	████████	████████
	Weibull	████	████	████████	████	████	████████	████████
	Log-normal	████	████	████████	████	████	████████	████████
	Gen Gamma	████	████	████████	████	████	████████	████████
	Log-logistic	████	████	████████	████	████	████████	████████
	Gompertz	████	████	████████	████	████	████████	████████
PFS distribution	KM with Log-logistic tail (base case)	████	████	████████	████	████	████████	████████
	Exponential	████	████	████████	████	████	████████	████████
	Weibull	████	████	████████	████	████	████████	████████
	Log-normal	████	████	████████	████	████	████████	████████
	Gen Gamma	████	████	████████	████	████	████████	████████
	Log-logistic	████	████	████████	████	████	████████	████████
TTD distribution	KM with Exponential tail (base case)	████	████	████████	████	████	████████	████████
	Exponential	████	████	████████	████	████	████████	████████
	Weibull	████	████	████████	████	████	████████	████████
	Log-normal	████	████	████████	████	████	████████	████████
	Gen Gamma	████	████	████████	████	████	████████	████████
	Log-logistic	████	████	████████	████	████	████████	████████
	Gompertz	Does not converge						
Alternative NMA network	ITT (base case)	████	████	████████	████	████	████████	████████
	ITT exclude Keynote	████	████	████████	████	████	████████	████████

	ITT exclude Paramount	■	■	■	■	■	■	■
Alternative NMA model	NMA - Fract Poly (FE) (base case)	■	■	■	■	■	■	■
	NMA - PH	■	■	■	■	■	■	■
	NMA - Fract Poly (RE)	■	■	■	■	■	■	■
Treatment stopping rule	At 2 years (base case)	■	■	■	■	■	■	■
	No treatment stopping rule	■	■	■	■	■	■	■
Treatment effect duration	5 years (base case)	■	■	■	■	■	■	■
	105 months	■	■	■	■	■	■	■
	150 months	■	■	■	■	■	■	■
	195 months	■	■	■	■	■	■	■
	240 months (lifetime)	■	■	■	■	■	■	■
Wastage	With vial sharing (base case)	■	■	■	■	■	■	■
	No vial sharing	■	■	■	■	■	■	■
Utility values	IMpower150 (Proximity to death) (base case)	■	■	■	■	■	■	■
	IMpower150 (Pre/Post progression)	■	■	■	■	■	■	■
	Chouaid et al. 2013	■	■	■	■	■	■	■
	Nafees et al. 2008	■	■	■	■	■	■	■
Subsequent treatments	Base case	■	■	■	■	■	■	■
	Impower 150	■	■	■	■	■	■	■
AE disutility	No (base case)	■	■	■	■	■	■	■
	Yes	■	■	■	■	■	■	■

Table 8 Scenario analysis results- ITT population vs. Pemetrexed plus platinum – list price

	Description	Atezo+Bev+CP			Pem+platinum			ICER
		Total LYs	Total QALYs	Total costs	Total LYs	Total QALYs	Total costs	(£/QALY)
OS distribution	Exponential (base case)	■	■	■	■	■	■	■
	Weibull	■	■	■	■	■	■	■
	Log-normal	■	■	■	■	■	■	■
	Gen Gamma	■	■	■	■	■	■	■
	Log-logistic	■	■	■	■	■	■	■
	Gompertz	Does not converge						
PFS distribution	KM with Log-logistic tail (base case)	■	■	■	■	■	■	■
	Exponential	■	■	■	■	■	■	■
	Weibull	■	■	■	■	■	■	■
	Log-normal	■	■	■	■	■	■	■
	Gen Gamma	■	■	■	■	■	■	■
	Log-logistic	■	■	■	■	■	■	■
	Gompertz	■	■	■	■	■	■	■
TTD distribution	KM with Exponential tail (base case)	■	■	■	■	■	■	■
	Exponential	■	■	■	■	■	■	■
	Weibull	■	■	■	■	■	■	■
	Log-normal	■	■	■	■	■	■	■
	Gen Gamma	■	■	■	■	■	■	■
	Log-logistic	■	■	■	■	■	■	■
	Gompertz	Does not converge						
Alternative NMA network	ITT (base case)	■	■	■	■	■	■	■
	ITT exclude Keynote	■	■	■	■	■	■	■
	ITT exclude Paramount	Does not converge						
Alternative NMA model	NMA - Fract Poly (FE) (base case)	■	■	■	■	■	■	■
	NMA - PH	■	■	■	■	■	■	■
	NMA - Fract Poly (RE)	■	■	■	■	■	■	■
	At 2 years (base case)	■	■	■	■	■	■	■

Treatment stopping rule	No treatment stopping rule	■	■	■	■	■	■	■
Treatment effect duration	5 years (base case)	■	■	■	■	■	■	■
	105 months	■	■	■	■	■	■	■
	150 months	■	■	■	■	■	■	■
	195 months	■	■	■	■	■	■	■
	240 months (lifetime)	■	■	■	■	■	■	■
Wastage	With vial sharing (base case)	■	■	■	■	■	■	■
	No vial sharing	■	■	■	■	■	■	■
Utility values	IMpower150 (Proximity to death) (base case)	■	■	■	■	■	■	■
	IMpower150 (Pre/Post progression)	■	■	■	■	■	■	■
	Chouaid et al. 2013	■	■	■	■	■	■	■
	Nafees et al. 2008	■	■	■	■	■	■	■
Subsequent treatments	Base case	■	■	■	■	■	■	■
	Impower 150	■	■	■	■	■	■	■
AE disutility	No (base case)	■	■	■	■	■	■	■
	Yes	■	■	■	■	■	■	■

1.2.1 ERG analyses

Table 9 - Table 11 show the ERG base case results for the three populations with list price for all treatments.

Table 9 ERG base case results for ITT population– list price

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+platinum w Pem maint	■	■	■	■
Atezo+Bev+CP	■	■	■	■

Table 10 ERG base case results for PD-L1 population– list price

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+platinum w Pem maint	████████	██████		████████
Atezo+Bev+CP	████████	██████	████████	

Table 11 ERG base case results for EGFR/ALK population – list price

Technologies	Total costs (£)	Total QALYs	ICER (£) fully incremental analysis	ICER (£) pairwise; Atezo+Bev+CP vs comparator
Pem+platinum w Pem maint	████████	██████		████████
Atezo+Bev+CP	████████	██████	████████	

Table 12 shows the scenario analyses with the ERG base case for the ITT population with list price for all treatments.

Table 12 ERG scenario analysis for ITT population – list price

	Description	Atezo+Bev+CP		Pem+platinum+Pem Maintenance		ICER
		Total QALYs	Total costs	Total QALYs	Total costs	
OS distribution	Weibull (base case)	████	██████	████	██████	██████
	Exponential	████	██████	████	██████	██████
	Log-logistic	████	██████	████	██████	██████
PFS distribution	KM+log-logistic (base case)	████	██████	████	██████	██████
	KM + Exponential	████	██████	████	██████	██████
	KM+Weibull	████	██████	████	██████	██████
TTD distribution	KM + Exponential and pemetrexed follows PFS (base case)	████	██████	████	██████	██████
	Bevacizumab until progression	████	██████	████	██████	██████
Alternative NMA network/model	ITT FP excluding PARAMOUNT (FE) (base case)	████	██████	████	██████	██████
	ITT FP (RE)	████	██████	████	██████	██████
	ITT PH (excluding PARAMOUNT)	████	██████	████	██████	██████
Treatment stopping rule/treatment effect	2 years treatment + 3 years OS effect (base case)	████	██████	████	██████	██████

	2 years OS	■	■	■	■	■
	5 years OS	■	■	■	■	■
	3 years PFS	■	■	■	■	■
	No stopping rule or effect cap	■	■	■	■	■
Utility values	IMPower150 EQ-5D, using time from death + disutilities (base case)	■	■	■	■	■
	IMPower EQ-5D health states	■	■	■	■	■
AE disutility	disutilities per grade 3+ treatment related AE (base case)	■	■	■	■	■
	No AE disutilities	■	■	■	■	■
Subsequent treatments	Base case	■	■	■	■	■
	IMpower150	■	■	■	■	■
	Exclude nivolumab	■	■	■	■	■
	Include nintedanib + docetaxel	■	■	■	■	■

1.2.2 Additional scenario analysis - subsequent treatments

We have included an additional scenario for subsequent (second line) treatments in which nintedanib in combination with docetaxel is an available option for patients progressing on pemetrexed-based chemotherapy. This scenario analysis is not reported in the main ERG report. Costs for nintedanib were taken from NICE technology appraisal TA347 (i.e. 21 day cycle cost of nintedanib of nintedanib £1434.07; docetaxel £20.02; treatment given for 5.35 months). We assumed that 15% of patients received nintedanib and docetaxel, and kept the

proportion of all other treatments unchanged. The model rescales the proportion on all treatments to equal 100%. (Rescaled proportion for patients receiving nintedanib 13%).

Table 13 shows the additional scenario analysis in the ERG base case with subsequent treatment for nintedanib + docetaxel for the ITT population (based on PAS discount for atezolizumab and bevacizumab).

Table 13 ERG scenario analysis for ITT population including nintedanib + docetaxel – (PAS price for atezolizumab and bevacizumab)

	Description	Atezo+Bev+CP		Pem+platinum+Pem Maintenance		ICER (£/QALY)
		Total QALYs	Total costs	Total QALYs	Total costs	
Subsequent treatments	Base case	■	■	■	■	Dominant
	Include nintedanib + docetaxel	■	■	■	■	Dominant