

**LIVERPOOL REVIEWS AND
IMPLEMENTATION GROUP (LRiG)**

**Lapatinib and trastuzumab in
combination with an aromatase
inhibitor for the first-line treatment
of metastatic hormone receptor
positive breast cancer which over-
expresses HER2**

ERRATUM

Base case results: TRA+ANA vs ANA

The base case cost-effectiveness results based on the AG model are shown in Table . A modest expected mean health gain per patient (less than 8 months life extension, and about 0.5 additional QALYs) is generated by a substantial additional cost of more than £35,000 per patient most of which is incurred in the first 5 years. The cost-effectiveness ratio is stable over long time periods and exceeds £70,000 per QALY gained.

Univariate sensitivity analysis

Results from a sensitivity analysis covering the main model variables are shown in Table . The ICER is most sensitive to the health state utility parameter values, and to the cost of TRA, and discounting rates, but very insensitive to most of the other variables. In all cases the ICER remains above £61,000 per QALY indicating that uncertainty in any single parameter value is unlikely to alter the cost effectiveness of TRA+ANA relative to conventional thresholds.

Table 29 Cost-effectiveness results for base case analysis of TRA+ANA vs ANA (discounted) using AG model

Treatment	Cost per patient						Outcomes per patient		ICER
Time horizon (years)	Drugs	Monitoring	Adverse events	BSC	Terminal care	Total costs	Life years	QALYs	£ / QALY gained
ANA									
10	£549	£602	-	£11,101	£1,632	£13,884	2.204	1.235	
20	£549	£602	-	£11,194	£1,647	£13,992	2.220	1.243	
30	£549	£602	-	£11,194	£1,648	£13,993	2.220	1.243	
TRA+ANA									
10	£35,197	£1,843	£90	£11,471	£1,695	£50,296	2.783	1.725	
20	£36,251	£1,898	£92	£11,549	£1,696	£51,487	2.823	1.755	
30	£36,370	£1,905	£93	£11,557	£1,696	£51,621	2.827	1.759	
Incremental									
10	£34,648	£1,241	£90	£370	£63	£36,412	0.579	0.490	£74,312
20	£35,702	£1,297	£92	£355	£49	£37,495	0.603	0.513	£73,135
30	£35,821	£1,303	£93	£363	£49	£37,628	0.607	0.516	£72,919

Table 30 Univariate sensitivity analysis of the cost-effectiveness results of TRA+ANA vs ANA to variations in main variables in AG model (base case with 20 year horizon)

Model variable	Variation in value		ICER for:	
	low	high	low	high
Base case	-	-	£73,135	
Discount rate – costs	0%	6%	£77,944	£70,351
Discount rate – outcomes	0%	6%	£68,003	£76,409
Dispensing costs: community	£5	£10	£73,103	£73,192
Dispensing costs: hospital	£7	£11	£73,045	£73,225
Frequency of cardiac monitoring (p.a.)	3	6	£72,854	£73,707
ECHO as % of scans	50%	100%	£73,416	£72,713
Frequency of PFS follow-up & CT scan (p.a.)	2	6	£72,525	£73,790
Proportion of progressed patients on exemestane	0%	100%	£73,330	£72,940
Net extra cost of AEs in TRA+ANA group	£0	£1,000	£72,955	£74,759
Net extra disutility of AEs in TRA+ANA group	0	-0.01	£73,135	£74,479
Utility in PFS: ANA only	-10%	10%	£67,822	£79,352
Utility in PFS: TRA+ANA	-10%	10%	£90,840	£61,206
Utility in PFS: both groups	-10%	10%	£82,784	£65,500
Utility in PPS	-10%	10%	£71,944	£74,366
Administration of TRA costs	-10%	10%	£72,228	£74,042
Acquisition cost of TRA costs	-10%	10%	£67,269	£79,001
Cost of cardiac scan	-10%	10%	£72,228	£74,042
BSC annual costs	-10%	10%	£73,046	£73,224
Terminal care costs	-10%	10%	£73,125	£73,145

Probabilistic sensitivity analysis

Probabilistic sensitivity was explored running 1000 random iterations for all variables subject to measurable parameter uncertainty, using the base case scenario over a 20 year horizon.

The PSA results are compared with the corresponding deterministic results in Table .

Table 31 Comparison of deterministic and probabilistic cost-effectiveness results for TRA+ANA vs ANA (base case with 20 year horizon)

	Incremental cost	Incremental QALYs	ICER
Deterministic	£37,495	0.448	£73,135
PSA	£33,085	0.463	£71,470

The scatterplot of iteration results in the cost-effectiveness plane (Figure) indicates a strong positive correlation between incremental cost and incremental benefit. Figure confirms that there is no measurable probability of the combination therapy being cost effective at a willingness-to-pay threshold of £40,000 per QALY gained, and only a 3.2% probability at £50,000 per QALY gained.

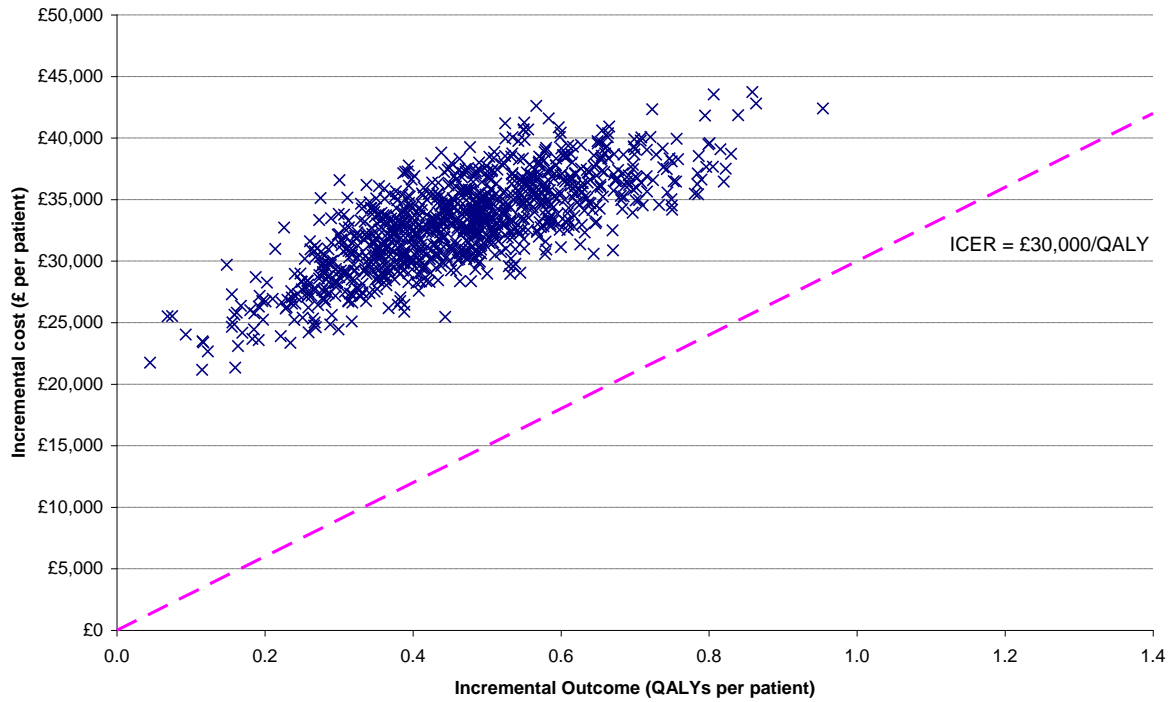


Figure 18 PSA of TRA+ANA vs ANA only: scatterplot of 1000 probabilistic iterations

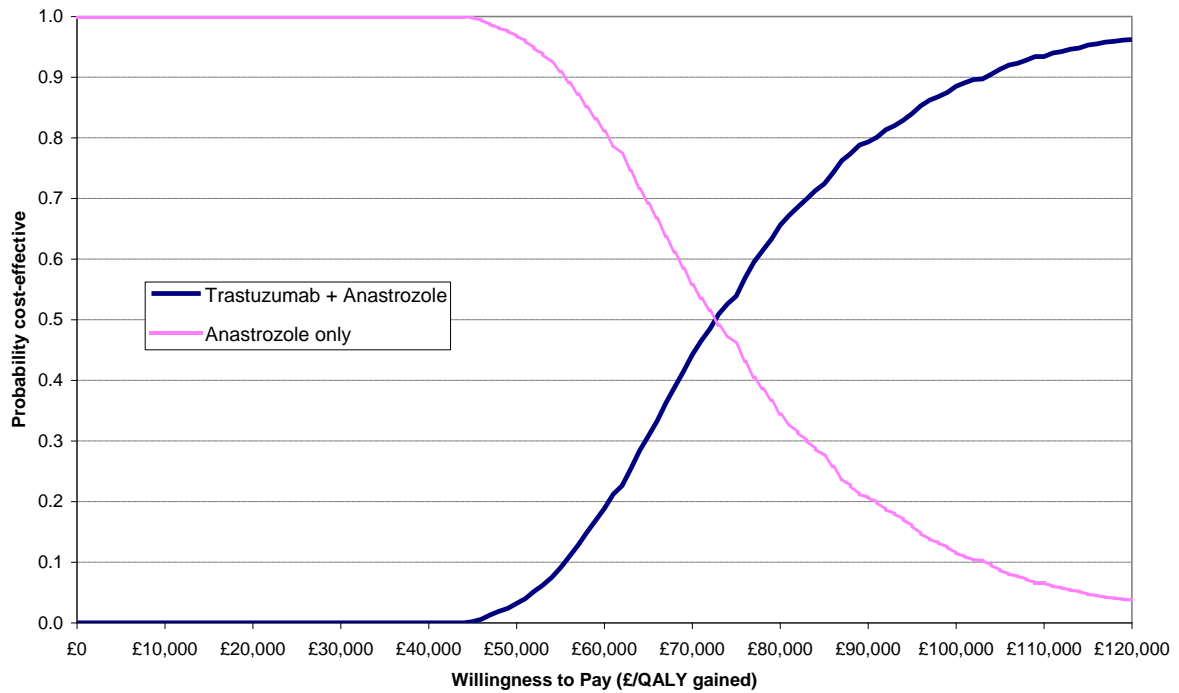


Figure 19 PSA of TRA+ANA vs ANA only: cost-effectiveness acceptability curve