PEMBROLIZUMAB FOR PATIENTS PREVIOUSLY TREATED WITH IPILIMUMAB

RISK ANALYSIS - THE IMPACT OF DIFFERENT DURATIONS OF NHS FUNDING FOR PEMBROLIZUMAB ON COST EFFECTIVENESS

MSD was aware when it made the submission to NICE that there was a marked difference between the reference case deterministic ICER value and that from the PSA. This was driven by the continuing use, and therefore cost, of pembrolizumab extending for a minority of patients into decades. To demonstrate the impact of this we also presented in our submission a scenario analysis where the cost of treatment (drug acquisition and administration) ceased at 2 years, based on the maximum treatment duration of therapy within the Phase III, KEYNOTE 006 study (patients previously untreated with ipilimumab). The efficacy data used for this analysis was the same as for the base case analysis. The PSA ICER from this scenario was significantly lower and more aligned with that of the deterministic reference case.

[redacted]

MSD believes that the Committee will want to better quantify the potential cost to the NHS of continuing treatment use, [redacted] We have therefore provided a number of additional analyses below. The analyses demonstrate that it is only a small (theoretical) increase in the number of patients driving the uncertainty around the cost-effectiveness of pembrolizumab.

[redacted]

SUMMARY OF ICERS ASSUMING DIFFERENT DURATIONS OF NHS REIMBURSEMENT FOR PEMBROLIZUMAB AND PROPORTION OF PATIENTS IN PFS (POTENTIALLY TREATED) AT THOSE TIME-POINTS

Table 1. ICERs and proportion of patients in PFS (and potentially on treatment with pembrolizumab) considering different NHS reimbursement times, for patients previously treated with ipilimumab*

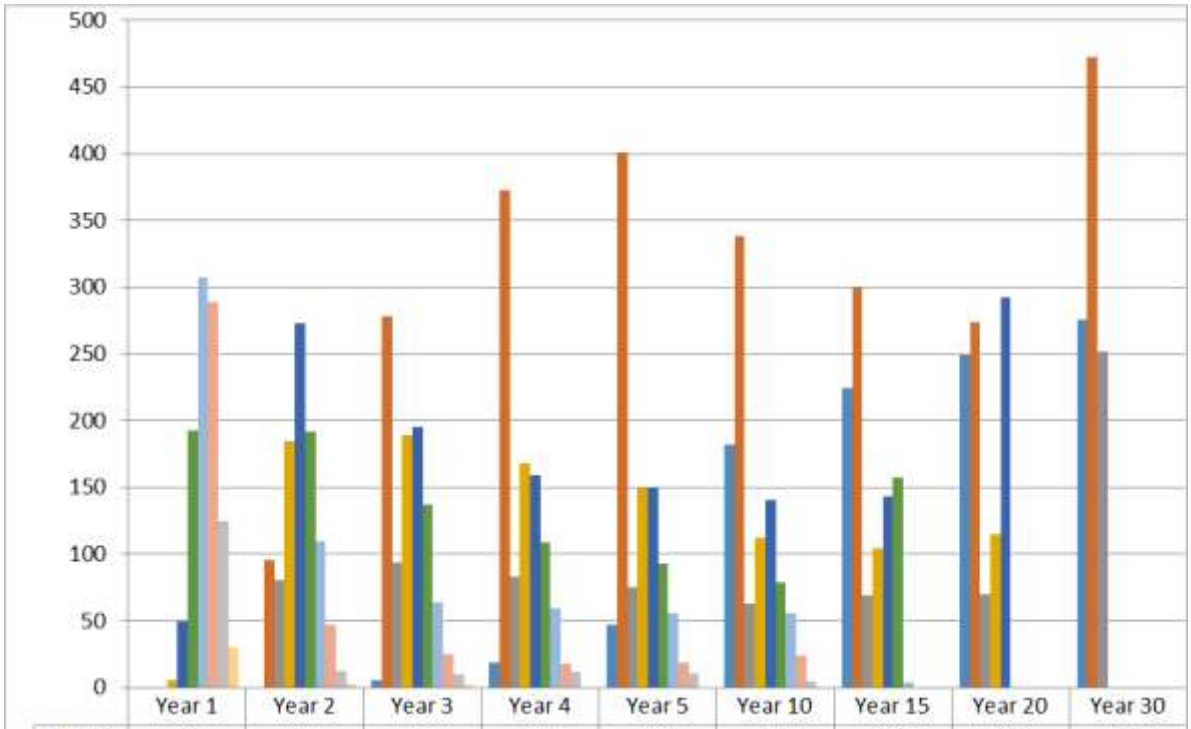
	ICERs*		Proportion of patients in PFS (potentially on pembrolizumab treatment) from post NHS reimbursement point	
NHS reimbursement times	Deterministic	Probabilistic	Deterministic	Probabilistic
Reference case: lifetime (30 years)	£42,923	£67,615	0.62%	0.52%
Up to 2 years	£31,764	£33,623	7.38%	8.46%
Up to 3 years	£34,480	£37,842	3.72%	6.28%
Up to 4 years	£35,942	£40,189	2.27%	4.97%
Up to 5 years	£36,912	£42,635	1.59%	4.45%
Up to 10 years	£39,161	£52,820	0.75%	4.35%
Up to 15 years	£40,435	£60,236	0.64%	3.58%
Up to 20 years	£41,422	£65,907	0.63%	2.42%

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

The probabilistic sensitivity analysis runs 1,000 simulations. Each of these simulations reflects the average result for a cohort of patients with a different set of simulated input parameter values (drawn randomly from a

set of probabilistic distributions). The graph below reflects the number of simulations (over 1,000) according to the average proportion of patients treated with pembrolizumab and still in PFS (and therefore, potentially on treatment). It takes into account different intervals (0% patients in PFS; >0% and up to 1% of patients in PFS; >1% and up to 2%; > 2% and up to 5%; etc.) and takes into account different time periods. For example, if we take into account NHS reimbursement for years, for the majority of simulations there were between 10% and 20% of patients in PFS (and potentially, still on treatment) at the end of year 2. On the other hand, if we take into account NHS reimbursement of 5 years, a small number of simulations (47, or 4.7%) resulted in 0% of patients in PFS (and therefore not on treatment) at the end of year 5, while in the majority of simulations there were up to 5% of patients in PFS (in 625 simulations, or approximately 63%).

Figure 1. Summary of the number of simulations (over 1,000) resulting in a proportion of patients in PFS equal to 0%, >0% and up to 1%, >1% and up to 2%, >2% and up to 5%, >5% and up to 10%, >10% and up to 15%, >15% and up to 20%, >20% and up to 30%, and >30% and up to 40%, when considering different NHS reimbursement periods



	Year 1	Year 2	Year 3	Year 4	Year 5	Year 10	Year 15	Year 20	Year 30
0.0%	0	0	6	19	47	182	224	249	276
1.0%	0	96	278	373	401	338	299	274	472
2.0%	0	81	94	83	75	63	69	70	252
5.0%	6	185	189	168	149	112	104	115	0
10.0%	50	273	195	159	149	141	143	292	0
15.0%	193	192	137	109	93	79	157	0	0
20.0%	307	110	64	59	56	56	4	0	0
25.0%	289	47	25	18	19	24	0	0	0
30.0%	125	13	10	12	11	5	0	0	0
40.0%	30	3	2	0	0	0	0	0	0

REFERENCE CASE: NHS REIMBURSEMENT OF PEMBROLIZUMAB FOR A LIFETIME (I.E. 30 YEARS)

Table 2. ICERs when considering NHS reimbursement for pembrolizumab of 30-years for patients previously treated with ipilimumab*

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,594	1.11	1.57				
Pembrolizumab	£92,741	2.25	3.10	£77,147	1.14	1.53	£67,615
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51				
Pembrolizumab	£66,955	2.26	3.10	£50,995	1.188	1.592	£42,923

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 2. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 30-years for patients

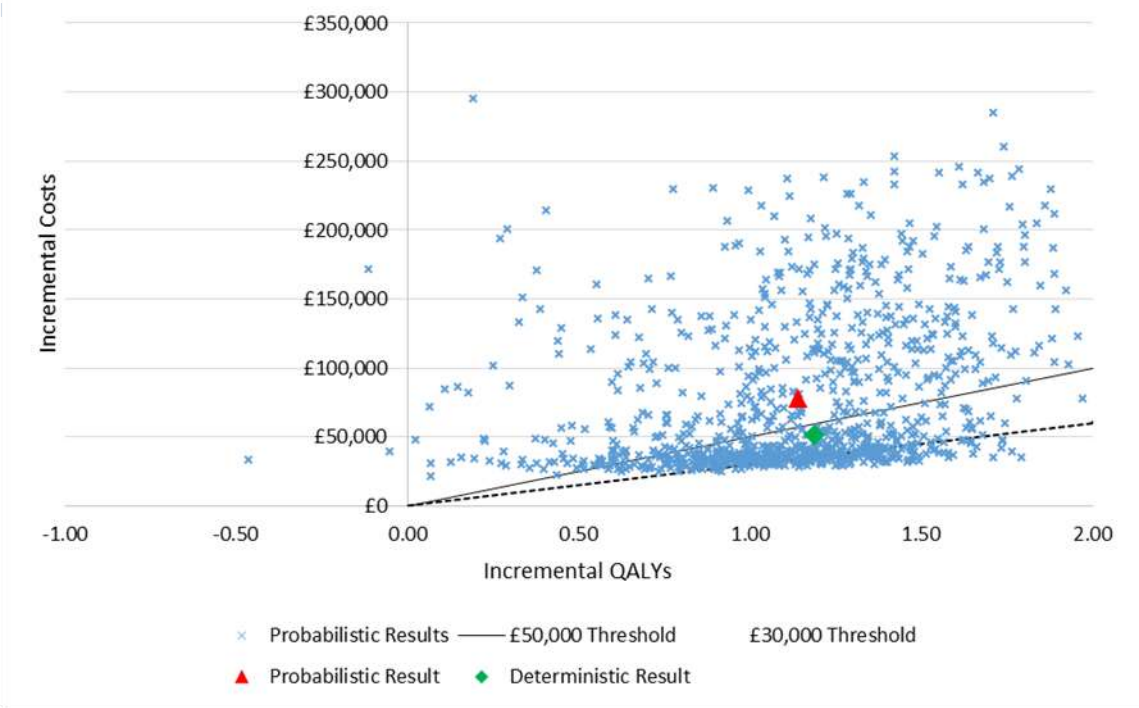
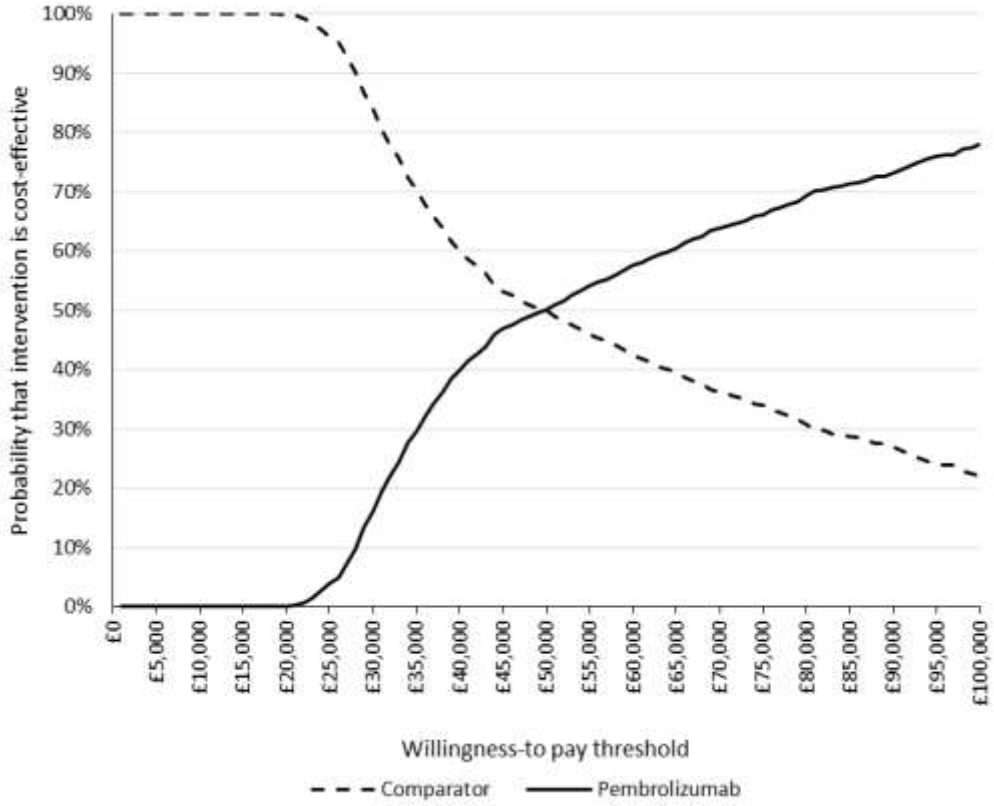


Figure 3. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement of pembrolizumab for 30-years for patients previously treated with ipilimumab



NHS REIMBURSEMENT OF PEMBROLIZUMAB FOR 2 YEARS

Table 3. ICERs when considering NHS reimbursement for pembrolizumab of 2-years for patients previously treated with ipilimumab*

Probabilistic Results

	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,463	1.14	1.59				
Pembrolizumab	£53,454	2.27	3.09	£37,991	1.13	1.51	£33,623

Deterministic Results

	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51				
Pembrolizumab	£53,698	2.26	3.10	£37,738	1.19	1.59	£31,764

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 4. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 2-years for patients previously treated with ipilimumab

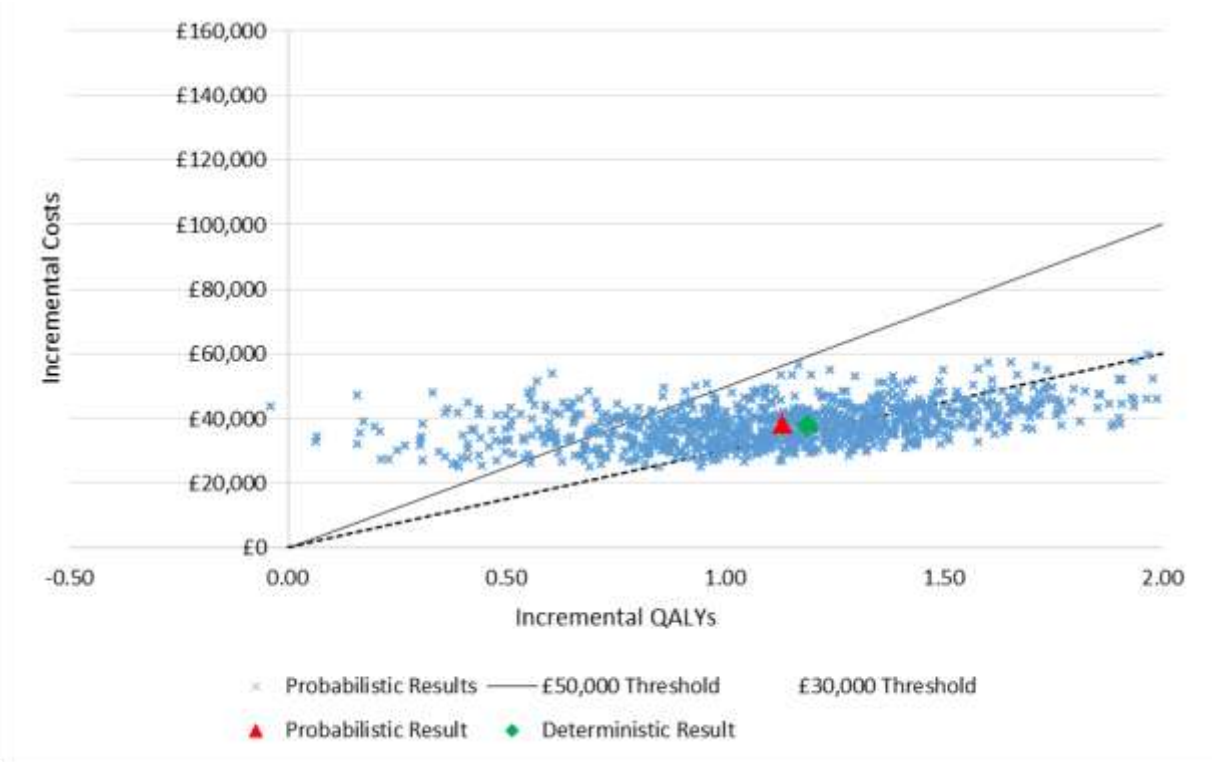
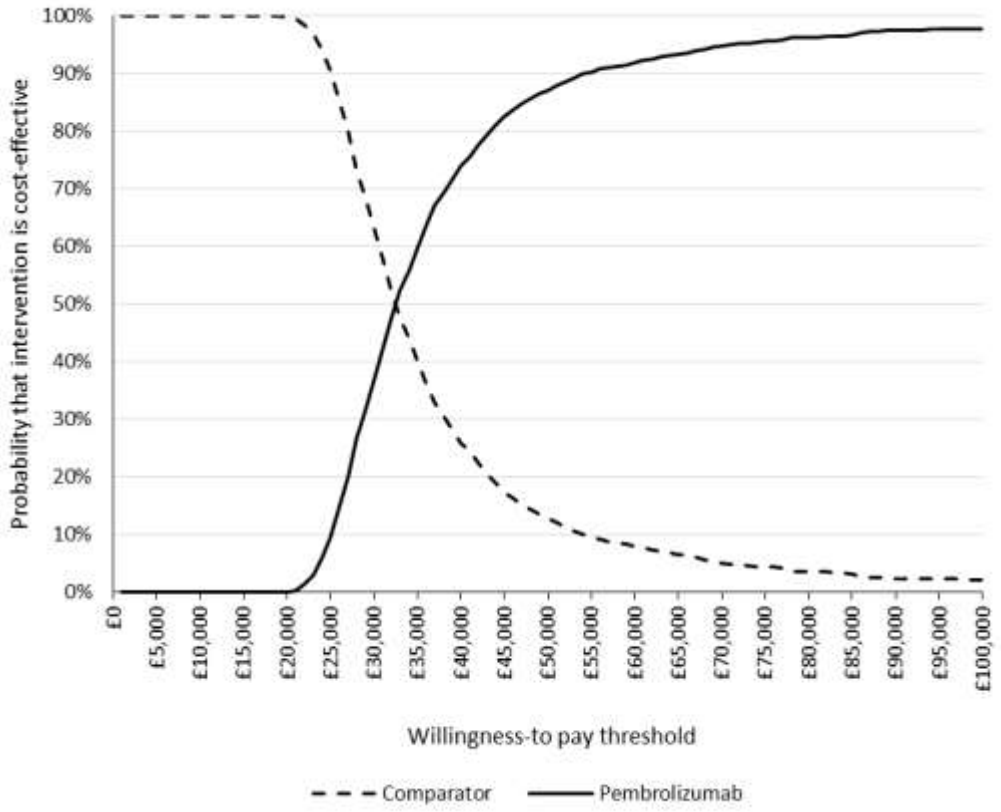


Figure 5. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement for pembrolizumab of 2-years for patients previously treated with ipilimumab



NHS REIMBURESMENT OF PEMBROLIZUMAB FOR 3 YEARS

Table 4.

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,699	1.15	1.61	£43,004	1.14	1.52	£37,842
Pembrolizumab	£58,703	2.29	3.12				
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51	£40,965	1.19	1.59	£34,480
Pembrolizumab	£56,925	2.26	3.10				

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 6. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 3-years for patients

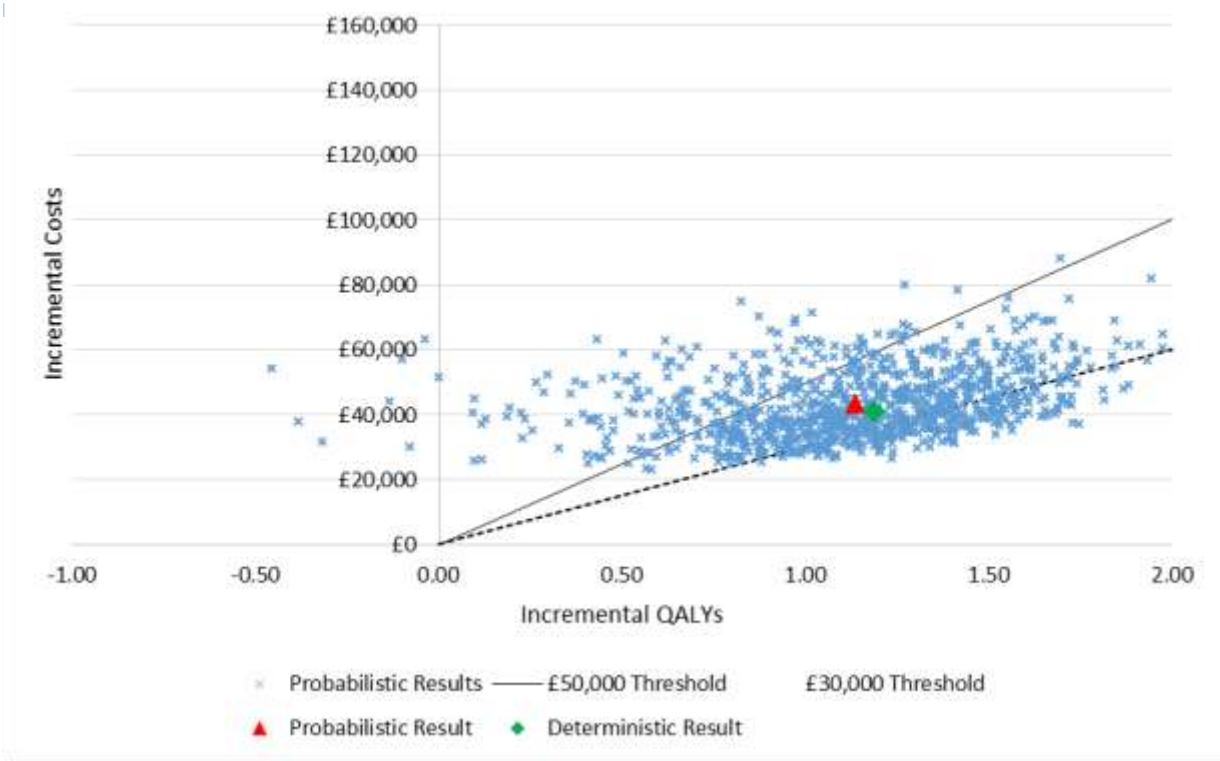
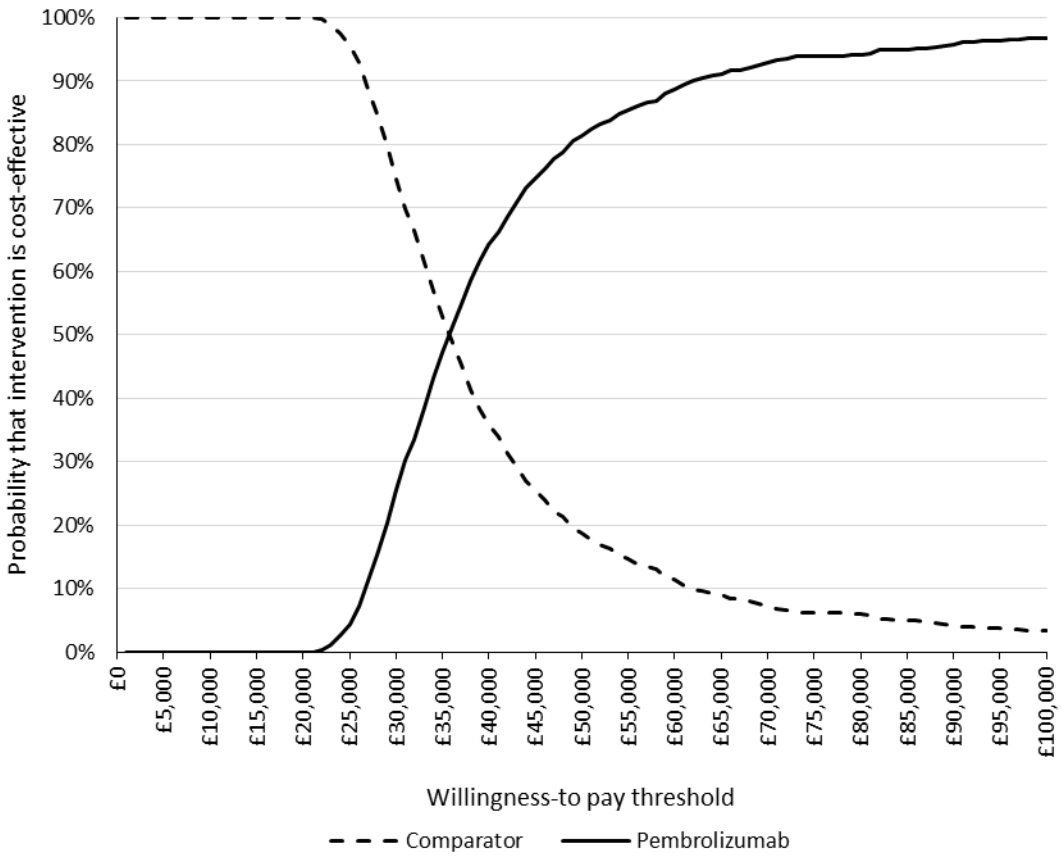


Figure 7. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement for pembrolizumab of 3-years for patients previously treated with ipilimumab



NHS REIMBURSEMENT OF PEMBROLIZUMAB FOR 4 YEARS

Table 5. ICERs when considering NHS reimbursement for pembrolizumab of 4-years for patients previously treated with ipilimumab*

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,837	1.12	1.57	£45,634	1.14	1.53	£40,189
Pembrolizumab	£61,470	2.25	3.10				
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51	£42,700	1.19	1.59	£35,942
Pembrolizumab	£58,660	2.26	3.10				

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 8. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 4-years for patients previously treated with ipilimumab

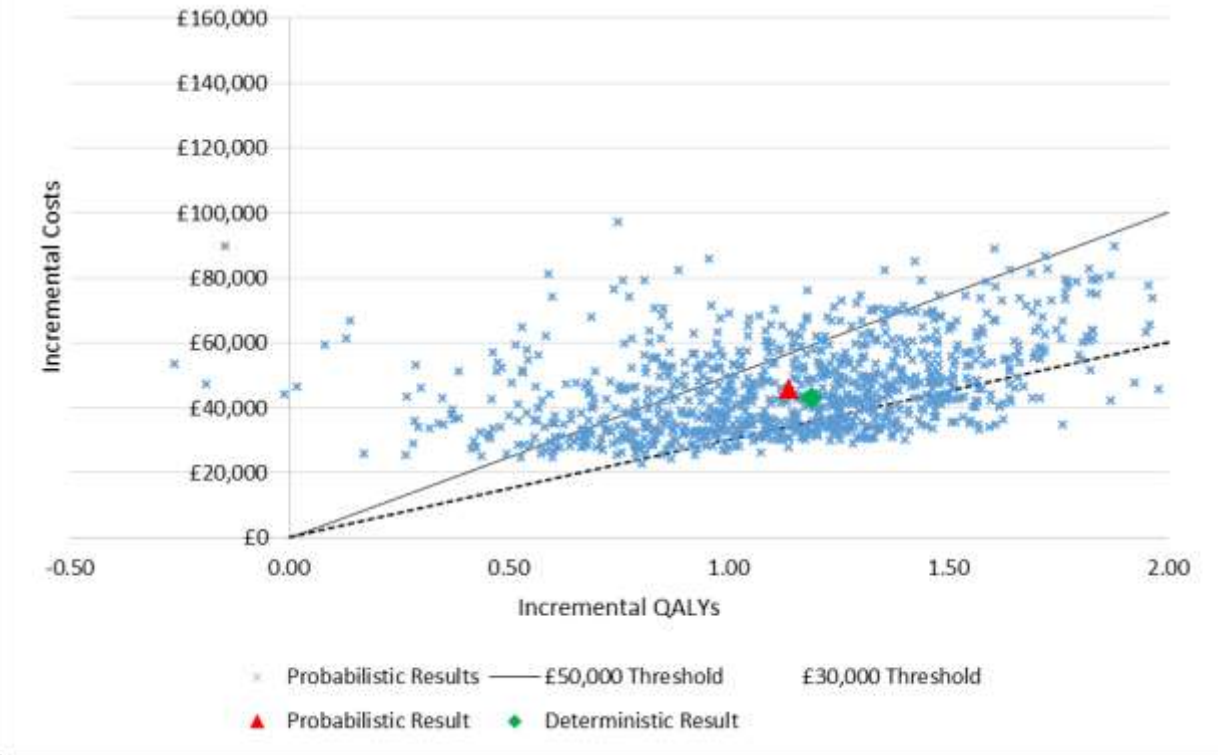
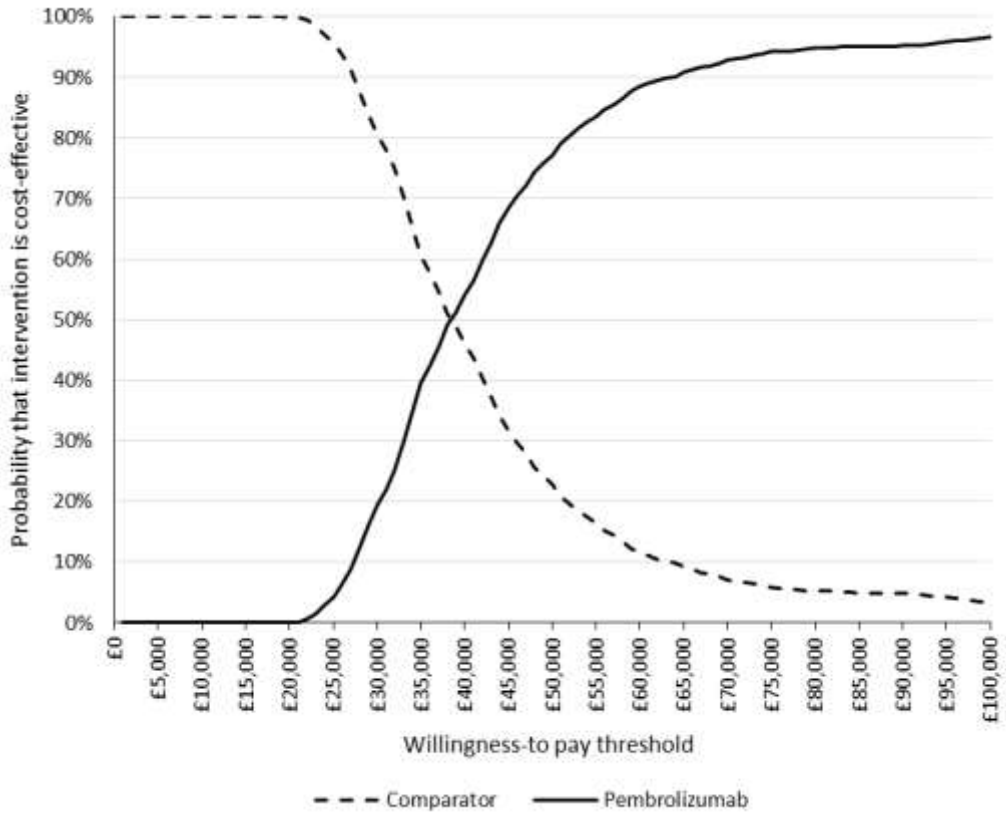


Figure 9. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement for pembrolizumab of 4-years for patients previously treated with ipilimumab



NHS REIMBURSEMENT OF PEMBROLIZUMAB OF 5 YEARS

Table 6. ICERs when considering NHS reimbursement for pembrolizumab of 5-years for patients previously treated with ipilimumab*

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,541	1.12	1.58	£47,988	1.13	1.51	£42,635
Pembrolizumab	£63,529	2.25	3.09				
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51	£43,854	1.19	1.59	£36,912
Pembrolizumab	£59,814	2.26	3.10				

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 10. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 5-years for patients

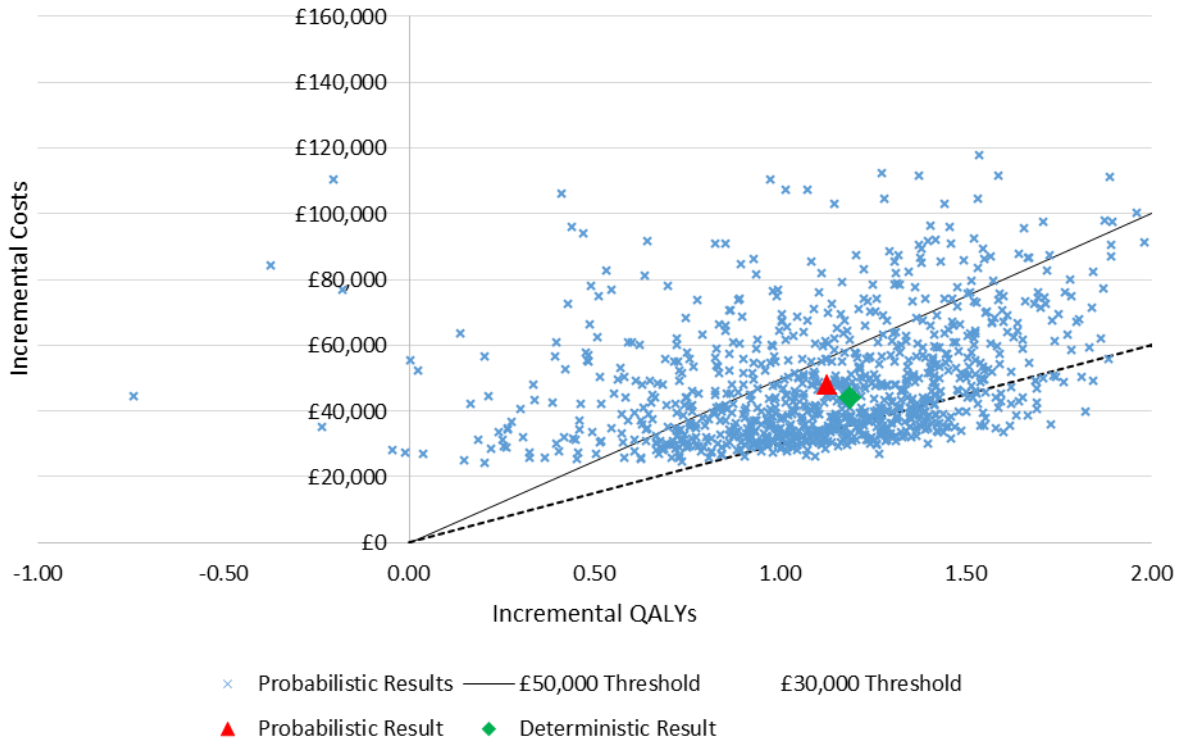
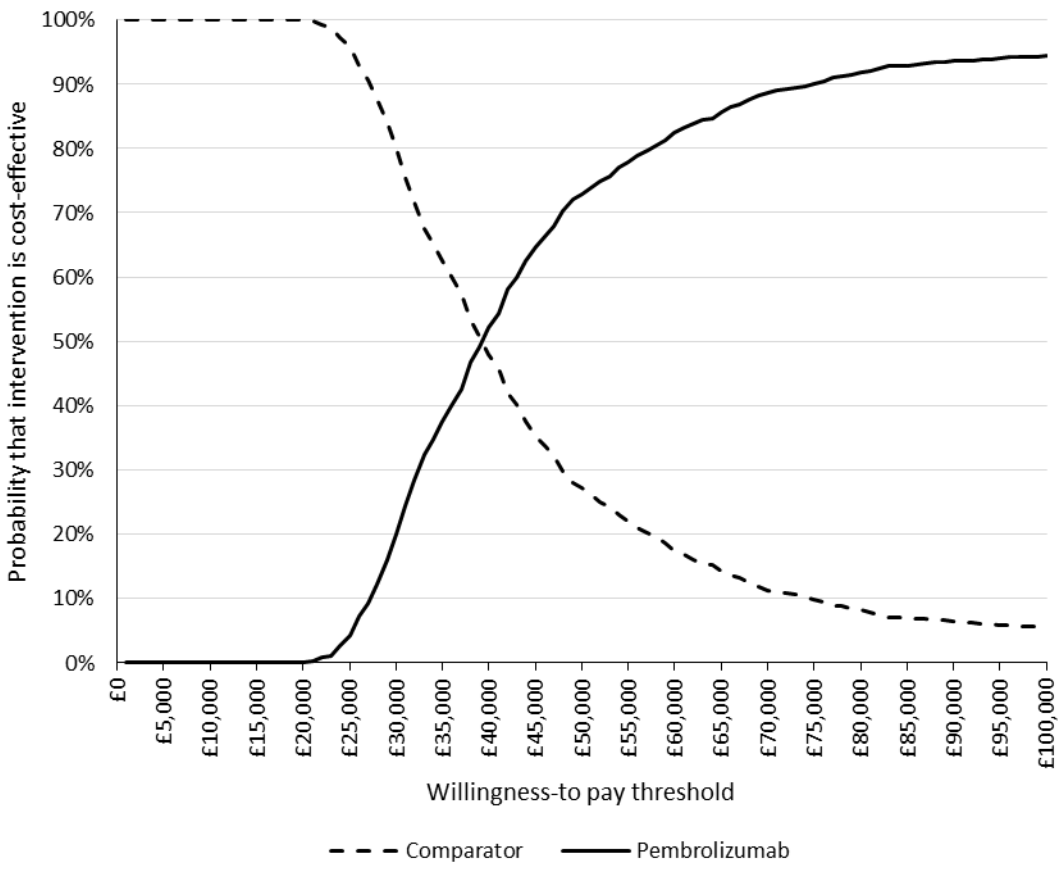


Figure 11. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement for pembrolizumab of 5-years for patients previously treated with ipilimumab



NHS REIMBURSEMENT OF PEMBROLIZUMAB FOR 10 YEARS

Table 7. ICERs when considering NHS reimbursement for pembrolizumab of 10-years for patients previously treated with ipilimumab*

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,644	1.12	1.57	£60,566	1.15	1.53	£52,820
Pembrolizumab	£76,210	2.27	3.11				
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51	£46,525	1.19	1.59	£39,161
Pembrolizumab	£62,485	2.26	3.10				

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 12. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 10-years for patients previously treated with ipilimumab

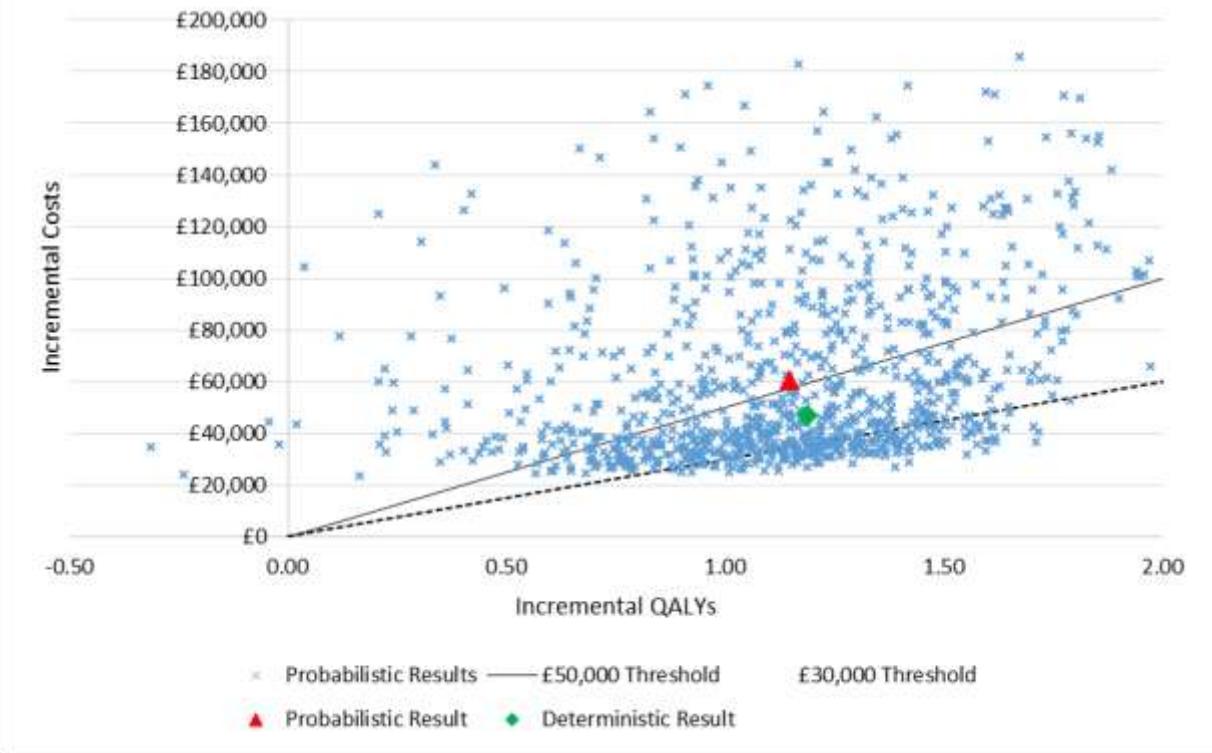
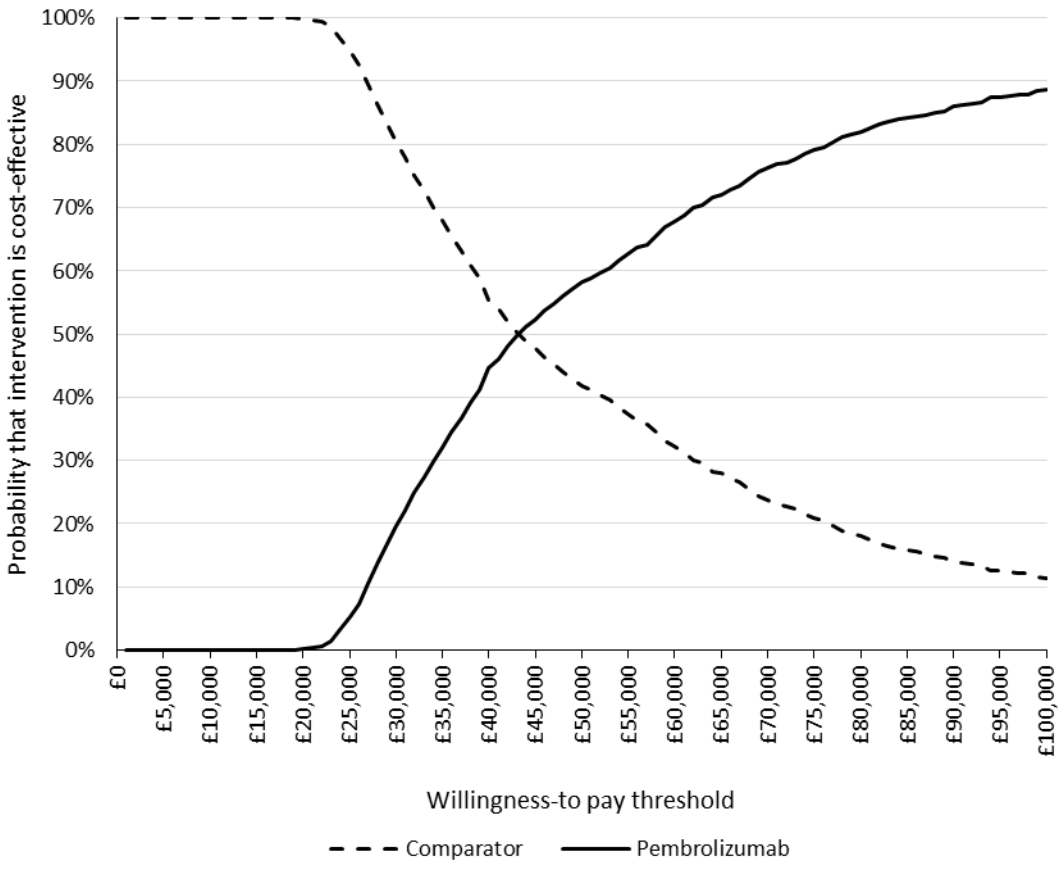


Figure 13. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement for pembrolizumab of 10-years for patients previously treated with ipilimumab



NHS REIMBURSEMENT OF PEMBROLIZUMAB FOR 15 YEARS

Table 8. ICERs when considering NHS reimbursement for pembrolizumab of 15-years for patients previously treated with ipilimumab*

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,547	1.12	1.57	£68,525	1.14	1.53	£60,236
Pembrolizumab	£84,072	2.25	3.10				
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51	£48,038	1.19	1.59	£40,435
Pembrolizumab	£63,998	2.26	3.10				

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 14. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 15-years for patients previously treated with ipilimumab

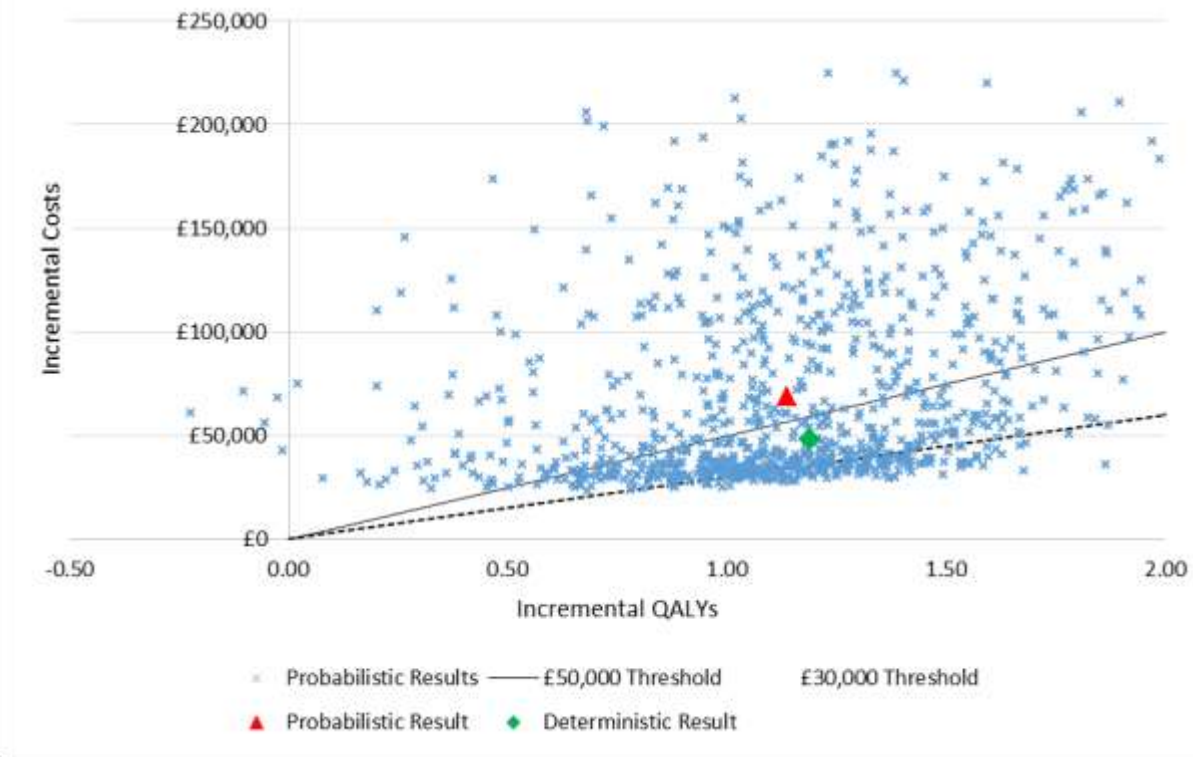
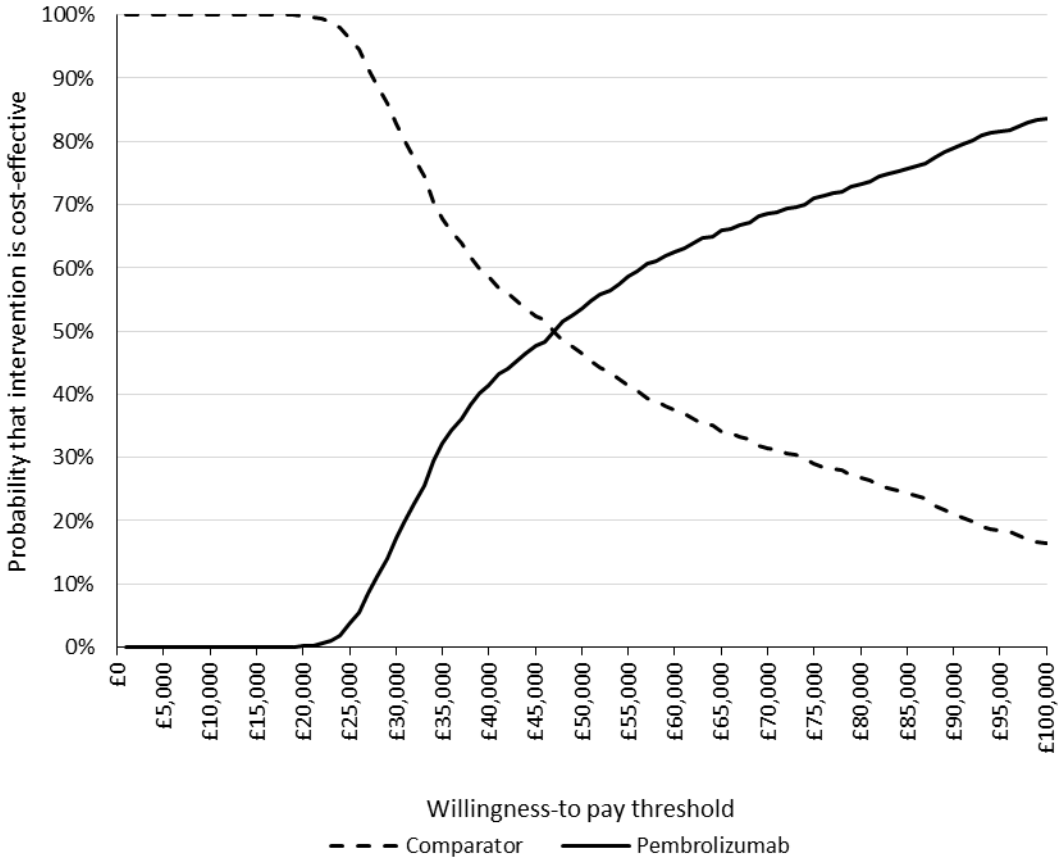


Figure 15. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement of pembrolizumab for 15-years for patients previously treated with ipilimumab



NHS REIMBURSEMENT OF PEMBROLIZUMAB FOR 20 YEARS

Table 9. ICERs when considering NHS reimbursement for pembrolizumab of 20-years for patients previously treated with ipilimumab*

Probabilistic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,589	1.13	1.58				
Pembrolizumab	£90,196	2.26	3.10	£74,607	1.13	1.52	£65,907
Deterministic Results							
	Total Costs	Total QALYs	Total LYs	Incremental costs	Incremental QALYs	Incremental LYS	ICER
BSC	£15,960	1.07	1.51				
Pembrolizumab	£65,172	2.26	3.10	£49,212	1.19	1.59	£41,422

*ICER: pembrolizumab (PAS discount incorporated) vs. BSC

Figure 16. Cost-effectiveness plane for the PSA results when considering NHS reimbursement of pembrolizumab for 20-years for

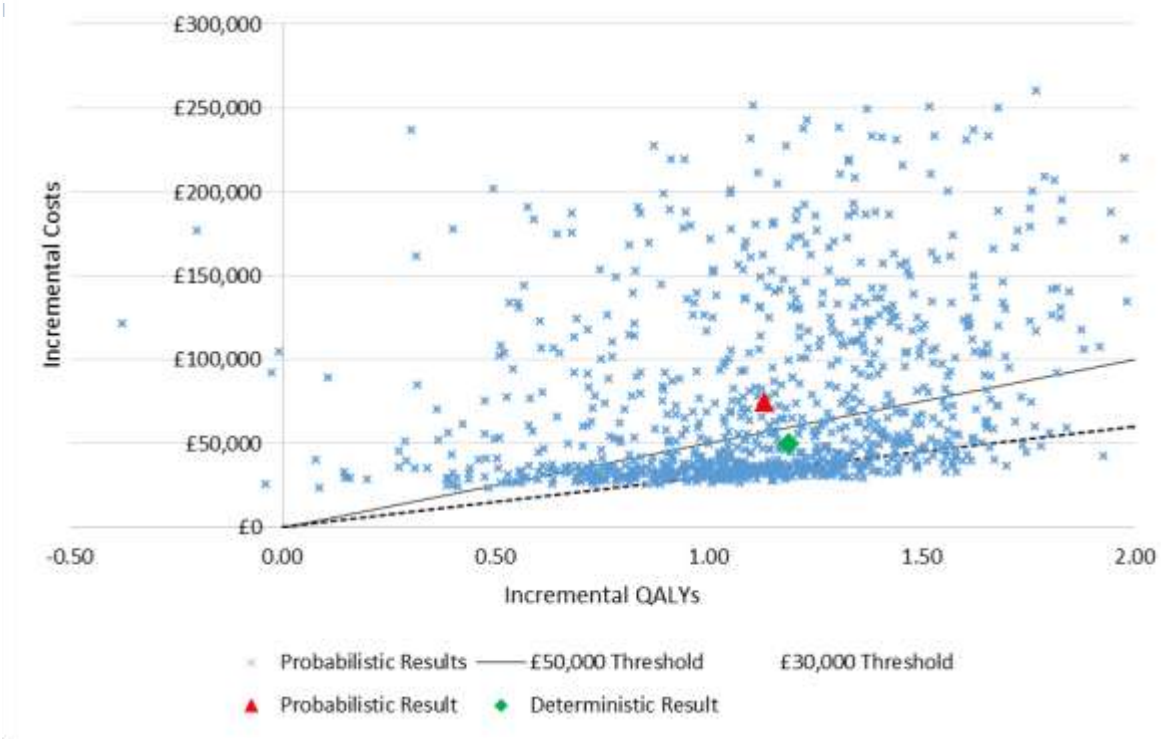
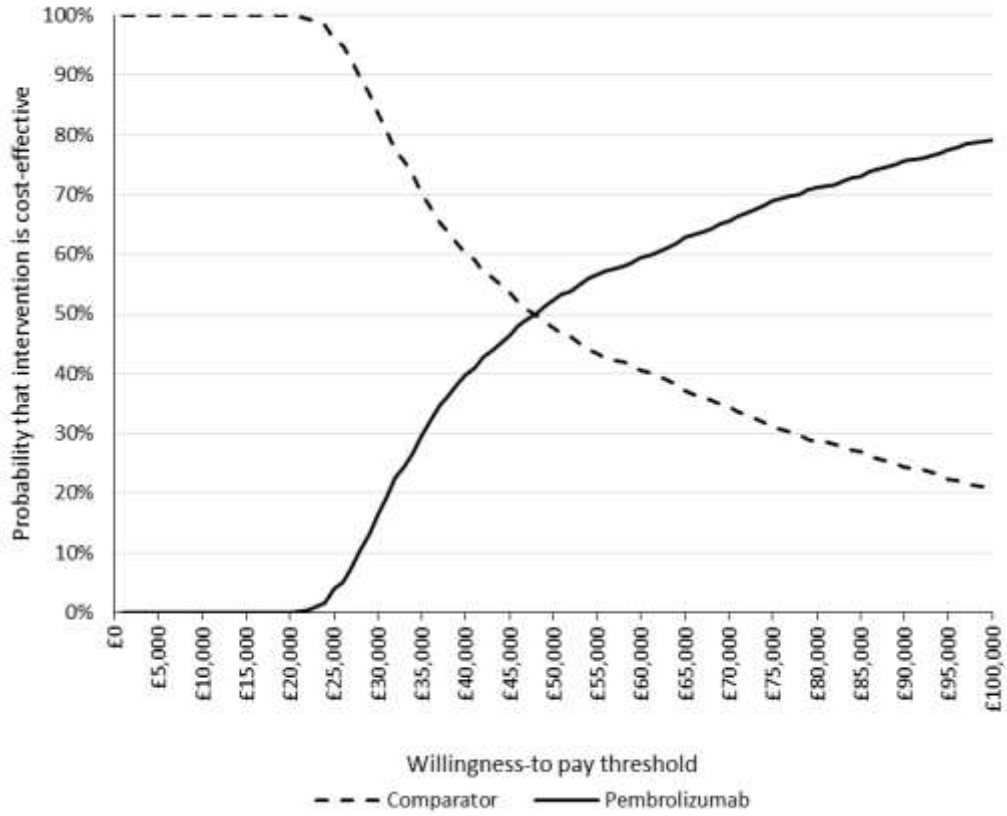



Figure 17. Cost-effectiveness acceptability curves for the PSA results when considering NHS reimbursement of pembrolizumab for 20-years for patients previously treated with ipilimumab