7. PenTAG Economic Assessment

7.4. Results

We first present the base case analysis, which we believe to be closest to the NICE reference case. Deterministic results for the base case analysis are given in Section 7.4.1.1 (page 2) and probabilistic results are given in Section 7.4.1.2 (page 12).

Next we present scenario analyses which explore structural and other uncertainties in the economic assessment. Structural uncertainty in the extrapolation of graft survival is explored in two scenario analyses in Section 7.4.2.1 (page 32). Although it is believed that unit costs for drug acquisition have been identified appropriately and in line with the reference case, we also explore the impact of using list prices for all drugs, and conduct a two-way threshold analysis on costs relating to belatacept in Section 7.4.2.2 (page 46).

Summary cost-effectiveness results are presented in the following form throughout, with regimens sorted in order of ascending effectiveness (total QALYs):

- Total costs
- Incremental costs versus the previous regimen
- Total QALYs
- Incremental QALYs versus the previous regimen
- ICER (versus the previous regimen on the cost-effectiveness frontier unless the regimen is dominated or extended dominated)
- Incremental net health benefit at £20,000 and £30,000 per QALY versus the referent regimen (the regimen on the cost-effectiveness frontier with the lowest total QALYs)

For probabilistic cost-effectiveness results the following are also presented:

- The probability that each regimen is cost-effective (i.e., gives the greatest net health benefit of all regimens being compared) at £20,000 and £30,000 per QALY

Note that throughout costs and ICERs are reported rounded to the nearest £1 and QALYs are reported to four decimal places. This should not be taken as an indication of the precision of these estimates but to allow for third-party checking of the accuracy of calculations.

7.4.1. Base case analysis

7.4.1.1. Deterministic results

Induction agents

We present the cost-effectiveness of induction agents basiliximab and rabbit ATG and the comparator of no induction in the context of three different maintenance regimens:

- Ciclosporin, azathioprine and corticosteroids
- Ciclosporin, mycophenolate mofetil and corticosteroids
- Tacrolimus, mycophenolate mofetil and corticosteroids

Note that while other regimens including basiliximab are modelled (BAS+SRL+MMF, BAS+BEL+MMF, BAS+CSA+MPS) these cannot be meaningfully compared to any other regimens to estimate the cost-effectiveness of basiliximab.

Summary cost-effectiveness results are given in Table 207.

Table 207. Summary of cost-effectiveness results for induction agents

Induction agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY
With CSA+AZA						*vs. Basiliximab*	
No induction	£101,595	—	10.7711	—	Dominated	-0.2994	-0.2436
Rabbit ATG	£104,570	+£2,975	10.8182	+0.0471	Dominated	-0.4011	-0.2956
Basiliximab	£98,244	-£6,326	10.9029	+0.0848	—	—	—
With CSA+MMF						*vs. Basiliximab*	
No induction	£97,429	—	10.9145	—	Dominated	-0.2207	-0.1838
Rabbit ATG	£101,940	+£4,511	10.9281	+0.0135	Dominated	-0.4327	-0.3206
Basiliximab	£95,219	-£6,720	11.0247	+0.0966	—	—	—
With TAC+MMF						*vs. Basiliximab*	
No induction	£92,226	—	10.8884	—	Dominated	-0.1906	-0.1603
Rabbit ATG	£97,146	+£4,920	10.9047	+0.0163	Dominated	-0.4203	-0.3080
Basiliximab	£90,405	-£6,741	10.9880	+0.0832	—	—	—

Basiliximab

Basiliximab was compared to no induction and to rabbit ATG in three comparisons. In all three comparisons basiliximab was predicted to dominate no induction and rabbit ATG. Therefore basiliximab is predicted to be cost-effective at £20,000 and £30,000 per QALY.

Rabbit ATG

Rabbit ATG was compared to no induction and to basiliximab in three comparisons. In all three comparisons rabbit ATG was predicted to be dominated by basiliximab. Therefore rabbit ATG is not predicted to be cost-effective at £20,000 and £30,000 per QALY.

As shown in Table 238 (in Appendix 9, page 602), rabbit ATG induction results in greater induction therapy costs than basiliximab and greater costs of infection prophylaxis (since KTRs at intermediate risk of CMV require prophylaxis if receiving rabbit ATG induction). These cost increases are partially offset by a reduction in costs of acute rejection treatment (due to reduced incidence of acute rejection).

Summary

In all comparisons basiliximab was dominant over no induction and rabbit ATG and was the only cost-effective induction agent.

Maintenance agents

We present the cost-effectiveness results for the following maintenance agents:

- Immediate-release tacrolimus (TAC);
- Prolonged-release tacrolimus (TAC-PR);
- Mycophenolate mofetil (MMF);
- Mycophenolate sodium (MPS);
- Sirolimus (SRL);

- Everolimus (EVL);
- Belatacept (BEL).

These are compared to each other as appropriate and also to ciclosporin (CSA) or azathioprine (AZA). All maintenance agents were modelled with concomitant treatment which would be corticosteroids plus mycophenolate mofetil, azathioprine, ciclosporin or immediate-release tacrolimus according to the evidence base plus optional induction therapy (basiliximab or rabbit ATG). Comparisons are made holding all concomitant treatments equal. Summary results are given in Table 208.

Table 208. Summary of cost-effectiveness results for maintenance agents

Maintenance agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY
With MMF						*vs. TAC*	
TAC-PR	£106,529	—	10.7920	—	Dominated	-0.8116	-0.5732
TAC	£92,226	-£14,303	10.8884	+0.0964	—	—	—
CSA	£97,429	+£5,203	10.9145	+0.0261	£199,118	-0.2340	-0.1473
With AZA						*vs. TAC*	
CSA	£101,595	—	10.7711	—	Dominated	-0.5124	-0.3745
TAC	£93,319	-£8,276	10.8696	+0.0986	—	—	—
With BAS+MMF						*vs. TAC*	
SRL	£114,549	—	10.9010	—	Dominated	-1.2941	-0.8917
TAC	£90,405	-£24,144	10.9880	+0.0869	—	—	—
CSA	£95,219	+£4,815	11.0247	+0.0367	£131,035	-0.2040	-0.1237
BEL	£209,409	+£114,189	11.2941	+0.2694	£423,890	-5.6441	-3.6607
With rATG+MMF						*vs. TAC*	
TAC	£97,146	—	10.9047	—	—	—	—
CSA	£101,940	+£4,794	10.9281	+0.0234	£205,214	-0.2163	-0.1364

Table 208. Summary of cost-effectiveness results for maintenance agents (cont.)

Maintenance agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY
With CSA						*vs. MMF*	
AZA	£101,595	—	10.7711	—	Dominated	-0.3518	-0.2824
MMF	£97,429	-£4,166	10.9145	+0.1435	—	—	—
EVL	£176,154	+£78,725	10.9659	+0.0514	£1,532,379	-3.8849	-2.5728
With TAC						*vs. MMF*	
SRL	£125,539	—	10.6023	—	Dominated	-1.9518	-1.3966
AZA	£93,319	-£32,220	10.8696	+0.2674	Dominated	-0.0734	-0.0552
MMF	£92,226	-£1,093	10.8884	+0.0188	—	—	—
With BAS+CSA						*vs. MMF*	
AZA	£98,244	—	10.9029	—	Dominated	-0.2730	-0.2226
MMF	£95,219	-£3,025	11.0247	+0.1218	—	—	—
MPS	£111,540	+£16,321	11.1377	+0.1130	£144,449	-0.7030	-0.4310
With rATG+CSA						*vs. MMF*	
AZA	£104,570	—	10.8182	—	Dominated	-0.2414	-0.1976
MMF	£101,940	-£2,631	10.9281	+0.1099	—	—	—

Immediate-release tacrolimus

Immediate-release tacrolimus was compared to ciclosporin (four comparisons), prolonged-release tacrolimus (one comparison), sirolimus (one comparison) and belatacept (one comparison).

When used in combination with mycophenolate mofetil and corticosteroids, immediate-release tacrolimus dominated prolonged-release tacrolimus and was less costly and less effective than ciclosporin. The ICER of ciclosporin versus immediate-release tacrolimus was £199,118 per QALY and therefore immediate-release tacrolimus was the only cost-effective agent in this comparison at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

When used in combination with azathioprine and corticosteroids, immediate-release tacrolimus dominated ciclosporin.

When used in combination with basiliximab induction, mycophenolate mofetil and corticosteroids, immediate-release tacrolimus dominated sirolimus and was less costly and less expensive than ciclosporin and belatacept. The ICERs for ciclosporin and belatacept in this comparison were £131,035 and £423,890 per QALY respectively and therefore immediate-release tacrolimus was the only cost-effective agent in this comparison at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

When used in combination with rabbit ATG induction, mycophenolate mofetil and corticosteroids, immediate-release tacrolimus was less costly and less effective than ciclosporin. The ICER of ciclosporin was £255,592 per QALY and therefore immediate-release tacrolimus was the only cost-effective agent in this comparison at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

In three comparisons (all with mycophenolate mofetil), immediate-release tacrolimus was predicted be less effective than ciclosporin. In all comparisons, however, immediate-release tacrolimus was predicted to result in greater life expectancy and more years with functioning graft (see Table 239 in Appendix 9, page **Error! Bookmark not defined.**). The QALY loss arises because of the reduction in health-related quality of life in KTRs who develop NODAT; 10.6% of KTRs are predicted to develop NODAT with immediate-release tacrolimus versus 5.0% of KTRs for ciclosporin. If the utility decrement for NODAT is removed (and NODAT

therefore only affects costs, graft survival and death with functioning graft), then immediate-release tacrolimus is more effective than ciclosporin in all comparisons and therefore is dominant (see Table 243 in Appendix 9, page **Error! Bookmark not defined.**).

Prolonged-release tacrolimus

Prolonged-release tacrolimus was compared to ciclosporin and immediate-release tacrolimus in combination with mycophenolate mofetil and corticosteroids. Prolonged-release tacrolimus was dominated by both ciclosporin and immediate-release tacrolimus in this comparison.

Mycophenolate mofetil

Mycophenolate mofetil was compared to azathioprine (four comparisons), sirolimus (one comparison), everolimus (one comparison) and mycophenolate sodium (one comparison).

Mycophenolate mofetil dominated azathioprine in all four comparisons.

When used in combination with immediate-release tacrolimus and corticosteroids, mycophenolate mofetil dominated sirolimus.

When used in combination with ciclosporin and corticosteroids, mycophenolate mofetil was less costly and less effective than everolimus. The ICER of everolimus was £1,532,379 per QALY and therefore mycophenolate mofetil was the only cost-effective agent in this comparison at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

When used in combination with basiliximab induction, ciclosporin and corticosteroids, mycophenolate mofetil was less costly and less expensive than mycophenolate sodium. The ICER of mycophenolate sodium was £144,449 per QALY and therefore mycophenolate mofetil was the only cost-effective agent in this comparison at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Mycophenolate sodium

Mycophenolate sodium was compared to azathioprine and mycophenolate mofetil in combination with basiliximab induction, ciclosporin and corticosteroids. Mycophenolate sodium was more costly and more effective than azathioprine and mycophenolate mofetil. The ICER of mycophenolate sodium was £144,449 per QALY and therefore mycophenolate

sodium was not cost-effective at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Mycophenolate sodium was considerably more costly than mycophenolate mofetil, with discounted maintenance immunosuppression costs more than double those of mycophenolate mofetil, although there were some predicted savings in dialysis expenditure (see Table 238 in Appendix 10, page 602). Mycophenolate sodium was predicted to lead to increased time with functioning graft and increased life expectancy versus mycophenolate mofetil, which is why it was predicted to give increased QALYs (see Table 239 in Appendix 10, page 602).

Sirolimus

Sirolimus was compared to ciclosporin, immediate-release tacrolimus and belatacept in one comparison (in combination with basiliximab induction, mycophenolate mofetil and corticosteroids) and to azathioprine and mycophenolate mofetil in one comparison (in combination with immediate-release tacrolimus and corticosteroids).

Sirolimus was dominated by ciclosporin and tacrolimus in the first comparison and was dominated by azathioprine and mycophenolate mofetil in the second comparison.

Everolimus

Everolimus was compared to azathioprine and mycophenolate mofetil in combination with ciclosporin and corticosteroids. Everolimus was more costly and more effective than azathioprine and mycophenolate mofetil. The ICER of everolimus was £1,532,379 per QALY and therefore everolimus was not cost-effective at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Belatacept

Belatacept was compared to ciclosporin, immediate-release tacrolimus and sirolimus in combination with basiliximab induction, mycophenolate mofetil and corticosteroids. Belatacept was more costly and more effective than all comparators. The ICER of belatacept was £423,890 per QALY and therefore belatacept was not cost-effective at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Summary

Only immediate-release tacrolimus and mycophenolate mofetil were cost-effective at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Prolonged-release tacrolimus and sirolimus were dominated in their relevant comparisons while mycophenolate sodium, everolimus and belatacept were all the most costly and most effective treatment in their relevant comparisons, but with ICERs significantly above £30,000 per QALY.

Comparing all regimens

When all regimens are simultaneously compared, the following regimens are dominated or extended dominated (if indicated):

- TAC+SRL
- TAC-PR+MMF
- CSA+AZA
- TAC+AZA
- TAC+MMF
- CSA+MMF
- BAS+SRL+MMF
- BAS+CSA+AZA
- rATG+CSA+AZA
- CSA+EVL
- rATG+TAC+MMF (extended dominated)
- rATG+CSA+MMF (extended dominated)

Four regimens were neither dominated nor extended dominated and therefore lay on the cost-effectiveness frontier and the cost-effectiveness results for these are presented in Table

209. BAS+TAC+MMF was predicted to be the only cost-effective regimen at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Table 209. Cost-effectiveness of all regimens on the cost-effectiveness frontier

Regimen	Discounted costs		Discounted QALYs		ICER	INHB	
	Total	Inc.	Total	Inc.		£20k	£30k
BAS+TAC+MMF	£90,405	—	10.9880	—	—	—	—
BAS+CSA+MMF	£95,219	+£4,815	11.0247	+0.0367	£131,035	-0.2040	-0.1237
BAS+CSA+MPS	£111,540	+£16,321	11.1377	+0.1130	£144,449	-0.9070	-0.5548
BAS+BEL+MMF	£209,409	+£97,869	11.2941	+0.1564	£625,761	-5.6441	-3.6607

Additional results

Additional results for the deterministic base case (including disaggregated discounted costs and additional clinical outcomes) can be found in Appendix 9.

7.4.1.2. Probabilistic results

The PenTAG model was run for 10,000 PSA iterations. Non-linearities in models often manifest in substantially different results between probabilistic and deterministic analyses. Figure 95 demonstrates that there are no significant discrepancies in terms of total costs for each regimen. Figure 96 indicates that there are some discrepancies in terms of total QALYs for each regimen between the probabilistic and deterministic analyses, but there appears to be no systemic bias.

Figure 95. Comparison of deterministic and probabilistic costs in PenTAG model

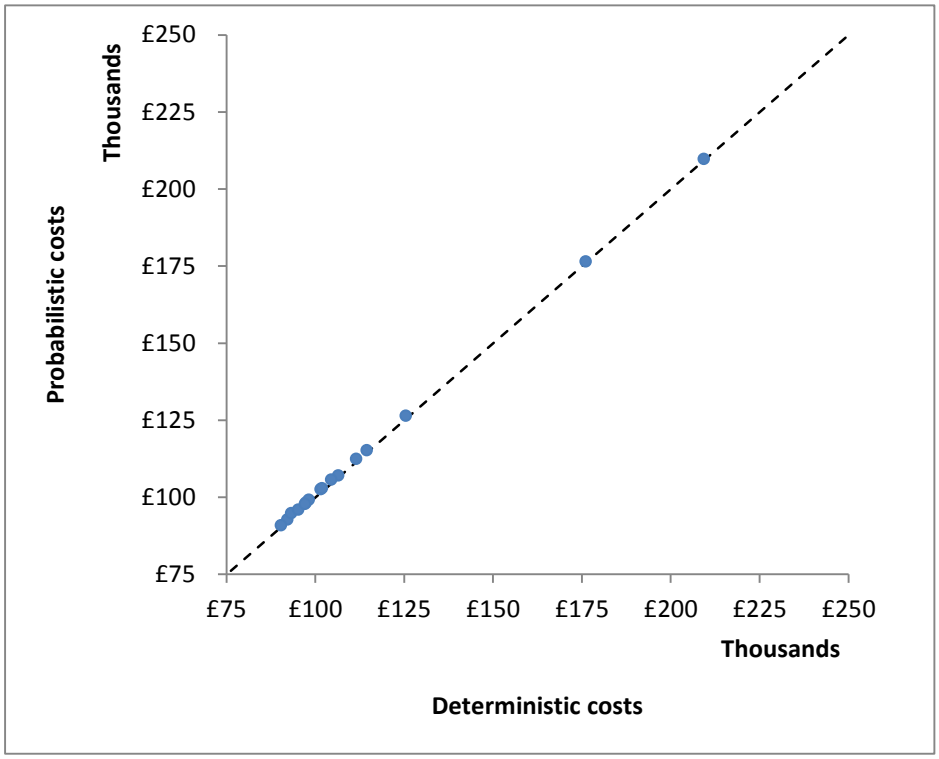
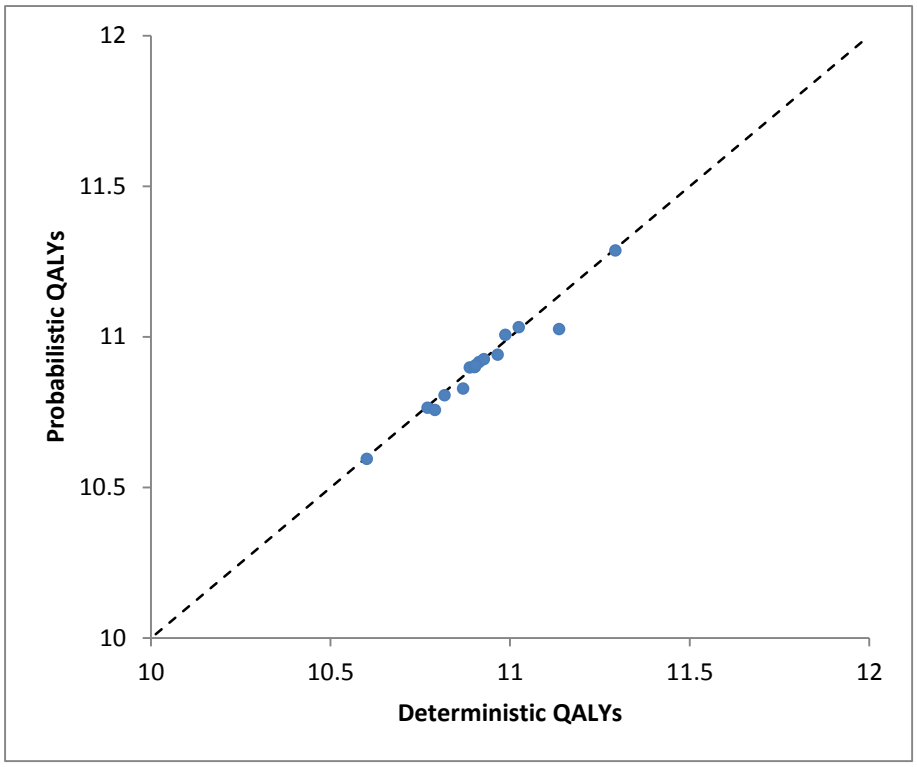


Figure 96. Comparison of deterministic and probabilistic QALYs in PenTAG model



The most significant outlier appears to be BAS+CSA+MPS, which is predicted to result in 11.1377 QALYs in the deterministic analysis but only 11.0244 in the probabilistic analysis. It was ascertained that this outlier effect is due to the significant uncertainty in the probability of mortality within the first 12 months for this regimen – the 95% CI of the odds ratio of mortality for MPS versus MMF is 0.058–7.23. When the probability of mortality drawn from the PSA distribution is extremely low the regression formulae for estimating the appropriate hazard ratio for death with functioning graft perform badly, and in some cases even a hazard ratio of zero results in above target mortality due to the mortality following graft loss. Noting that in the deterministic base case MPS was not cost-effective at £20,000 or £30,000 per QALY (the ICER of MPS versus MMF was over £100,000 per QALY) we have not attempted to compensate for this discrepancy in our analyses.

Induction agents

Probabilistic cost-effectivess results for induction agents (Table 210) were not significantly altered from the deterministic results (Table 207). No induction and rabbit ATG continued to be dominated by basiliximab in all three comparisons.

Table 210. Summary of probabilistic cost-effectiveness results for induction agents

Induction agent	Discounted costs		Discounted QALYs		ICER	Incremental net health benefit		Probability cost-effective	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY	£20k/QALY	£30k/QALY
With CSA+AZA						*vs. Basiliximab*			
No induction	£102,504	—	10.7634	—	Dominated	-0.3028	-0.2471	0.68%	0.55%
Rabbit ATG	£105,683	+£3,179	10.8048	+0.0415	Dominated	-0.4203	-0.3115	5.78%	6.83%
Basiliximab	£99,159	-£6,524	10.8989	+0.0941	—	—	—	93.54%	92.62%
With CSA+MMF						*vs. Basiliximab*			
No induction	£98,219	—	10.9155	—	Dominated	-0.2294	-0.1914	1.81%	1.34%
Rabbit ATG	£102,831	+£4,613	10.9250	+0.0094	Dominated	-0.4506	-0.3357	3.29%	4.10%
Basiliximab	£95,938	-£6,893	11.0309	+0.1059	—	—	—	94.90%	94.56%
With TAC+MMF						*vs. Basiliximab*			
No induction	£92,660	—	10.8972	—	Dominated	-0.2013	-0.1703	2.68%	2.30%
Rabbit ATG	£97,750	+£5,090	10.9047	+0.0075	Dominated	-0.4482	-0.3324	2.84%	3.99%
Basiliximab	£90,802	-£6,948	11.0055	+0.1008	—	—	—	94.48%	93.71%

Basiliximab

Basiliximab was predicted to dominate no induction and rabbit ATG in all three comparisons (as in the deterministic results). Basiliximab was cost-effective at £20,000 per QALY in 93.5–94.9% of PSA iterations across comparisons and at £30,000 per QALY in 92.6–94.6% of iterations.

Rabbit ATG

Rabbit ATG was predicted to be dominated by basiliximab in all three comparisons (as in the deterministic results). Rabbit ATG was cost-effective at £20,000 per QALY in 2.8–5.8% of PSA iterations across comparisons and at £30,000 per QALY in 4.0–6.8% of iterations.

Cost-effectiveness acceptability curves

Cost-effectiveness acceptability curves are shown in Figure 97, Figure 98 and Figure 99 for the three comparisons. While these have not been presented as cost-effectiveness acceptability frontiers (in which only the regimen with the greatest expected net health benefit is shown for each cost-effectiveness threshold), the only effect this would have would be to remove the curves for no induction and rabbit ATG, since basiliximab is predicted to give the greatest expected net health benefit across the cost-effectiveness threshold range explored (£1,000 to £50,000 per QALY).

Figure 97. Cost-effectiveness acceptability curves for induction agents in combination with ciclosporin, azathioprine and corticosteroids

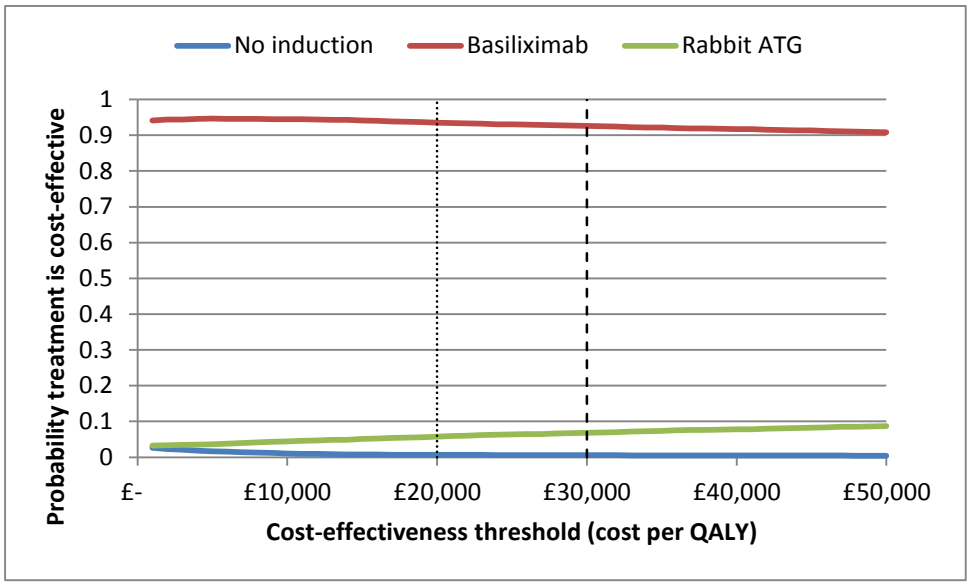


Figure 98. Cost-effectiveness acceptability curves for induction agents in combination with ciclosporin, mycophenolate mofetil and corticosteroids

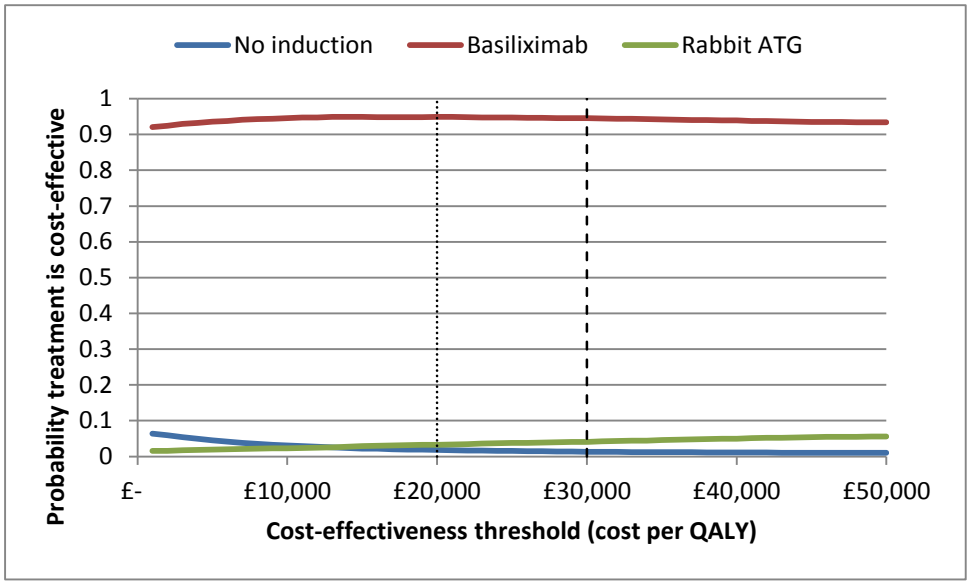
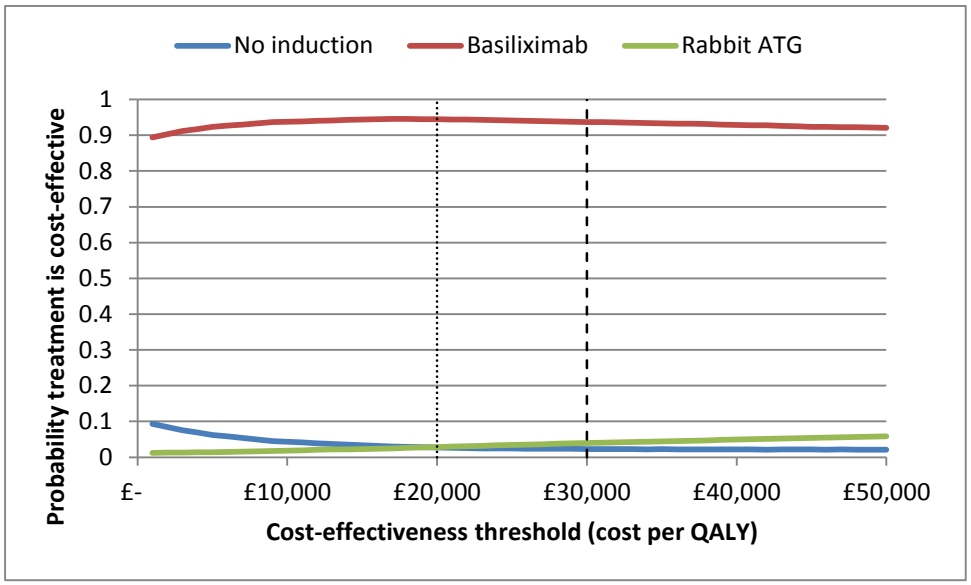


Figure 99. Cost-effectiveness acceptability curves for induction agents in combination with immediate-release tacrolimus, mycophenolate mofetil and corticosteroids



Summary

Basiliximab is predicted to be cost-effective with an error probability of 5.1–6.5% (cost-effectiveness threshold of £20,000 per QALY) to 5.4–7.4% (cost-effectiveness threshold of £30,000 per QALY). No induction and rabbit ATG are predicted not to be cost-effective.

Maintenance agents

A summary of cost-effectiveness results in the probabilistic analysis are given in Table 211. All treatments which were dominated in the deterministic analysis remain dominated in the probabilistic analysis. In addition, BAS+CSA+MPS is now predicted to be dominated by BAS+CSA+MMF, where in the deterministic analysis it was more costly and more effective with an ICER of over £100,000 per QALY. The treatment which was cost-effective at £20,000 and £30,000 per QALY in each comparison in the deterministic analysis remains cost-effective in the probabilistic analysis.

Table 211. Summary of probabilistic cost-effectiveness results for maintenance agents

Maintenance agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit		Probability cost-effective	
	Total	Inc.	Total	Inc.		£20k/QALY	£30k/QALY	£20k/QALY	£30k/QALY
With MMF						*vs. TAC*			
TAC-PR	£106,985	—	10.7557	—	Dominated	-0.8577	-0.6189	0.00%	£106,985
TAC	£92,660	-£14,325	10.8972	+0.1414	—	—	—	88.21%	£92,660
CSA	£98,219	+£5,558	10.9155	+0.0184	£302,909	-0.2596	-0.1669	11.79%	£98,219
With AZA						*vs. TAC*			
CSA	£102,504	—	10.7634	—	Dominated	-0.4497	-0.3210	6.29%	£102,504
TAC	£94,783	-£7,721	10.8270	+0.0636	—	—	—	93.71%	£94,783
With BAS+MMF						*vs. TAC*			
SRL	£115,212	—	10.8988	—	Dominated	-1.3273	-0.9204	0.00%	£115,212
TAC	£90,802	-£24,411	11.0055	+0.1067	—	—	—	87.06%	£90,802
CSA	£95,938	+£5,137	11.0309	+0.0254	£202,358	-0.2314	-0.1458	12.94%	£95,938
BEL	£209,677	+£113,738	11.2855	+0.2547	£446,594	-5.6637	-3.6824	0.00%	£209,677
With rATG+MMF						*vs. TAC*			
TAC	£97,750	—	10.9047	—	—	—	—	87.59%	£97,750
CSA	£102,831	+£5,082	10.9250	+0.0203	£250,785	-0.2338	-0.1491	12.41%	£102,831

Green highlight indicates cross-reference to original report

Table 211. Summary of probabilistic cost-effectiveness results for maintenance agents (cont.)

Maintenance agent	Discounted costs		Discounted QALYs		ICER	INHB		Probability cost-effective	
	Total	Inc.	Total	Inc.		£20k/QALY	£30k/QALY	£20k/QALY	£30k/QALY
With CSA						*vs. MMF*			
AZA	£102,504	—	10.7634	—	Dominated	-0.3664	-0.2950	9.13%	8.18%
MMF	£98,219	-£4,286	10.9155	+0.1522	—	—	—	90.87%	91.82%
EVL	£176,463	+£78,245	10.9395	+0.0240	£3,260,294	-3.8882	-2.5842	0.00%	0.00%
With TAC						*vs. MMF*			
SRL	£126,339	—	10.5931	—	Dominated	-1.9880	-1.4267	0.00%	0.00%
AZA	£94,783	-£31,557	10.8270	+0.2339	Dominated	-0.1763	-0.1409	35.68%	35.64%
MMF	£92,660	-£2,123	10.8972	+0.0702	—	—	—	64.32%	64.36%
With BAS+CSA						*vs. MMF*			
AZA	£99,159	—	10.8989	—	Dominated	-0.2930	-0.2393	12.52%	11.30%
MPS	£112,360	+£13,200	11.0244	+0.1255	Dominated	-0.8275	-0.5538	0.11%	0.62%
MMF	£95,938	-£16,421	11.0309	+0.0065	—	—	—	87.37%	88.08%
With rATG+CSA						*vs. MMF*			
AZA	£105,683	—	10.8048	—	Dominated	-0.2627	-0.2152	14.47%	13.13%
MMF	£102,831	-£2,852	10.9250	+0.1201	—	—	—	85.53%	86.87%

Immediate-release tacrolimus

Immediate-release tacrolimus was compared to ciclosporin (four comparisons), prolonged-release tacrolimus (one comparison), sirolimus (one comparison) and belatacept (one comparison).

In all comparisons immediate-release tacrolimus was the least costly intervention. It dominated prolonged-release tacrolimus when used in combination with MMF; it dominated ciclosporin when used in combination with AZA; and, it dominated sirolimus when used in combination with BAS+MMF. When used in combination with MMF or BAS+MMF or rATG+MMF, immediate-release tacrolimus was less effective than ciclosporin but the ICERs of ciclosporin versus immediate-release tacrolimus were over £200,000 per QALY. Immediate-release tacrolimus was less costly and less effective than belatacept when used in combination with BAS+MMF but the relevant ICER of belatacept (versus ciclosporin) was over £400,000 per QALY.

In all comparisons, immediate-release tacrolimus was predicted to be cost-effective at £20,000 to £30,000 per QALY. The probability of immediate-release tacrolimus being cost-effective (i.e., giving the greatest net health benefit in each comparison) at £20,000 and £30,000 per QALY ranged from 81.8% to 93.7%.

Prolonged-release tacrolimus

Prolonged-release tacrolimus was compared to immediate-release tacrolimus and ciclosporin in combination with MMF. Prolonged-release tacrolimus was predicted to be dominated by immediate-release tacrolimus and ciclosporin and therefore not predicted to be cost-effective at any cost-effectiveness threshold. The probability of prolonged-release tacrolimus being cost-effective was 0.0% at both £20,000 and £30,000 per QALY.

Mycophenolate mofetil

Mycophenolate mofetil was compared to azathioprine (four comparisons), mycophenolate sodium (one comparison), everolimus (one comparison) and sirolimus (one comparison).

Mycophenolate mofetil was predicted to dominate azathioprine in all comparisons, and to dominate sirolimus when used in combination with TAC, and to dominate mycophenoalte

sodium when used in combination with BAS+CSA. Mycophenolate mofetil was predicted to be less costly and less effective than everolimus when used in combination with CSA, but the ICER of everolimus (versus mycophenolate mofetil) was over £3,000,000 per QALY and therefore mycophenolate mofetil was predicted to be cost-effective at £20,000 to £30,000 per QALY.

In all comparisons, mycophenolate mofetil was predicted to be cost-effective at £20,000 to £30,000 per QALY. The probability of mycophenolate mofetil being cost-effective at £20,000 and £30,000 per QALY ranged from 64.3% to 91.8% across comparisons.

Mycophenolate sodium

Mycophenolate sodium was compared to mycophenolate mofetil and azathioprine in combination with BAS+CSA. Mycophenolate sodium was predicted to be dominated by mycophenolate mofetil and therefore was not predicted to be cost-effective at any cost-effectiveness threshold. The probability of mycophenolate sodium being cost-effective was 0.1% at £20,000 per QALY and 0.6% and £30,000 per QALY.

Sirolimus

Sirolimus was compared to immediate-release tacrolimus, belatacept and ciclosporin in combination with BAS+MMF. Sirolimus was predicted to be dominated by immediate-release tacrolimus and ciclosporin and therefore not predicted to be cost-effective at any cost-effectiveness threshold. The probability of sirolimus being cost-effective in combination with BAS+MMF was 0.0% at both £20,000 and £30,000 per QALY.

Sirolimus was also compared to mycophenolate mofetil and azathioprine in combination with TAC. Sirolimus was predicted to be dominated by mycophenolate mofetil and azathioprine and therefore not predicted to be cost-effective at any cost-effectiveness threshold. The probability of sirolimus being cost-effective in combination with TAC was 0.0% at both £20,000 and £30,000 per QALY.

Everolimus

Everolimus was compared to mycophenolate mofetil and azathioprine in combination with CSA. Everolimus was predicted to be more costly and more effective than all comparators. The relevant ICER for everolimus (versus mycophenolate mofetil) was over £3,000,000 per

QALY and therefore everolimus was not predicted to be cost-effective at £20,000 to £30,000 per QALY. The probability of everolimus being cost-effective was 0.0% at both £20,000 and £30,000 per QALY.

Belatacept

Belatacept was compared to immediate-release tacrolimus, sirolimus and ciclosporin in combination with BAS+MMF. Belatacept was predicted to be more costly and more effective than all comparators. The relevant ICER for belatacept (versus ciclosporin) was over £400,000 per QALY and therefore belatacept was not predicted to be cost-effective at £20,000 to £30,000 per QALY. The probability of belatacept being cost-effective was 0.0% at both £20,000 and £30,000 per QALY.

Cost-effectiveness acceptability curves

Figure 100 to Figure 107 show the cost-effectiveness acceptability curves (CEACs) for maintenance agents in the probabilistic analysis. As for induction agents, we have not presented these as cost-effectiveness acceptability frontiers because the agent with the highest probability of being cost-effective also gives the greatest expected net health benefit in the range explored.

Figure 100. CEACs for maintenance agents (CSA, TAC and TAC-PR) in combination with MMF

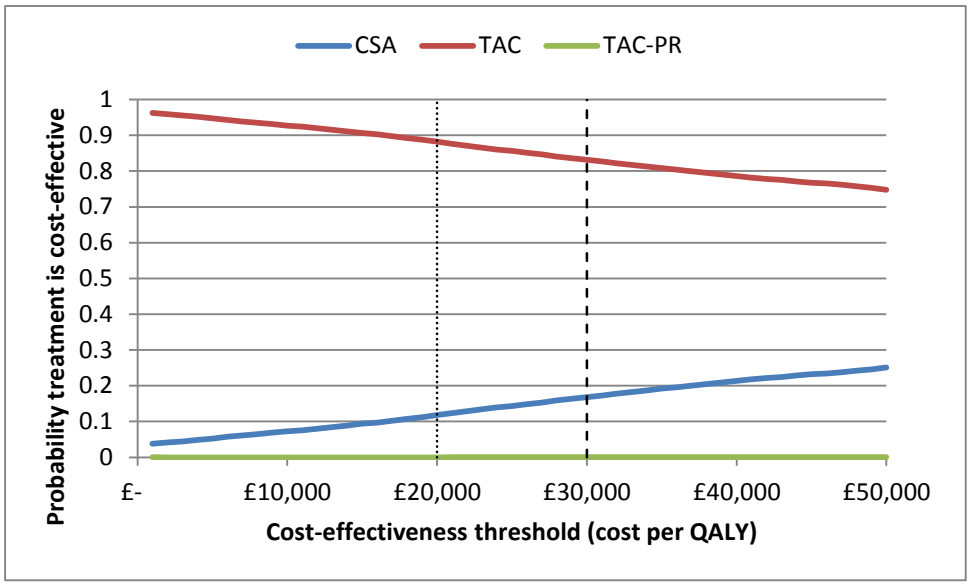


Figure 101. CEACs for maintenance agents (CSA and TAC) in combination with AZA

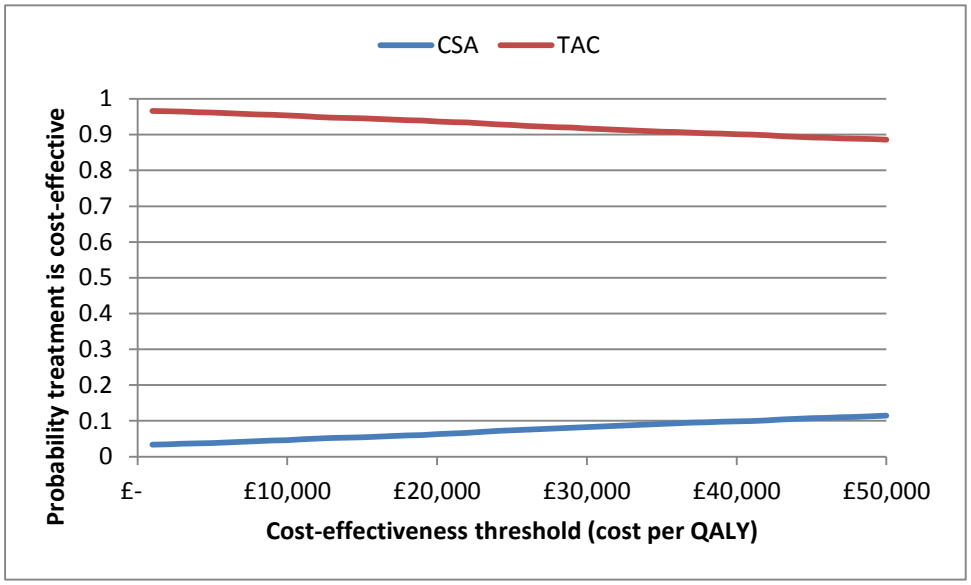


Figure 102. CEACs for maintenance agents (CSA, TAC, SRL and BEL) in combination with BAS+MMF

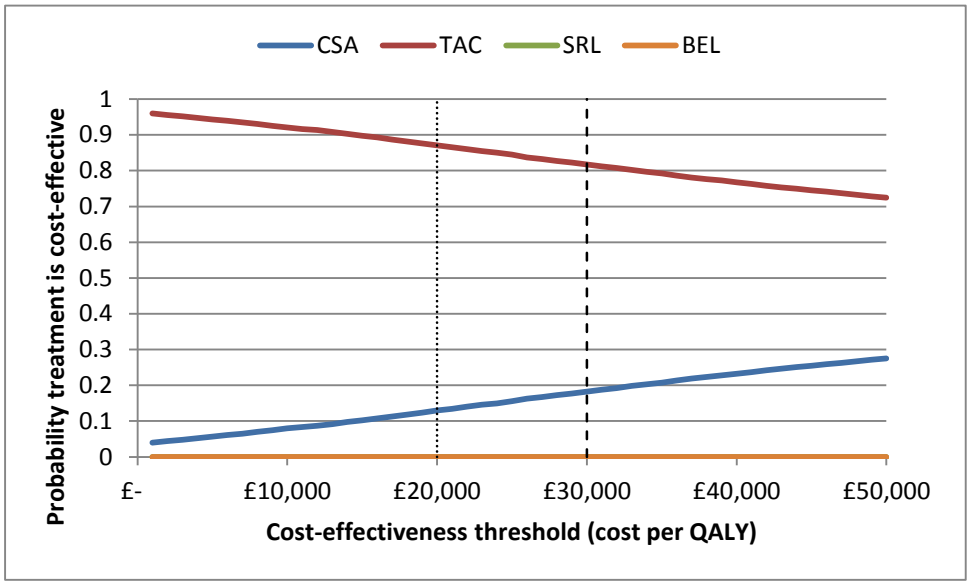


Figure 103. CEACs for maintenance agents (CSA and TAC) in combination with rATG+MMF

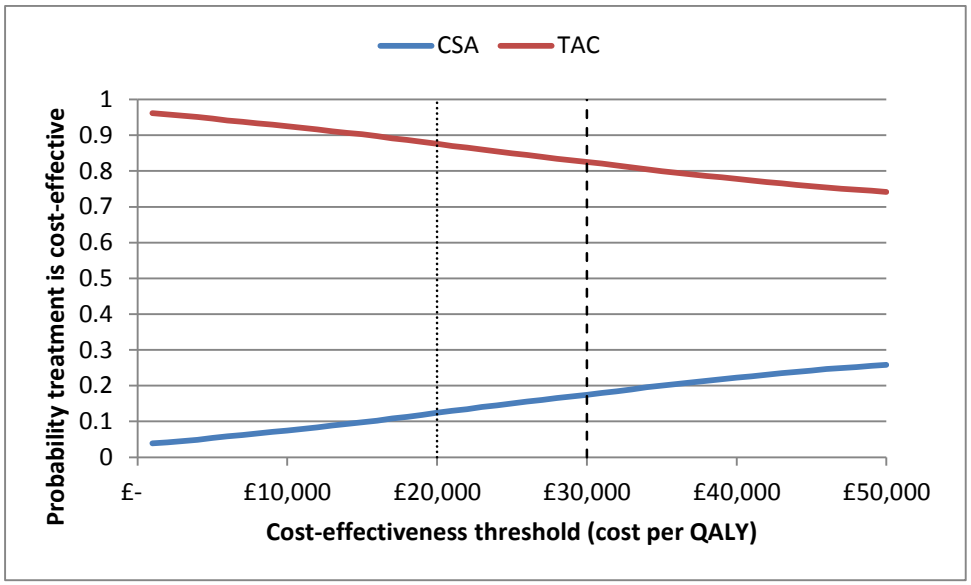


Figure 104. CEACs for maintenance agents (AZA, MMF and EVL) in combination with CSA

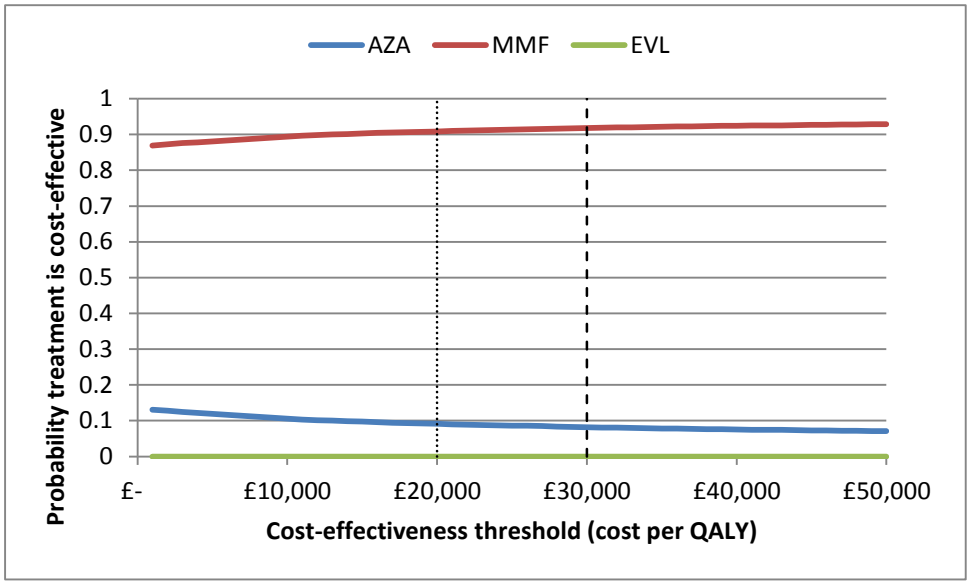


Figure 105. CEACs for maintenance agents (AZA, MMF and SRL) in combination with TAC

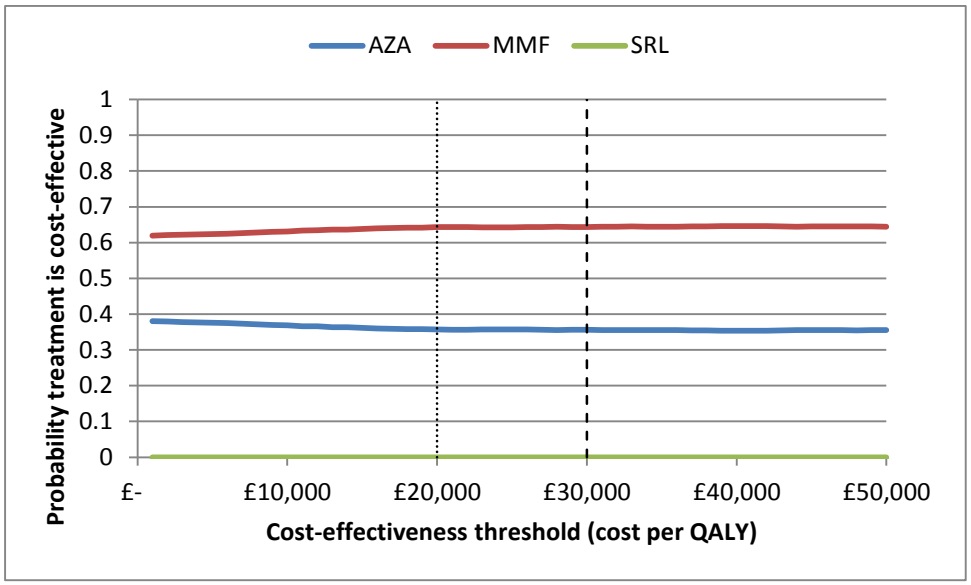


Figure 106. CEACs for maintenance agents (AZA, MMF and MPS) in combination with BAS+CSA

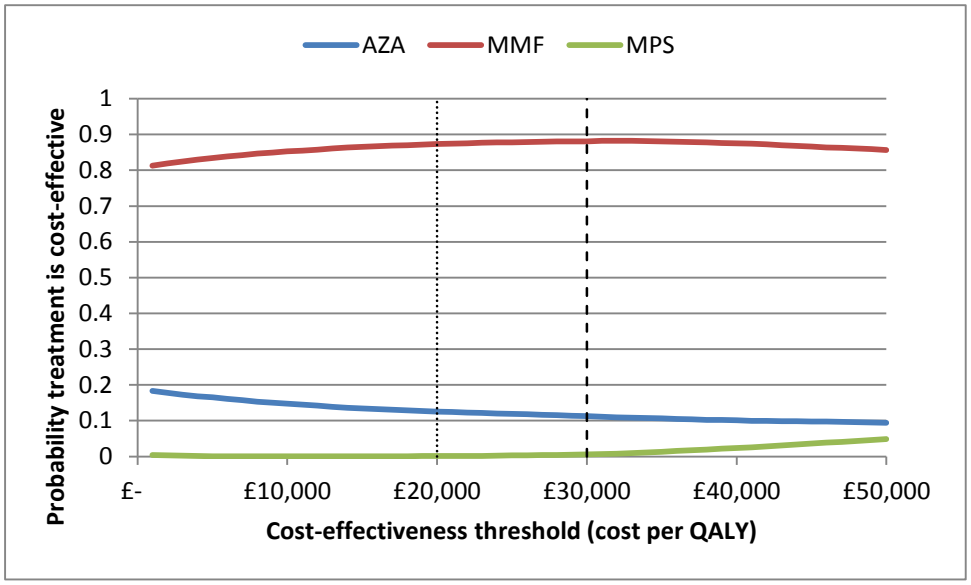
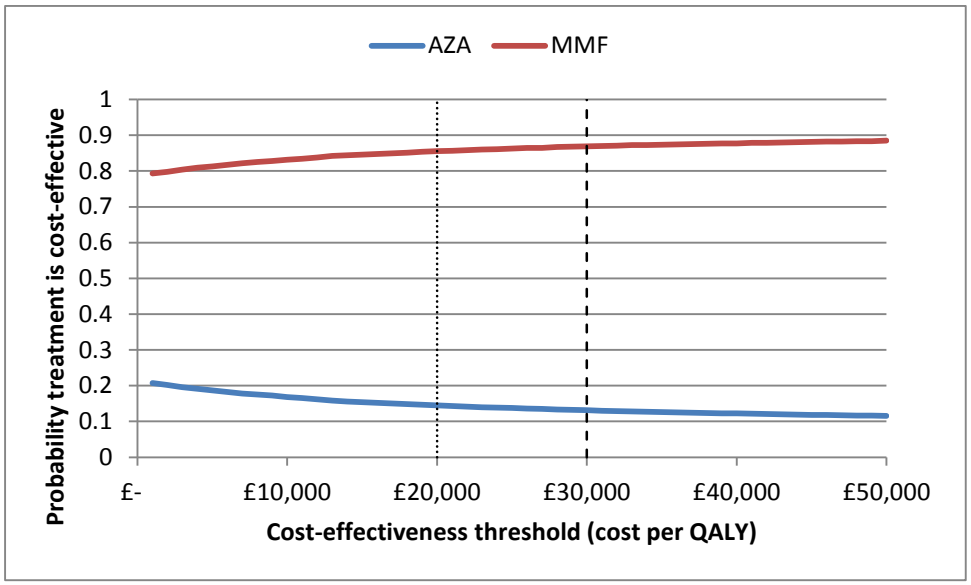


Figure 107. CEACs for maintenance agents (AZA and MMF) in combination with rATG+CSA



Summary

As in the deterministic analysis only immediate-release tacrolimus and mycophenolate mofetil were cost-effective at cost-effectiveness thresholds between £20,000 and £30,000 per QALY.

Prolonged-release tacrolimus, mycophenolate sodium and sirolimus were dominated in their relevant comparisons while everolimus and belatacept were all the most costly and most effective treatment in their relevant comparisons, but with ICERs significantly above £30,000 per QALY.

Comparing all regimens

When all regimens are compared simultaneously all regimens are dominated or extended dominated (rATG+TAC+MMF, rATG+CSA+MMF) except for BAS+TAC+MMF, BAS+CSA+MMF and BAS+BEL+MMF, which lie on the cost-effectiveness frontier. BAS+CSA+MPS is not predicted to be on the cost-effectiveness frontier in the probabilistic analysis whereas it was in the deterministic analysis. As explained in Section 7.4.1.2 (page 12) this may be due to a downward bias on probabilistic QALYs versus deterministic QALYs for this regimen due to non-linearities. The cost-effectiveness results for the regimens on the cost-effectiveness frontier are given in Table 212.

These results indicate that there is a 78.0–78.8% probability that a regimen on the cost-effectiveness frontier gives the maximum net health benefit at £20,000 to £30,000 per QALY. The probability that BAS+TAC+MMF gives the maximum net health benefit is 69.0% at £20,000 per QALY and 65.3% at £30,000 per QALY.

Table 212 also presents the cost-effectiveness results for regimens not on the cost-effectiveness frontier. All incremental costs and QALYs and INHBs are versus BAS+TAC+MMF. All these regimens are by definition dominated or extended dominated, although not in every case by BAS+TAC+MMF. Interestingly, at £20,000 per QALY there is a regimen not on the cost-effectiveness frontier (TAC+AZA) which is predicted to be more likely to be cost-effective than BAS+CSA+MMF and BAS+BEL+MMF (which are both on the frontier).

It is known that when the cost-effectiveness of an intervention is highly uncertain it can result in a flatteringly high probability of being cost-effective. A graphical representation which helps to identify this phenomenon is the rankogram,[417] which plots the probability distribution for the rank of an intervention according to a certain measure. We present rankograms of the net health benefit at £20,000 per QALY for all 16 regimens in Table 213. These suggest that the ranks of CSA+AZA, CSA+EVL, TAC+SRL, TAC-PR+MMF, BAS+TAC+MMF, BAS+SRL+MMF and BAS+BEL+MMF are fairly well or extremely well estimated (little dispersion in rank probability distribution) whereas the ranks for other regimens are less well estimated. The mean rank can also be calculated and is also presented in Table 213, demonstrating that the regimen with the greatest expected rank is BAS+TAC+MMF.

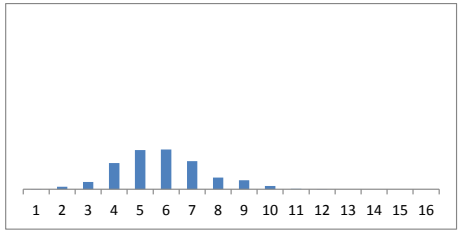
Table 212. Probabilistic cost-effectiveness results when all regimens are compared simultaneously

Regimen	Discounted costs		Discounted QALYs		ICER	Incremental net health benefit		Probability cost-effective	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY	£20k/QALY	£30k/QALY
Regimens on the cost-effectiveness frontier									
BAS+TAC+MMF	£90,802	—	11.0055	—	—	—	—	68.97%	65.32%
BAS+CSA+MMF	£95,938	+£5,137	11.0309	+0.0254	£202,358	-0.2314	-0.1458	8.97%	13.43%
BAS+BEL+MMF	£209,677	+£113,738	11.2855	+0.2547	£446,594	-5.6637	-3.6824	0.00%	0.00%
Probability a regimen on the cost-effectiveness frontier is cost-effective								77.94%	78.75%
Regimens not on the cost-effectiveness frontier									
TAC+SRL	£126,339	+£35,538	10.5931	-0.4124	Dominated	-2.1893	-1.5970	0.00%	0.00%
TAC-PR+MMF	£106,985	+£16,184	10.7557	-0.2498	Dominated	-1.0589	-0.7892	0.00%	0.00%
CSA+AZA	£102,504	+£11,703	10.7634	-0.2421	Dominated	-0.8273	-0.6322	0.00%	0.00%
rATG+CSA+AZA	£105,683	+£14,882	10.8048	-0.2006	Dominated	-0.9447	-0.6967	0.08%	0.11%
TAC+AZA	£94,783	+£3,981	10.8270	-0.1785	Dominated	-0.3775	-0.3112	16.86%	14.94%
TAC+MMF	£92,660	+£1,859	10.8972	-0.1083	Dominated	-0.2013	-0.1703	1.55%	1.21%
BAS+SRL+MMF	£115,212	+£24,411	10.8988	-0.1067	Dominated	-1.3273	-0.9204	0.00%	0.00%
BAS+CSA+AZA	£99,159	+£8,357	10.8989	-0.1066	Dominated	-0.5244	-0.3851	0.96%	1.26%
rATG+TAC+MMF	£97,750	+£6,948	10.9047	-0.1008	Dominated	-0.4482	-0.3324	2.18%	2.97%
CSA+MMF	£98,219	+£7,417	10.9155	-0.0900	Dominated	-0.4608	-0.3372	0.09%	0.12%
rATG+CSA+MMF	£102,831	+£12,030	10.9250	-0.0805	Dominated	-0.6820	-0.4815	0.33%	0.51%
CSA+EVL	£176,463	+£85,662	10.9395	-0.0660	Dominated	-4.3491	-2.9214	0.00%	0.00%
BAS+CSA+MPS	£112,360	+£21,558	11.0244	0.0189	Dominated	-1.0590	-0.6997	0.01%	0.13%
Probability a regimen not on the cost-effectiveness frontier is cost-effective								22.06%	21.25%

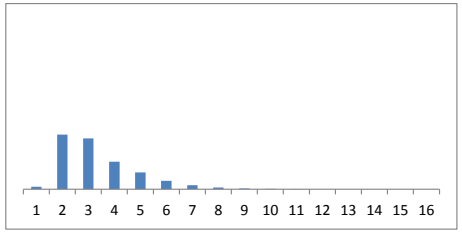
Table 213. Rankograms of net health benefit at £20,000 per QALY for each regimen

Regimen (mean rank)

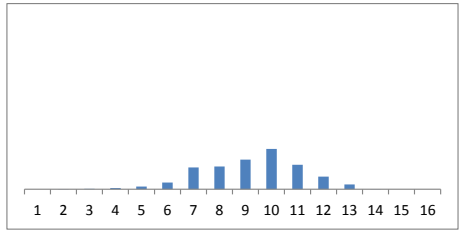
CSA+MMF (5.8)



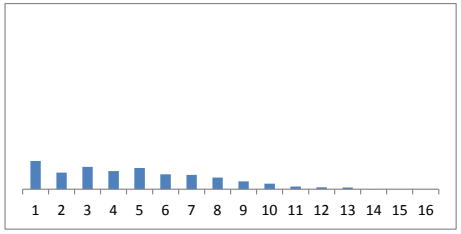
TAC+MMF (3.2)



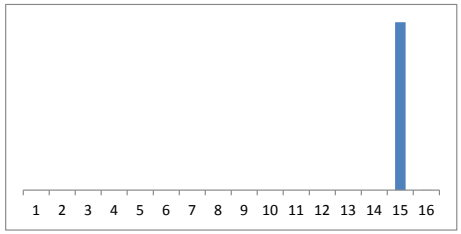
CSA+AZA (9.2)



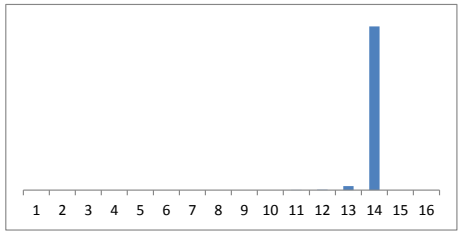
TAC+AZA (4.8)



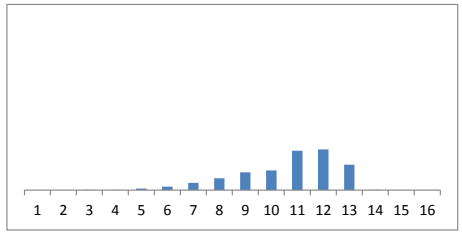
CSA+EVL (15.0)



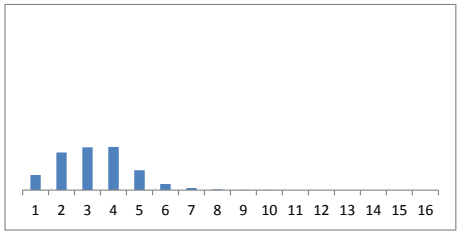
TAC+SRL (14.0)



TAC-PR+MMF (10.7)

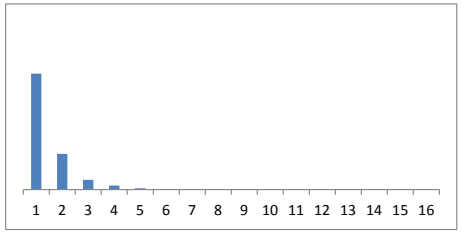


BAS+CSA+MMF (3.3)

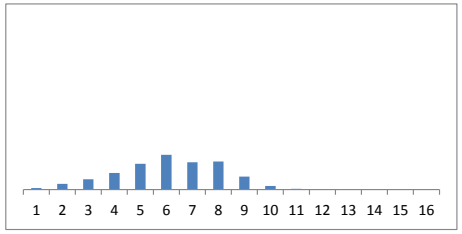


Regimen (mean rank)

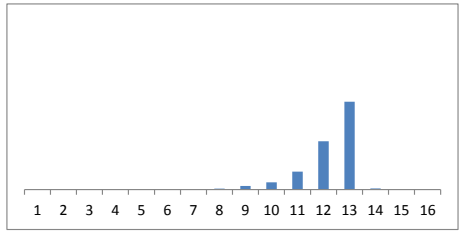
BAS+TAC+MMF (1.5)



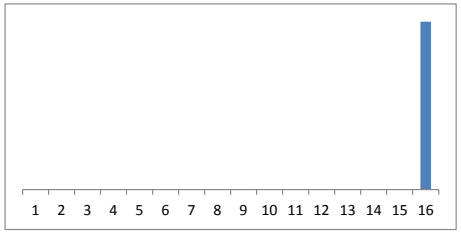
BAS+CSA+AZA (6.1)



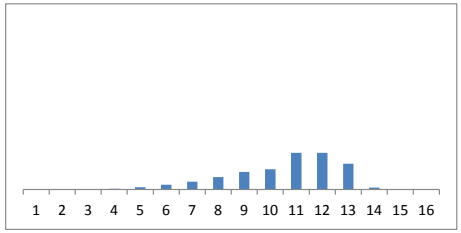
BAS+SRL+MMF (12.2)



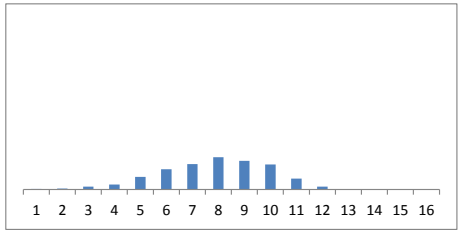
BAS+BEL+MMF (16.0)



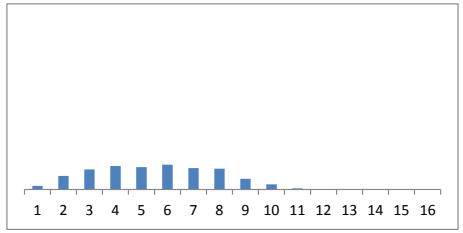
BAS+CSA+MPS (10.5)



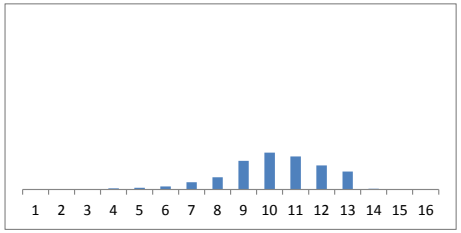
rATG+CSA+MMF (7.9)



rATG+TAC+MMF (5.5)



rATG+CSA+AZA (10.2)



7.4.2. Scenario analyses

7.4.2.1. Graft survival structural scenario analyses

Eliminating graft survival differences after a certain time

To explore what impact the model for death-censored graft survival had on cost-effectiveness a scenario analysis was conducted in which after *N* years the hazard rate of death-censored graft loss was equalised for all regimens (set equal to the baseline hazard function). This is equivalent to the conditional graft survival from time *N* years being identical across the regimens.

N was varied from 1 to 20; the base case is effectively *N* = 50. When *N* = 1 it is therefore assumed that acute rejection, eGFR and NODAT do not affect graft survival after 1 year and that long-term graft survival is determined solely by graft survival at 1 year. As *N* increases the surrogate relationship from acute rejection, eGFR and NODAT to graft survival is strengthened towards the base case.

Figure 108 shows the net health benefit of all regimens as *N* is varied from 1 to 20. Figure 109 shows a close up of the regimens with high net health benefit (BAS+CSA+MPS, TAC-PR+MMF, BAS+SRL+MMF, TAC+SRL, CSA+EVL and BAS+BEL+MMF are not visible in this figure).

Figure 108. Net health benefit of regimens as duration of surrogate effect on graft survival is varied

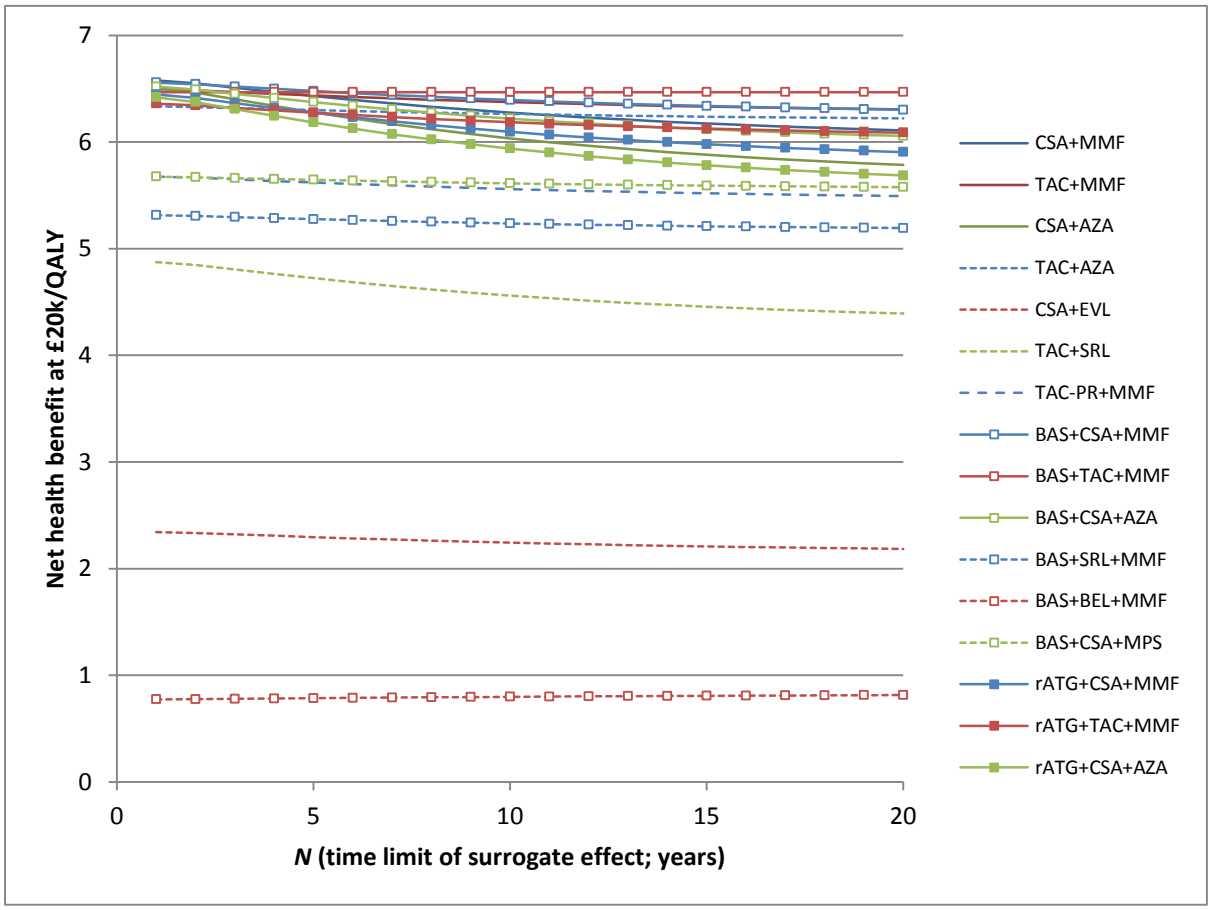


Figure 109. Net health benefit of regimens as duration of surrogate effect on graft survival is varied (close up)

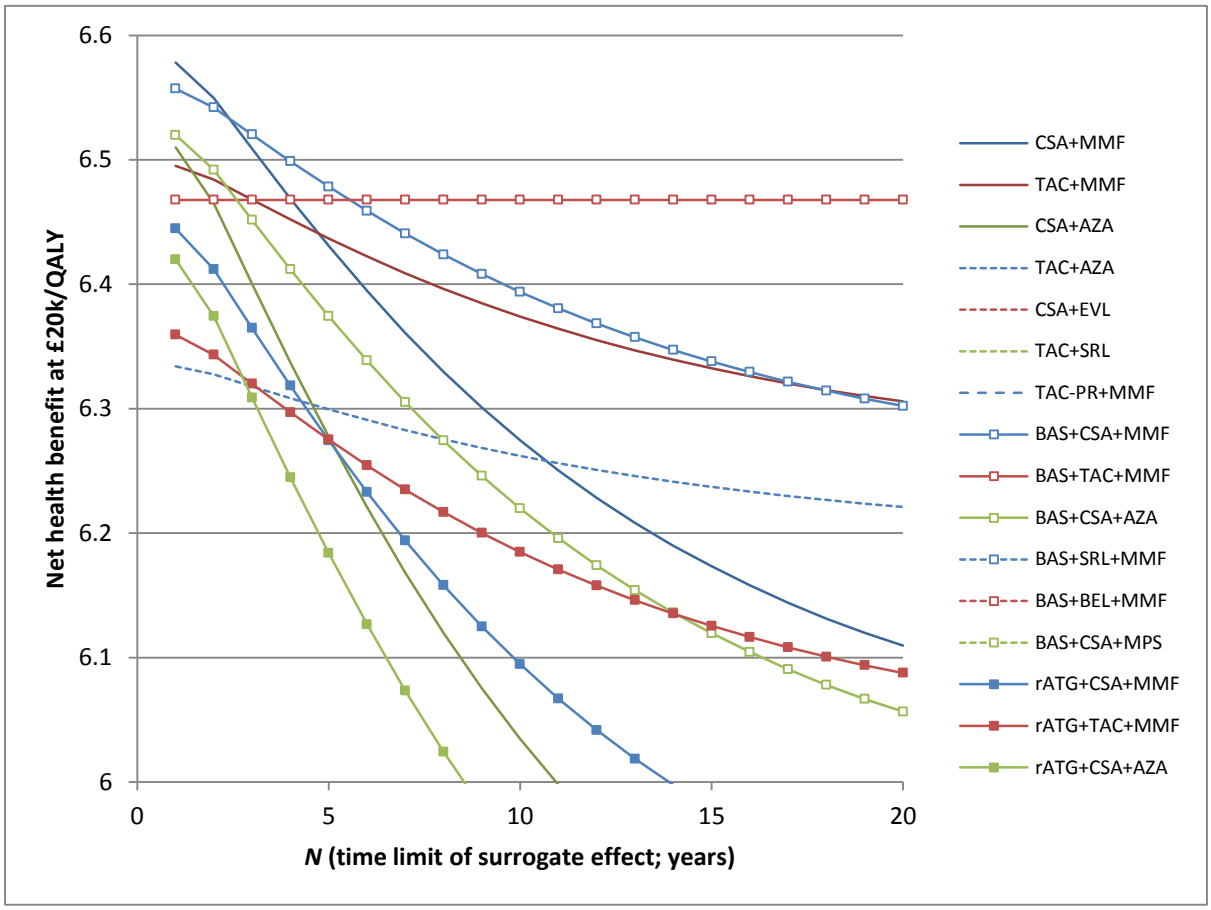


Table 214 and Table 215 respectively indicate the ranges of *N* for which induction and maintenance agents are cost-effective (i.e., give the greatest net health benefit in each comparison).

Table 214. Range of *N* for which each induction agent is cost-effective

Induction agent	Range of *N* for which induction agent is cost-effective	
	£20k/QALY	**£30k/QALY**
With CSA+AZA		
No induction	N/A	N/A
Basiliximab	1–20	1–20
Rabbit ATG	N/A	N/A
With CSA+MMF		
No induction	1–2	1
Basiliximab	3–20	2–20
Rabbit ATG	N/A	N/A
With TAC+MMF		
No induction	1–3	1–2
Basiliximab	4–20	3–20
Rabbit ATG	N/A	N/A

Table 215. Range of *N* for which each maintenance agent is cost-effective

Maintenance agent	Range of *N* for which maintenance agent is cost-effective	
	£20k/QALY	**£30k/QALY**
With MMF		
TAC-PR	N/A	N/A
TAC	5–20	8–20
CSA	1–4	1–7
With AZA		
CSA	1–4	1–5
TAC	5–20	6–20
With BAS+MMF		
SRL	N/A	N/A
TAC	6–20	9–20
CSA	1–5	1–8
BEL	N/A	N/A
With rATG+MMF		
TAC	5–20	8–20
CSA	1–4	1–7

Table 215. Range of *N* for which each maintenance agent is cost-effective (cont.)

Maintenance agent	Range of *N* for which maintenance agent is cost-effective	
	£20k/QALY	**£30k/QALY**
With CSA		
AZA	N/A	N/A
MMF	1–20	1–20
EVL	N/A	N/A
With TAC		
SRL	N/A	N/A
AZA	N/A	N/A
MMF	1–20	1–20
With BAS+CSA		
AZA	N/A	N/A
MMF	1–20	1–20
MPS	N/A	N/A
With rATG+CSA		
AZA	N/A	N/A
MMF	1–20	1–20

Table 215 indicates that TAC-PR, SRL, BEL, EVL and MPS were not cost-effective at £20,000 or £30,000 per QALY for any *N* from 1 to 20. MMF was cost-effective at £20,000 and £30,000 per QALY for all *N* from 1 to 20. For lower values of *N* (up to 4–8), CSA was cost-effective at £20,000 or £30,000 per QALY whereas for higher values (towards the base case), TAC was cost-effective at £20,000 and £30,000 per QALY.

As can be seen in Figure 109 once $N \geq 6$, BAS+TAC+MMF gives the greatest net health benefit. When $N < 6$, BAS+CSA+MMF, CSA+MMF, BAS+CSA+AZA, CSA+AZA and TAC+MMF give greater net health benefit than BAS+TAC+MMF for some N, although only BAS+CSA+MMF or CSA+MMF gives the greatest net health benefit for $N < 6$. Base case graft survival curves for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF are shown in Figure 110 and Figure 111.

Figure 110. Death-censored graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF (base case)

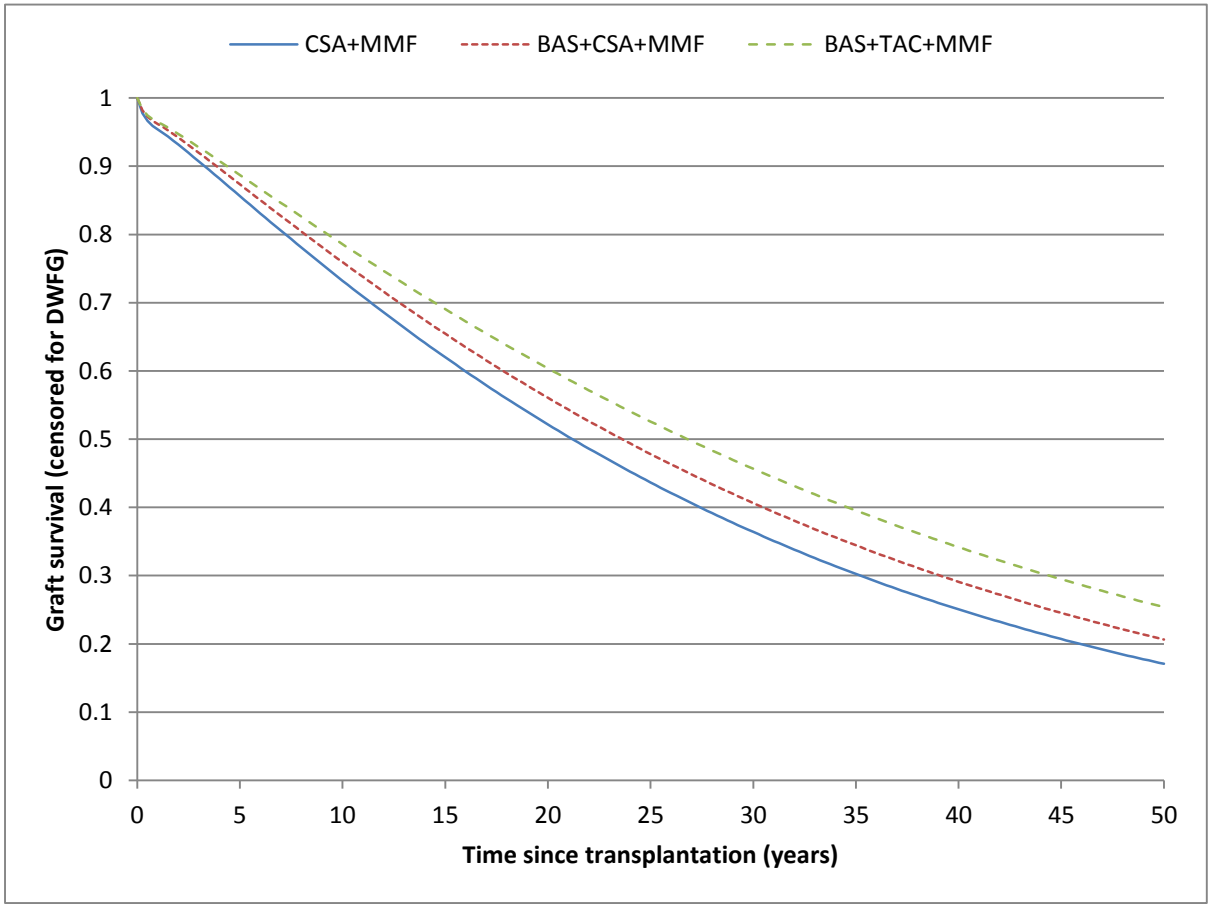
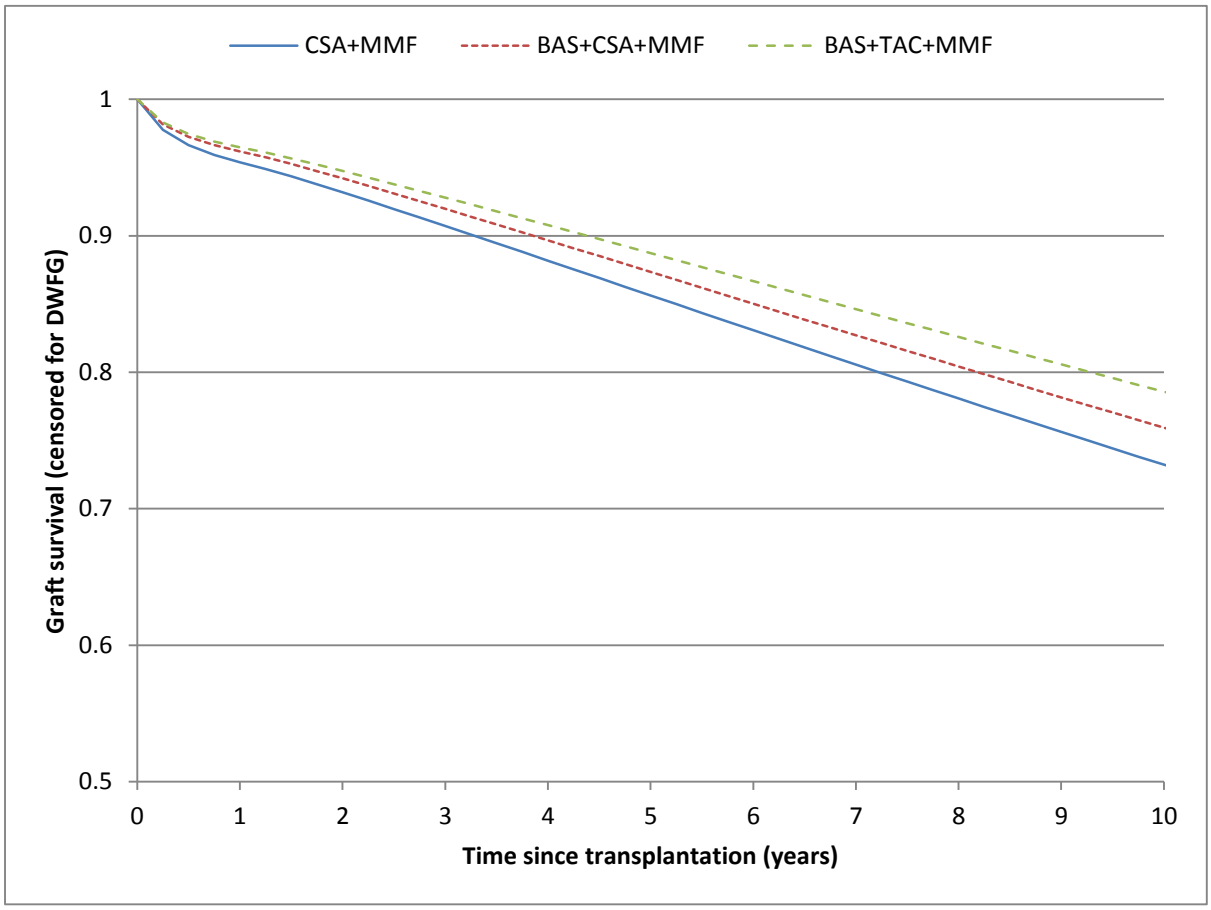


Figure 111. Death-censored graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF (base case; close up 0–10 years)



When *N* = 5, BAS+CSA+MMF gives the greatest net health benefit and the graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF are shown in Figure 112 and Figure 113. As expected, by reducing the duration of the surrogate effect the graft survival curves diverge significantly less than in the base case.

Figure 112. Death-censored graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF (*N* = 5)

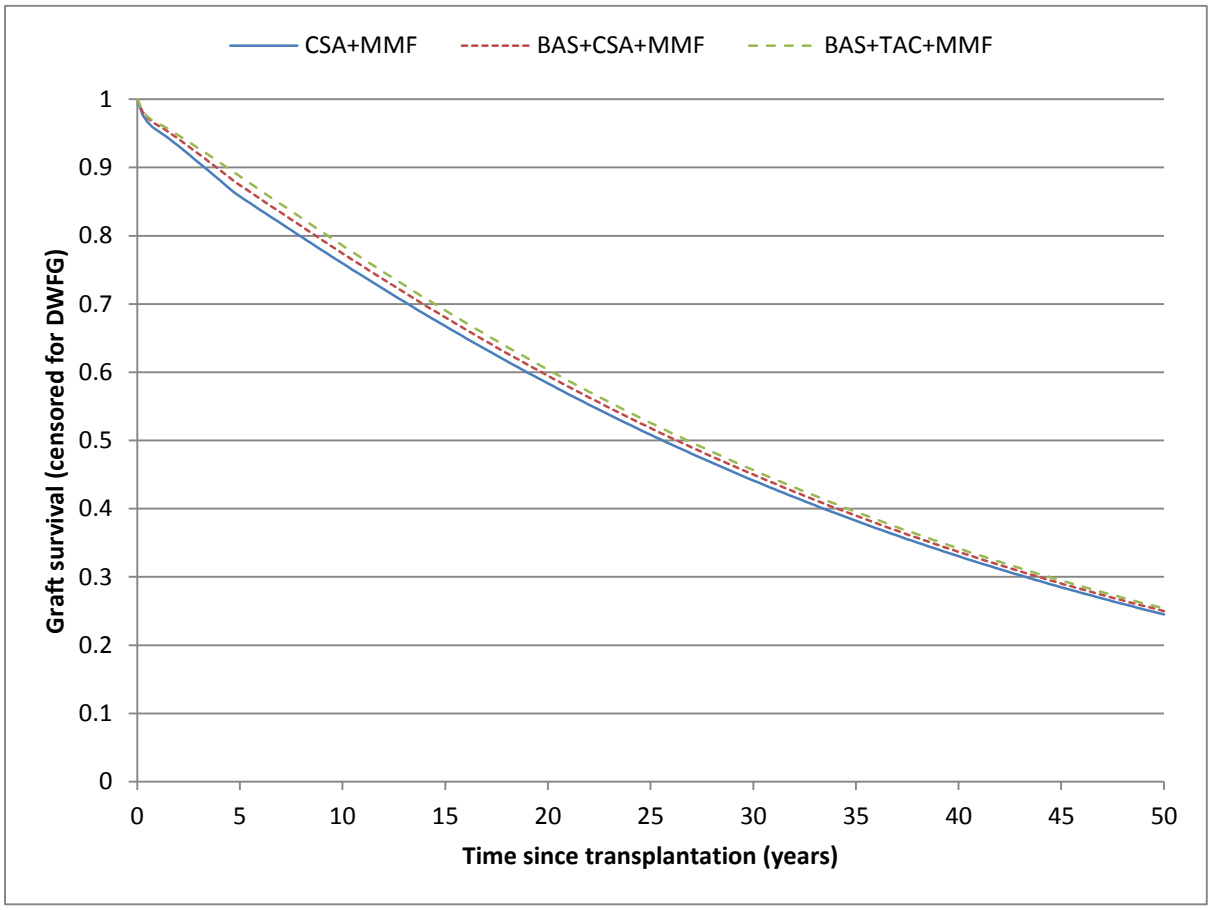
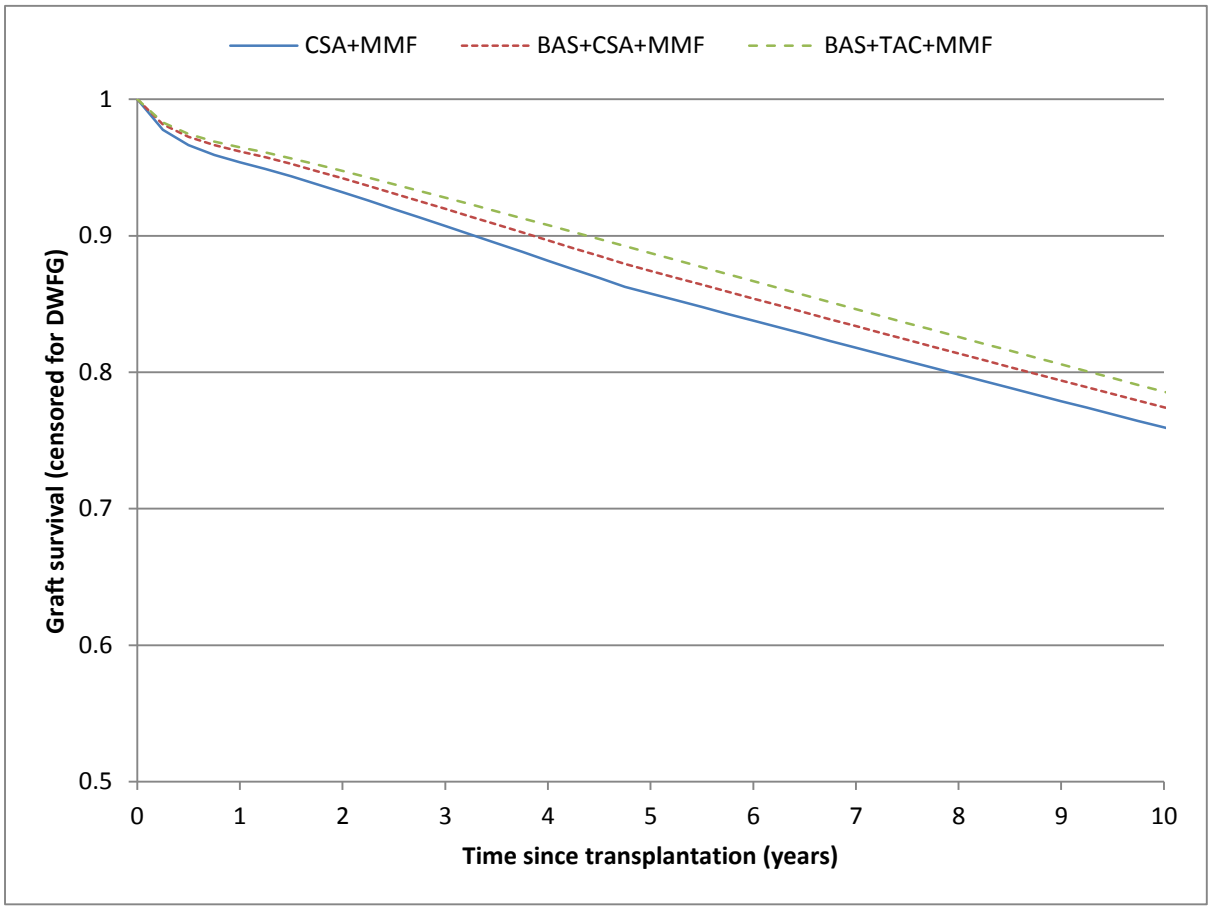


Figure 113. Death-censored graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF (N = 5; close up 0–10 years)



When *N* = 2, CSA+MMF gives the greatest net health benefit and the graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF are shown in Figure 114 and Figure 115. As there is now only one year of graft survival difference extrapolated according to the surrogate relationship, the graft survival curves are virtually identical. In this scenario CSA+MMF gives the greatest net health benefit but it is noteworthy that the net health benefit of CSA+MMF is quite sensitive to *N* and even in this scenario only four regimens are predicted to give greater net health benefit than BAS+TAC+MMF: CSA+MMF, TAC+MMF, BAS+CSA+MMF and BAS+CSA+AZA.

Figure 114. Death-censored graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF (N = 2)

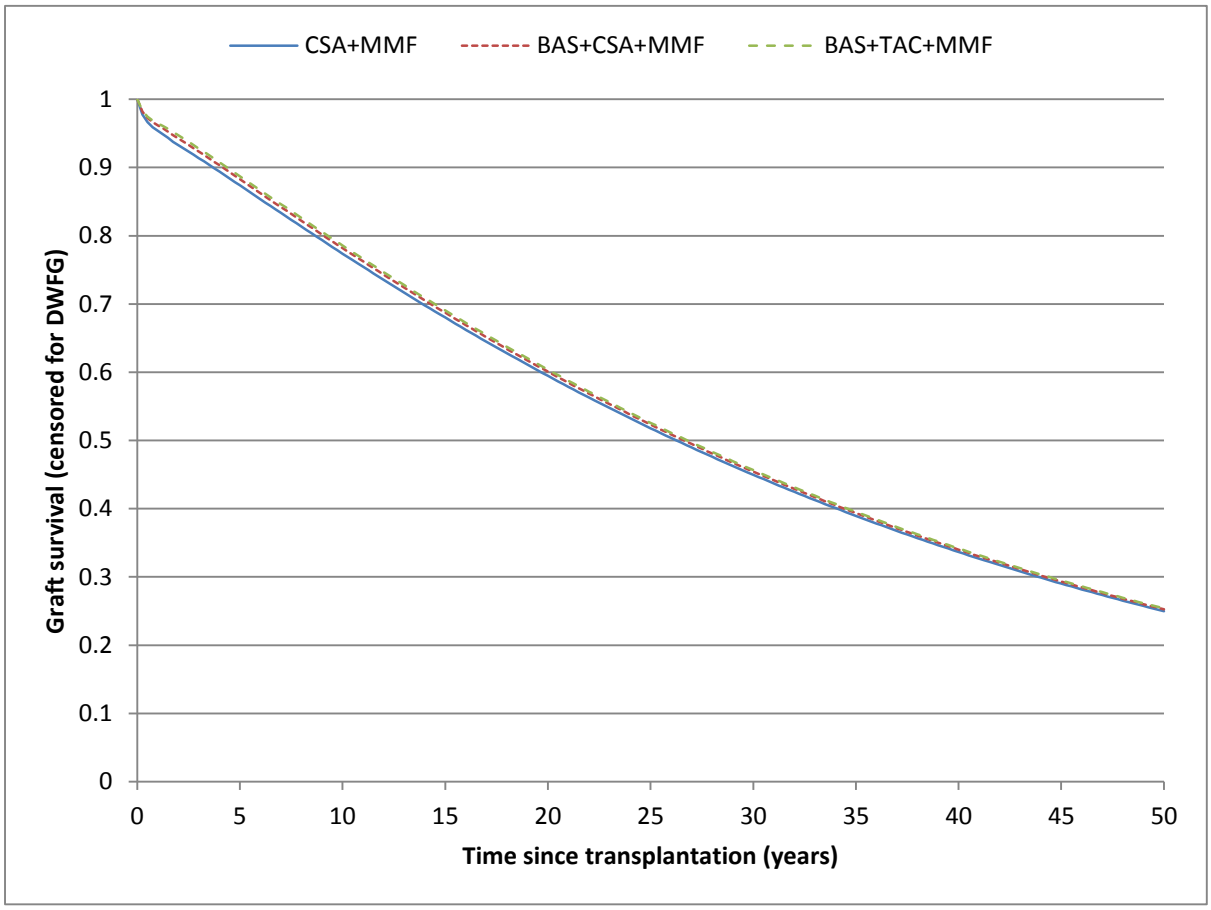
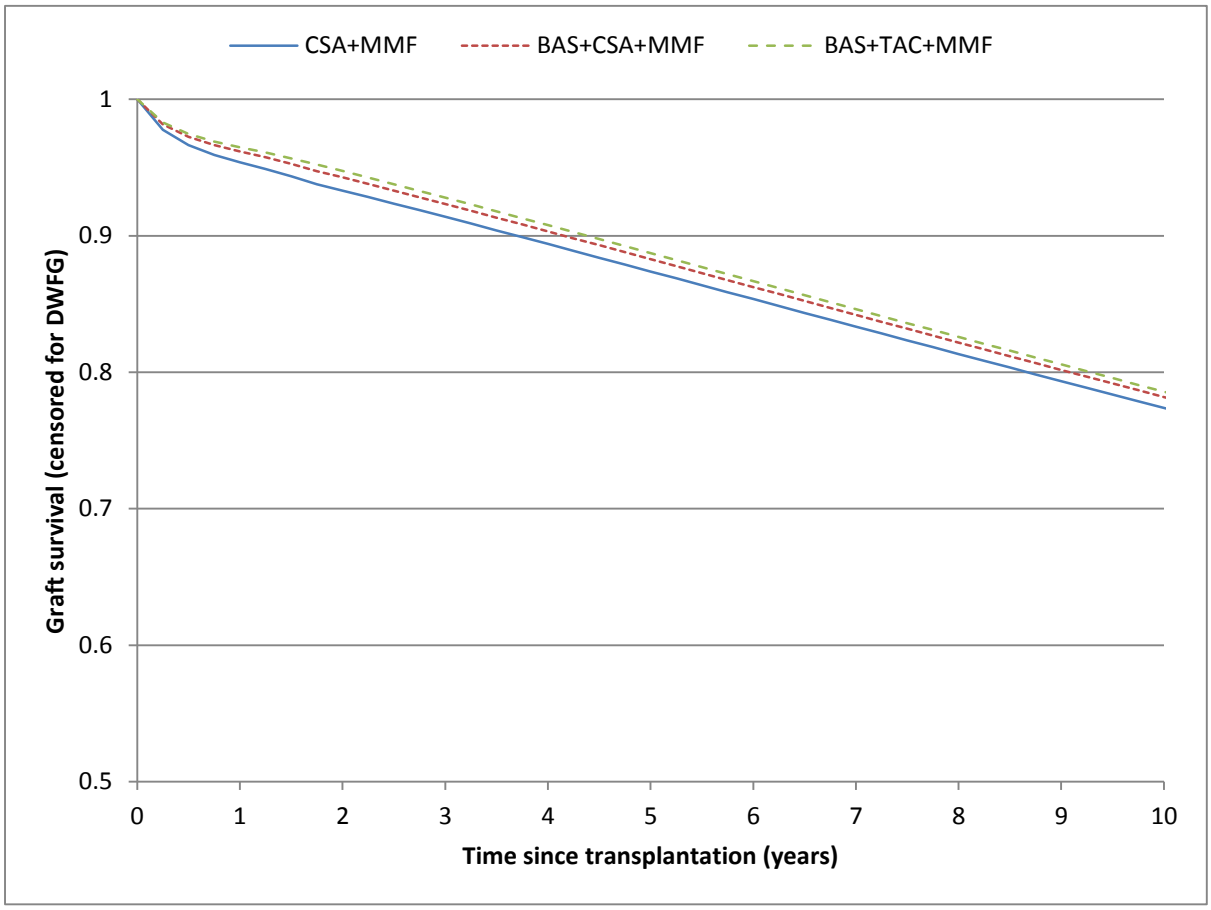


Figure 115. Death-censored graft survival for CSA+MMF, BAS+CSA+MMF and BAS+TAC+MMF (N = 2; close up 0–10 years)



Different gamma parameter for CNI-free regimens

It may be plausible that avoiding calcineurin inhibitors will prolong long-term graft survival by avoiding CNI nephrotoxicity. This possibility was investigated by reducing the gamma (γ) parameter in the Weibull model for graft survival (death-censored) for regimens without CNI, i.e., for BAS+SRL+MMF and BAS+BEL+MMF.

An offset was included for ln(γ) between −2 and 0 (equivalent to the base case). The incremental net health benefit for BAS+SRL+MMF and BAS+BEL+MMF versus BAS+TAC+MMF was calculated (since TAC was predicted to be the only cost-effective agent in combination with BAS+MMF at cost-effectiveness thresholds between £20,000 and £30,000 per QALY). The INHB was calculated at both £20,000 and £30,000 per QALY. As shown in Figure 116 and Figure 117 there is a cross-over for SRL but not for BEL across the

range explored, suggesting that SRL could be cost-effective at £20,000 to £30,000 per QALY if long-term graft survival were significantly better than extrapolated in the base case.

Figure 116. Incremental net health benefit (at £20,000 per QALY) of SRL and BEL versus TAC as gamma parameter of graft survival is varied

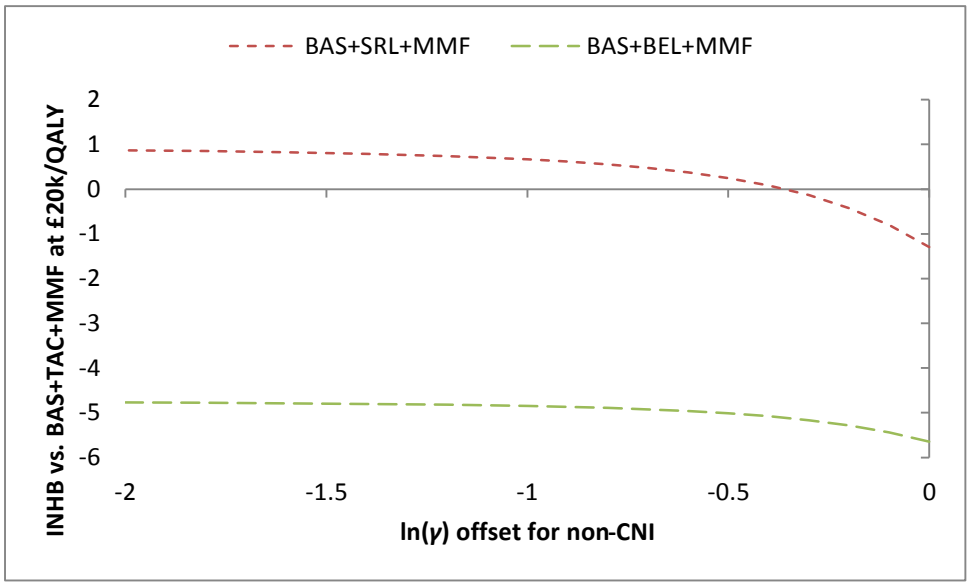
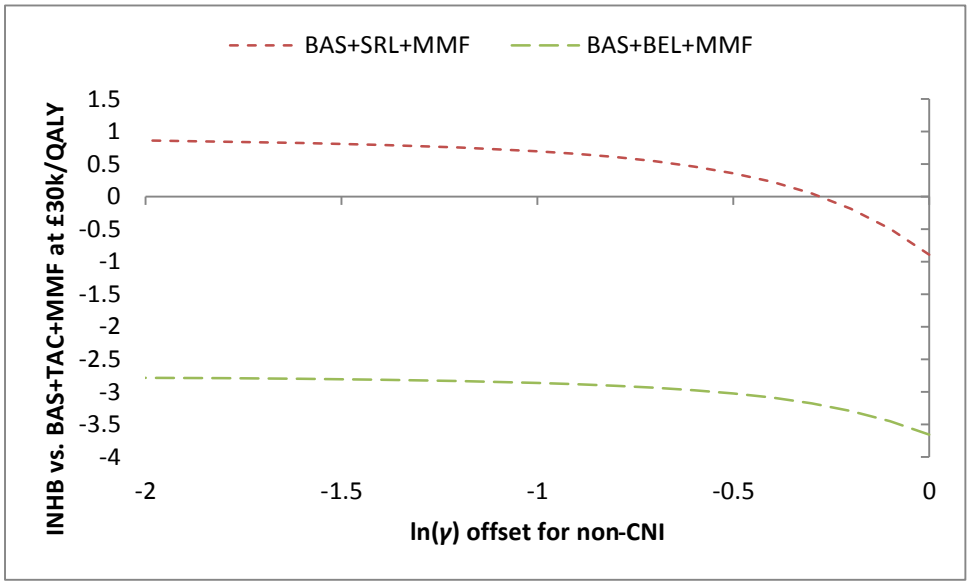


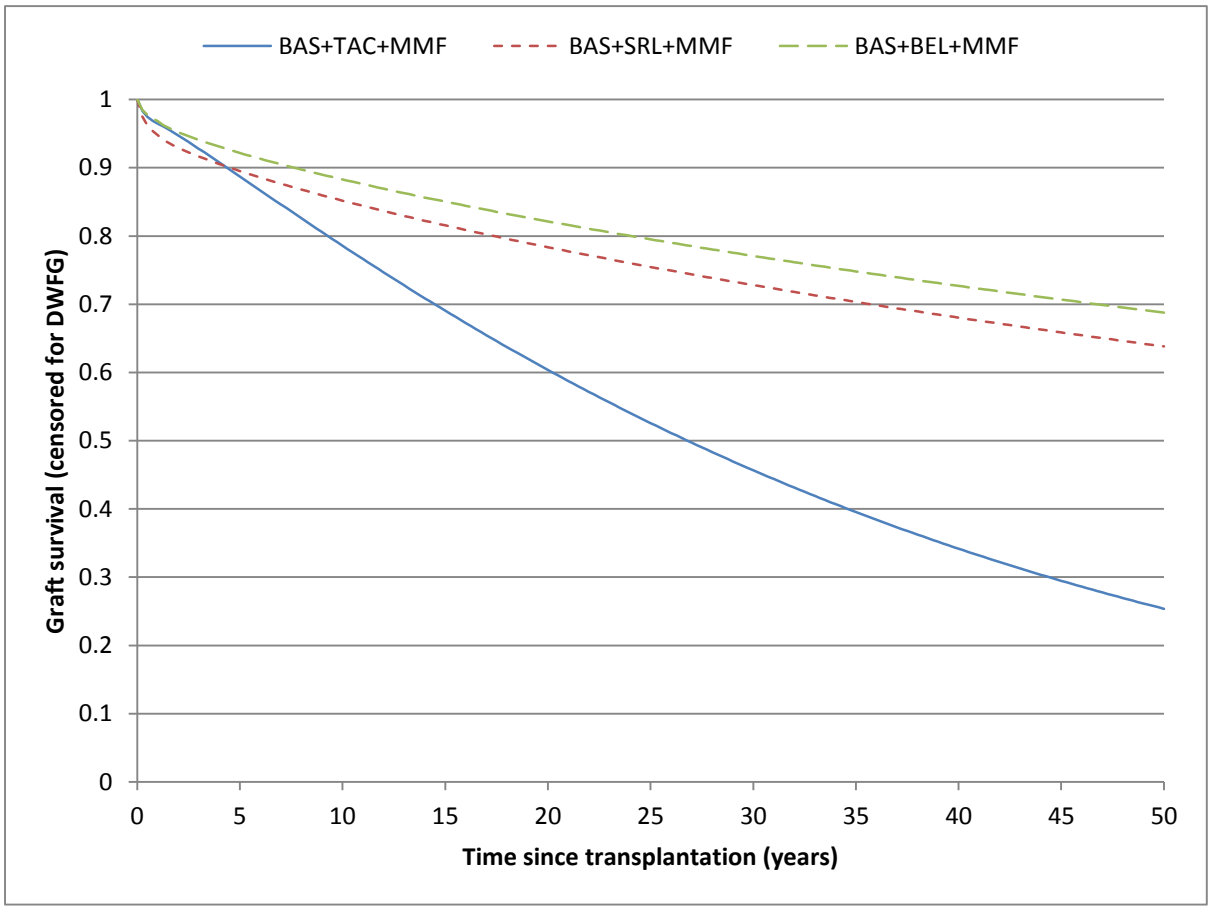
Figure 117. Incremental net health benefit (at £30,000 per QALY) of SRL and BEL versus TAC as gamma parameter of graft survival is varied



Cross-over at £20,000 per QALY occurs for SRL with a ln(γ) offset of −0.3582 (corresponding to γ=0.773), which leads to a reduction in total discounted costs from £114,549 to £99,859 and an increase in total discounted QALYs from 10.9010 to 11.4607.

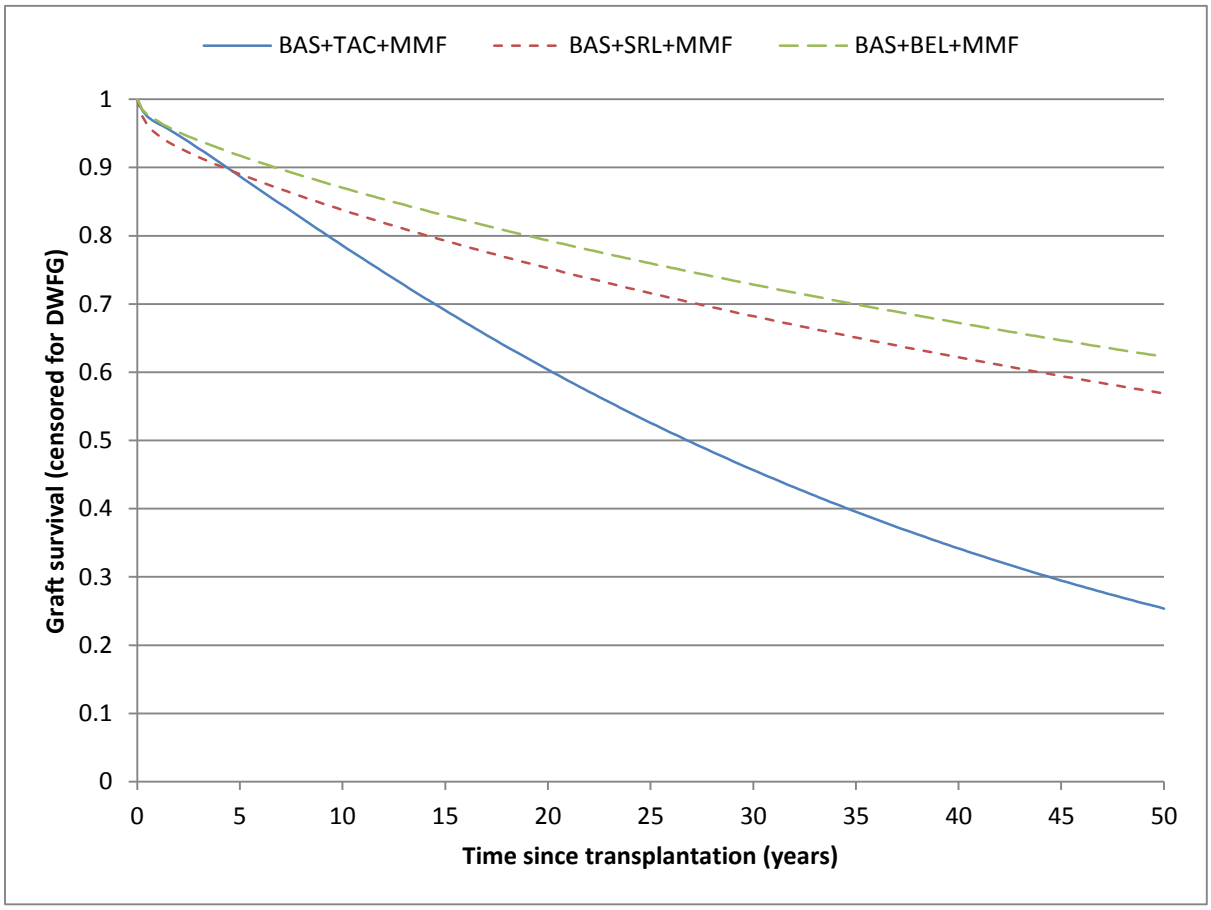
Death-censored graft survival in this scenario is shown in Figure 118. In this scenario TAC and SRL are equally cost-effective at £20,000 per QALY but BEL is not cost-effective.

Figure 118. Death-censored graft survival when non-CNI gamma parameter for graft survival is 0.773 for SRL and BEL versus 1.105 for TAC



Cross-over at £30,000 per QALY occurs for SRL with a ln(γ) offset of −0.2767 (corresponding to γ=0.838), which leads to a reduction in total discounted costs to £102,065 and an increase in total discounted QALYs to 11.3766. Death-censored graft survival in this scenario is shown in Figure 119. In this scenario TAC and SRL are equally cost-effective at £30,000 per QALY but BEL is not cost-effective.

Figure 119. Death-censored graft survival when non-CNI gamma parameter for graft survival is 0.838 for SRL and BEL versus 1.105 for TAC



7.4.2.2. Cost-related scenario analyses

List prices for drug acquisition costs

A scenario analysis was conducted in which the drug acquisition costs (for immunosuppression, NODAT and dyslipidaemia) were taken from list prices (BNF 68) rather than the CMU eMit database.

Unit costs for CSA, TAC, AZA and MMF increased, which as expected increased the total costs for all regimens (since there were no regimens not including at least one of CSA, TAC, AZA and MMF).

The cost-effectiveness results for induction agents were only marginally affected (Table 216). No induction and rabbit ATG continued to be dominated by basiliximab.

Table 216. Impact on cost-effectiveness of induction agents of using list prices for drug acquisition costs

Induction agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY
With CSA+AZA						*vs. Basiliximab*	
No induction	£104,711	—	10.7711	—	Dominated	-0.3077	-0.2491
Rabbit ATG	£107,627	+£2,916	10.8182	+0.0471	Dominated	-0.4064	-0.2992
Basiliximab	£101,194	-£6,433	10.9029	+0.0848	—	—	—
With CSA+MMF						*vs. Basiliximab*	
No induction	£103,302	—	10.9145	—	Dominated	-0.2218	-0.1846
Rabbit ATG	£107,807	+£4,504	10.9281	+0.0135	Dominated	-0.4335	-0.3212
Basiliximab	£101,069	-£6,738	11.0247	+0.0966	—	—	—
With TAC+MMF						*vs. Basiliximab*	
No induction	£104,443	—	10.8884	—	Dominated	-0.1815	-0.1542
Rabbit ATG	£109,376	+£4,933	10.9047	+0.0163	Dominated	-0.4119	-0.3023
Basiliximab	£102,803	-£6,573	10.9880	+0.0832	—	—	—

The cost-effectiveness results for maintenance agents showed some marked differences from the reference case analysis (Table 217). In general the INHB (at £20,000 per QALY) of TAC versus CSA decreased, in some cases causing it to become negative. Likewise, in general, the INHB of MMF versus AZA decreased, in some cases causing it to become negative. The cost-effectiveness of TAC-PR, SRL, EVL and MPS improved marginally but still none was predicted to be cost-effective in the range £20,000 to £30,000 per QALY. The cost-effectiveness of BEL was virtually unchanged with an ICER over £400,000 per QALY.

With a cost-effectiveness threshold in the range £20,000 to £30,000 per QALY the following changes were observed in cost-effectiveness:

- CSA instead of TAC was cost-effective in combination with MMF, BAS+MMF and rATG+MMF (TAC remained cost-effective in combination with AZA);
- AZA instead of MMF was cost-effective in combination with TAC (MMF remained cost-effective in combination with CSA, BAS+CSA and rATG+CSA).

Table 217. Impact on cost-effectiveness of maintenance agents of using list prices for drug acquisition costs

Maintenance agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY
With MMF						*vs. CSA*	
TAC-PR	£111,581	—	10.7920	—	Dominated	-0.5365	-0.3985
TAC	£104,443	-£7,139	10.8884	+0.0964	Dominated	-0.0831	-0.0641
CSA	£103,302	-£1,140	10.9145	+0.0261	—	—	—
With AZA						*vs. TAC*	
CSA	£104,711	—	10.7711	—	Dominated	-0.1744	-0.1491
TAC	£103,195	-£1,515	10.8696	+0.0986	—	—	—
With BAS+MMF						*vs. CSA*	
SRL	£119,577	—	10.9010	—	Dominated	-1.0491	-0.7406
TAC	£102,803	-£16,773	10.9880	+0.0869	Dominated	-0.1235	-0.0946
CSA	£101,069	-£1,734	11.0247	+0.0367	—	—	—
BEL	£215,325	+£114,256	11.2941	+0.2694	£424,137	-5.4434	-3.5391

Table 217. Impact on cost-effectiveness of maintenance agents of using list prices for drug acquisition costs (cont.)

Maintenance agent	Discounted costs		Discounted QALYs		ICER (cost per QALY)	Incremental net health benefit	
	Total	Incremental	Total	Incremental		£20k/QALY	£30k/QALY
With CSA						*vs. MMF*	
AZA	£104,711	—	10.7711	—	Dominated	-0.2139	-0.1904
MMF	£103,302	-£1,408	10.9145	+0.1435	—	—	—
EVL	£178,788	+£75,486	10.9659	+0.0514	£1,469,322	-3.7229	-2.4648
With TAC						*vs. AZA*	
SRL	£134,088	—	10.6023	—	Dominated	-1.8120	-1.2971
AZA	£103,195	-£30,893	10.8696	+0.2674	—	—	—
MMF	£104,443	+£1,247	10.8884	+0.0188	£66,470	-0.0436	-0.0228
With BAS+CSA						*vs. MMF*	
AZA	£101,194	—	10.9029	—	Dominated	-0.1280	-0.1260
MMF	£101,069	-£125	11.0247	+0.1218	—	—	—
MPS	£114,174	+£13,105	11.1377	+0.1130	£115,991	-0.5423	-0.3239
With rATG+CSA						*vs. AZA*	
AZA	£107,627	—	10.8182	—	—	—	—
MMF	£107,807	+£180	10.9281	+0.1099	£1,633	+0.1009	+0.1039

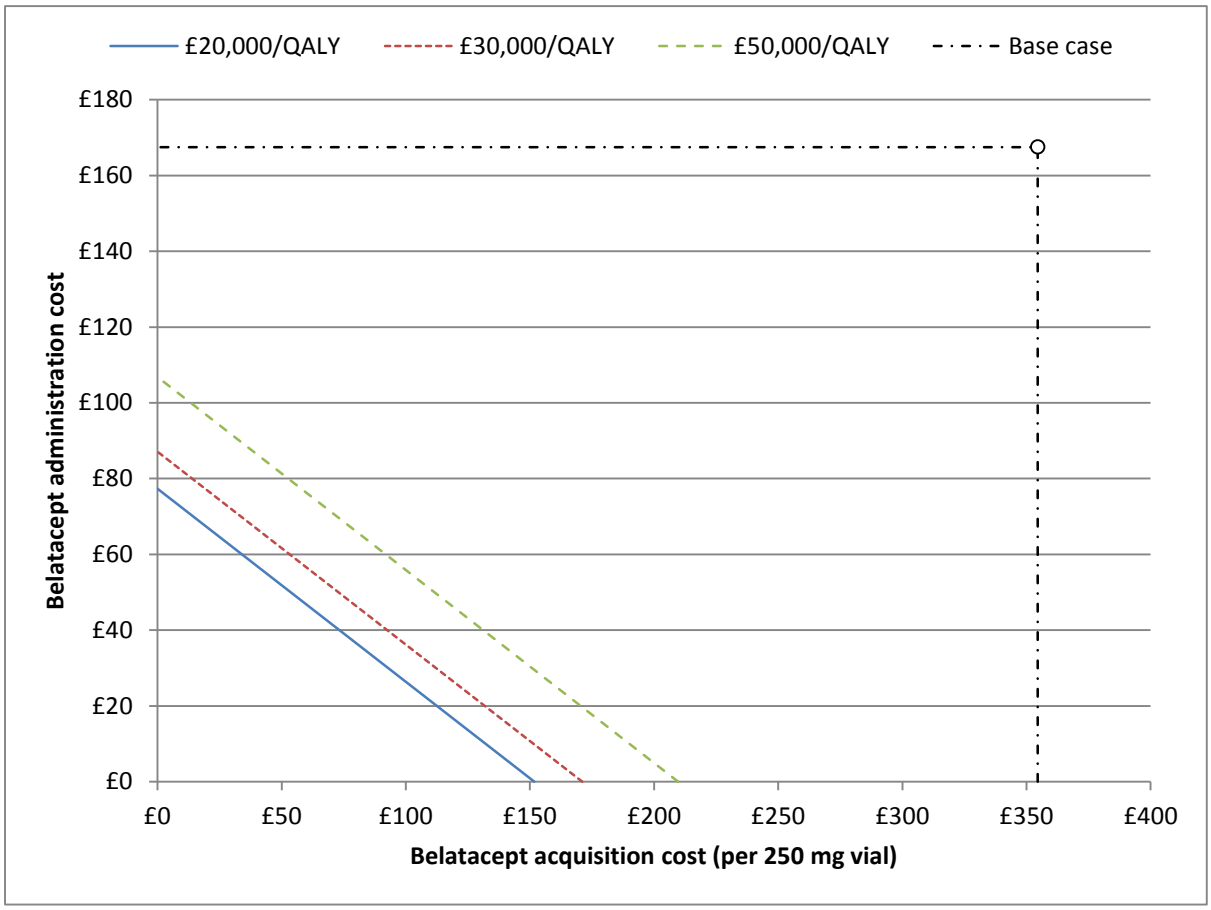
Threshold analysis on costs associated with belatacept

A two-way threshold analysis was conducted on the two costs associated with belatacept: drug administration and drug acquisition. It was found that the total discounted costs for BAS+BEL+MMF were exactly linearly dependent on both costs according to the following formula:

Cost(BAS+BEL+MMF) = 72,453.47 + 311.3796×Cost(Vial) + 158.5936×Cost(Belatacept admin)

This formula was used to calculate the ICER of BAS+BEL+MMF versus BAS+TAC+MMF. ICER isolines (lines of constant ICER) are straight lines in the 2D plot of the costs of IV administration and belatacept vials, as shown in Figure 120.

Figure 120. Threshold analysis on costs associated with belatacept



The threshold analysis indicated that if the administration cost in the base case is assumed to be correct, BAS+BEL+MMF is not predicted to be cost-effective at £20,000 to £30,000 per

QALY even at zero acquisition cost. Since the acquisition and administration costs are both NHS costs and are intrinsically related to treating the condition of interest with belatacept, both of these costs should be included in the reference-case analysis. The administration cost associated with belatacept is a genuine incremental cost associated with belatacept and not with other available treatments.[418] Even if administration costs are excluded for belatacept, BAS+BEL+MMF is not predicted to be cost-effective at £20,000 to £30,000 per QALY based on the current list price for drug acquisition. Bristol Myers Squibb argue for a cost of administration for belatacept of £153.57. At this cost of administration BAS+BEL+MMF is still not predicted to be cost-effective at £20,000 per QALY even at zero acquisition cost.