Confidential information removed

Economic evaluation of the Nexavar patient access scheme for patients with advanced RCC

Background

In response to the consultation on appraising medicines for end of life being undertaken by NICE, Bayer have proposed a patient access scheme to the Department of Health. This scheme provides the first pack of Nexavar (112 tablets, 200mg) free of charge to each patient commencing treatment for Nexavar for the treatment of renal cell carcinoma (RCC).

With the proposed change in advice to the appraisal committee from NICE, and the submitted patient access scheme, we would like the Committee to take into account the data and analysis provided within this document.

This updated submission contains the Bayer analysis of the cost-effectiveness of Nexavar taking the patient access scheme into account. In addition to the overall TARGET patient group, and as part of the patient access scheme, we would also like NICE to consider the data on those patients who had prior cytokine therapy, as well as our comments on the appropriateness and implications of a six week Markov cycle length and the application of the hazard ratio within the academic modelling.

The cost-effectiveness analysis is based on the input assumptions used by the academic group, PenTAG, in their original report.

Appraising medicines for end of life

The NICE consultation on end of life medicines outlines the following criteria for a drug for it to be considered under the “appraising medicines for end of life” strategy:

- The medicine is indicated, in its licence, for a patient population normally not exceeding 7000 new patients per annum, and;
- The medicine is indicated for the treatment of patients with a diagnosis of a terminal illness and who are not, on average, expected to live for more than 24 months, and;
- There is sufficient evidence to indicate that the medicine offers a substantial extension to life, compared to current NHS treatment.

Bayer believe that Nexavar meets these criteria. The final scope for the appraisal showed that the patient population was below 7,000 new patients per annum, and that patients with advanced RCC have a poor survival prognosis, with a median survival of between 6 and 12 months. Furthermore, Nexavar has been shown to substantially increase both progression free and overall survival in patients with RCC.

Patients who have had prior cytokine therapy: rationale for the sub group

In the original analysis, the academic group noted that the inclusion criteria for TARGET included patients who had the presence of histologically confirmed metastatic clear cell RCC who had progressed after one systemic treatment within the previous eight months. They noted that for 17% of patients recruited, this prior systemic therapy is not reported and consequently did not accept the evidence to support a first line setting in cytokine unsuitable patients, although this is a group for which Nexavar has a licensed indication.

The academic group therefore restricted their analysis of Nexavar to the second line setting but used the overall TARGET data set for this setting. Bayer acknowledge that one of the challenges in health technology assessment is that the data publicly available for a technology may not always represent the licensed indication. As a result, the TARGET dataset has been reanalysed for this specific patient subset (i.e. those who had received prior cytokine therapy and for whom Nexavar is a second line treatment) and we consequently would like the Committee to take it into consideration when evaluating the patient access scheme.

Clinical data

The clinical data are split into two groups:

1. The overall TARGET group (defined as equivalent to a second line advanced setting in the original assessment), which includes patients both with and without prior cytokine therapy
2. Prior cytokine group from TARGET (those where Nexavar is a second line treatment in the advanced setting)

Overall TARGET group

The clinical data for the overall TARGET group has been described in the original submission. The main clinical data used for the modelling is provided below for ease of reference.

Figure 1: Investigator progression-free survival in the phase III TARGET study (also show in Escudier et al. 2007 N Eng J Med 356;2)

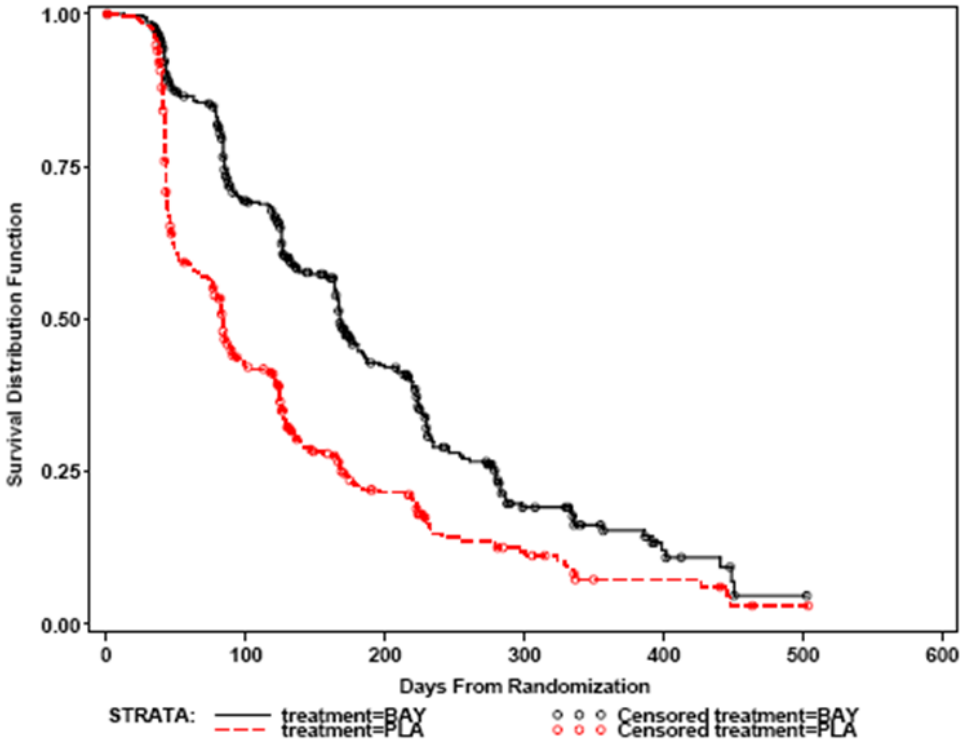
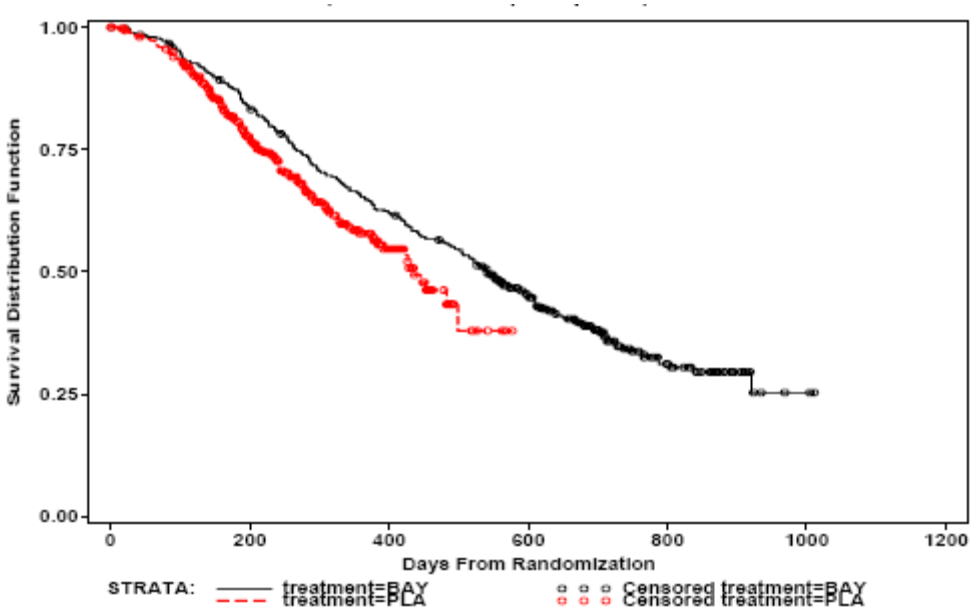


Figure 2: Kaplan-Meier Plot of Overall Survival Secondary Analysis (Placebo data Censored (cross-over) 30 Jun 2005): Intent to Treat (08 Sep 2006)



Prior cytokine group

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Model structure

A comparison of the key model parameters between the PenTAG report and the revised Bayer model is summarised below.

Table 1: Overview of the model key assumptions and structure

Model parameter	Bayer model	PenTAG model
Cycle length	28 days (equivalent to a pack of Nexavar; monthly is more relevant to prescribing and treatment decisions)	42 days
Comparator arm data	Weibull fit	Weibull fit
Nexavar arm data	Weibull fit (reflects the best available data more closely)	Hazard ratios
Half cycle correction	Yes	Yes
Health states	PFS, PD, death	PFS, PD, death
Treatment costs	As per PenTAG report	-
Utility values	As per PenTAG report	-

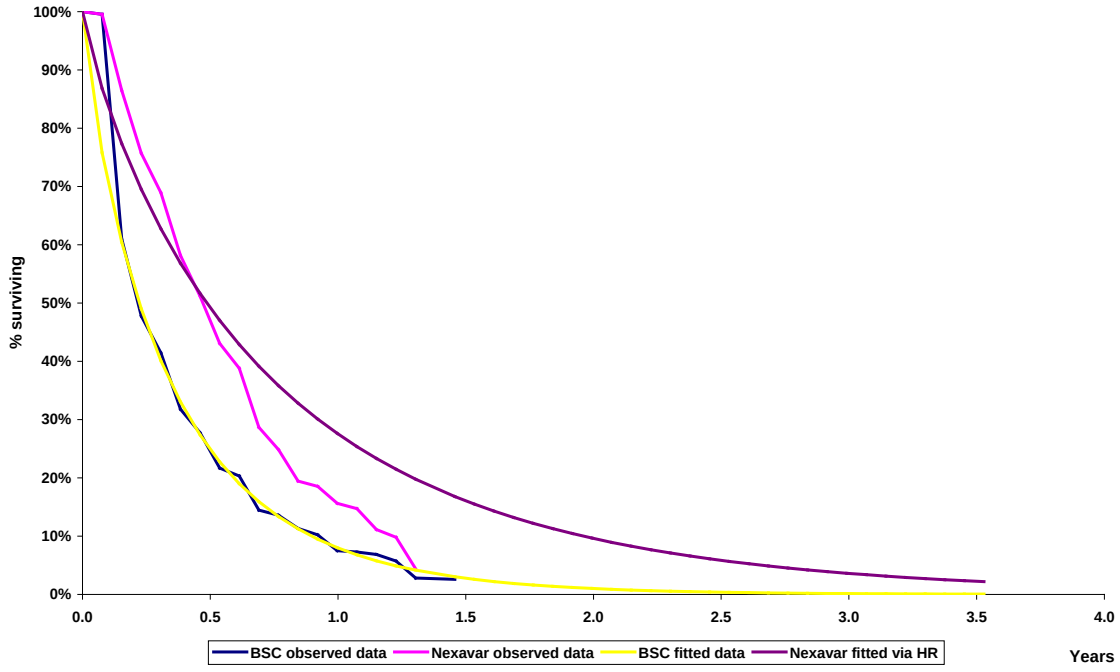
In the PenTAG model, the cycle length chosen was 42 days, which is equivalent to a cycle of sunitinib. The academic group did not investigate the impact of the cycle length on the results. Nexavar is administered in four week cycles, not six week cycles.

Treatment and supportive care decisions for patients receiving Nexavar are also based on a monthly basis rather than a six weekly basis. Therefore a monthly cycle is a more relevant time period to base the modelling of clinical, economic and outcomes for Nexavar. The original Bayer model used a 30.4 day (equivalent to one calendar month) cycle length to reflect this. For simplicity, the revised model used in the analysis here and incorporating the patient access scheme, uses a 28 day cycle which proxies the usual treatment decision time points and the treatment cycle length for patients on Nexavar. As a consequence of a shorter cycle length, the clinical outcomes from the model reflect more closely those observed in the clinical trials, improving the validity of the model.

Curve fitting

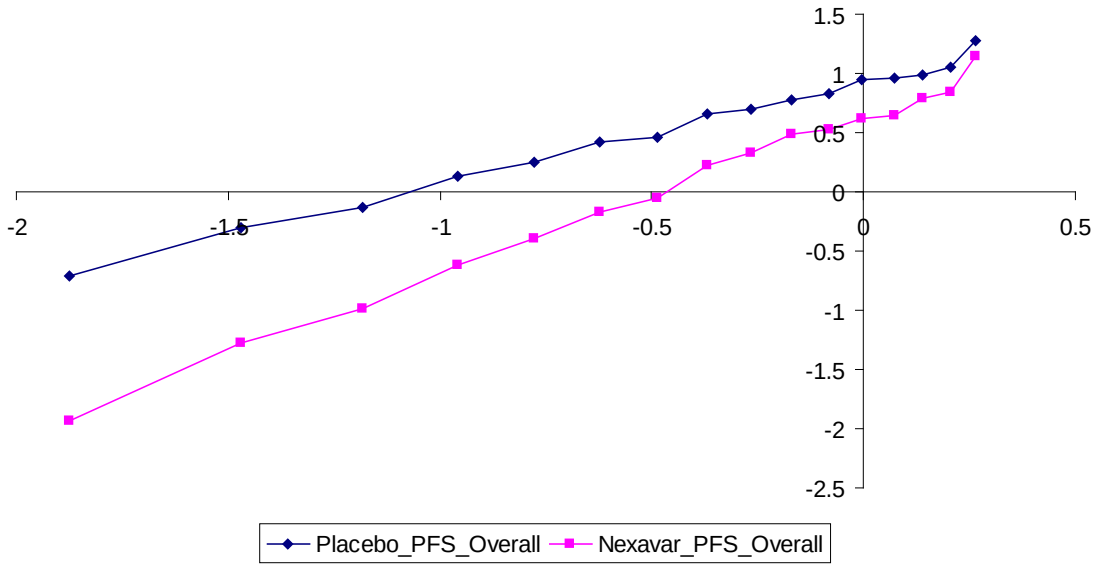
Bayer have previously stated that the use of hazard ratios does not necessarily provide an accurate reflection of the survival curves observed in the TARGET trial. The academic group in their response to Consultee comments (dated 30.06.08) acknowledged this. The figure below shows that modelling the PFS of Nexavar for the overall TARGET group by using the hazard ratio applied to a Weibull distribution does not provide a good fit to the data observed in the trial (HR as applied in the PenTAG model, HR=0.51).

Figure 5: Inaccuracy of using the HR in modelling Nexavar progression free survival



The application of the hazard ratio requires an assumption of proportional hazards. This has been tested, showing that the assumption of proportional hazards is not reasonable (see figure below).

Figure 6: Log-cumulative hazard plot to visually show proportional hazard assumption is not valid (e.g. PFS for the overall TARGET group)



Given that the applied HR approach has been proven to be invalid, Bayer believe that the BSC and Nexavar survival data should be modelled independently. This will improve the validity of the modelling undertaken as it will more closely match that data observed in the trial.

Therefore, a Weibull fit (for a consistent approach to that used within the academic model) has been applied to the survival data for both the placebo and Nexavar groups, using a technique similar to that used by PenTAG. As the Bayer and PenTAG models use different time units, the statistical parameters (shape and scale) are not directly transferable between the models. We have therefore provided the equivalent parameters that can be used when the Weibull function uses a monthly time estimate. Results from the model fitting are provided in the appendices.

Overall TARGET group

The Weibull parameters (shape and scale) used to provide curve estimation for the overall TARGET group are provided below.

Table 2: Overall group – Weibull parameters

Outcome	Weibull parameter	0.0767 year (28 day) – Bayer model		Equivalent monthly time estimate	
		BSC	Nexavar	BSC	Nexavar
Progression free survival	Shape	2.5281	1.9159	0.2876	0.0592
	Scale	0.8612	1.3506	0.8839	1.4090
Overall survival	Shape	0.5427	0.3808	0.0132	0.0122
	Scale	1.4663	1.4160	1.4905	1.3862

The associated Kaplan Meier curves and Weibull fitted curves for the overall TARGET group are shown below for PFS and OS.

Figure 7: Overall TARGET group – PFS

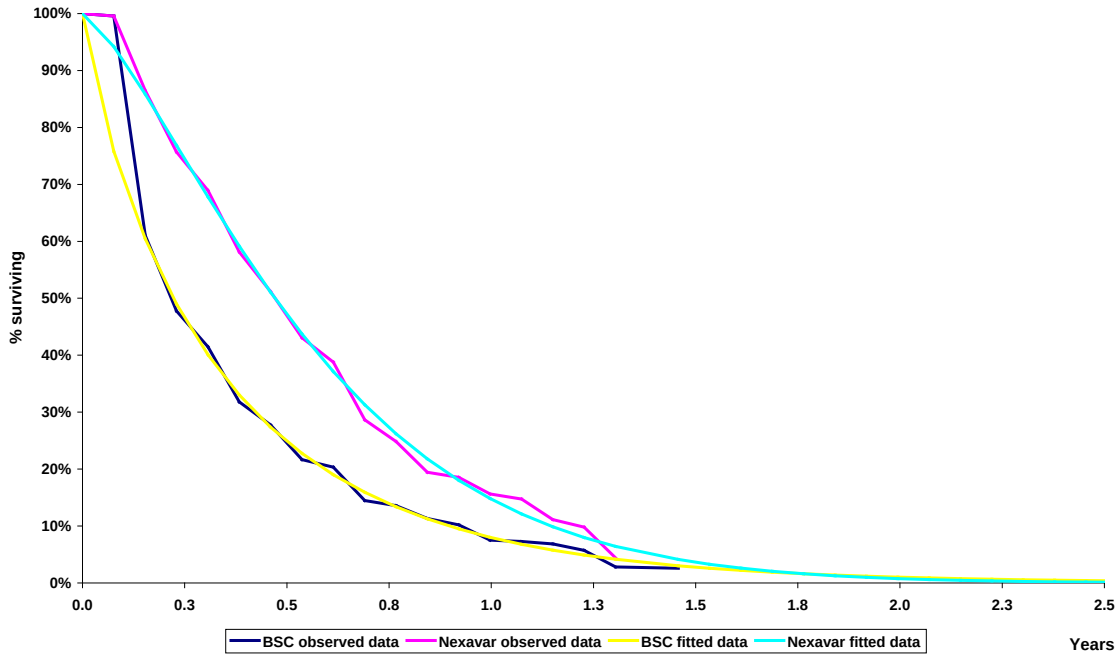
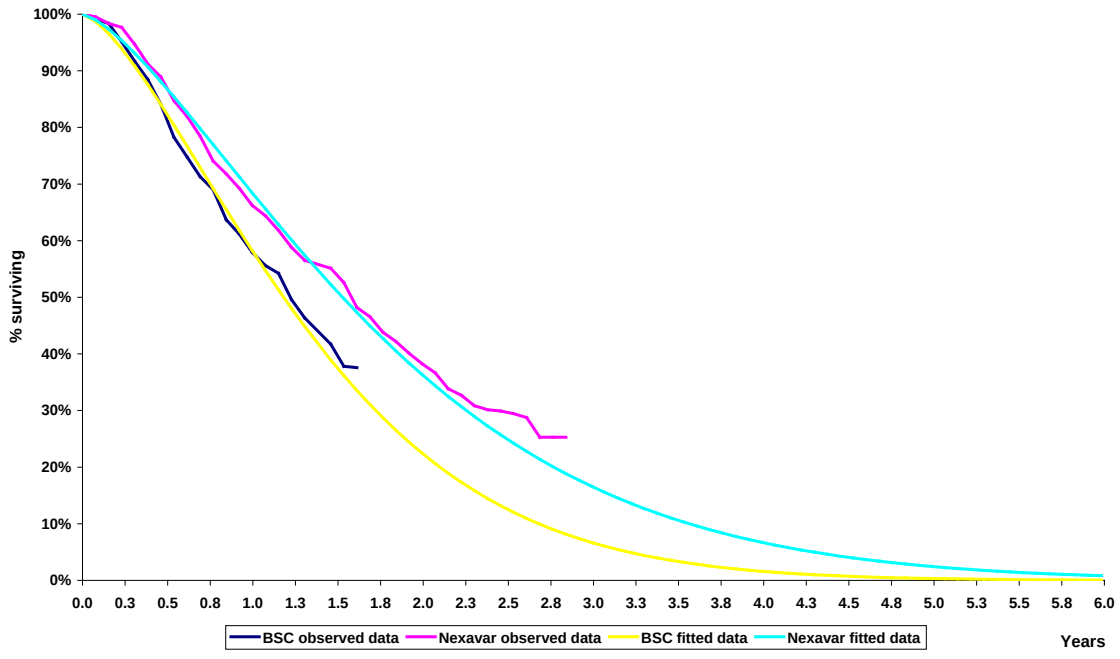


Figure 8: Overall TARGET group – OS



Prior cytokine group

The Weibull parameters (shape and scale) used to provide curve estimation for the prior cytokine subset are provided below.

Table 3: Prior cytokine group – Weibull parameters

Outcome	Weibull parameter	0.0767 year (28 day) – Bayer model		Equivalent monthly time estimate	
		BSC	Nexavar	BSC	Nexavar
Progression free survival	Shape	[redacted]	[redacted]	[redacted]	[redacted]
	Scale	[redacted]	[redacted]	[redacted]	[redacted]
Overall survival	Shape	[redacted]	[redacted]	[redacted]	[redacted]
	Scale	[redacted]	[redacted]	[redacted]	[redacted]

The associated Kaplan Meier curves and Weibull fitted curves for the prior cytokine patients are shown below for PFS and OS.

[redacted]

[redacted]

[redacted]

Cost assumptions

The cost assumptions used in the PenTAG analysis have been used in this revised analysis. As PenTAG used a 42 day Markov cycle, the associated cycle costs have been converted to a 28 day equivalent.

Table 4: Costs used within the model

Description	Bayer model (28 day cycle)	PenTAG model (42 day cycle)
PFS on treatment	£148.67	£223.00
PFS on BSC	£54.00	£81.00
PD	£290.00	£435.00
Cost of death	£0	£0
Adverse event (Nexavar)	£11 per patient	£11 per patient

The cost of a 28 day cycle of Nexavar is £2980.47 (112 tabs, 200mg). [redacted] The equivalent value of the first pack of Nexavar free of charge is £2980.47 and this is applied as a reduction in the overall drug cost within the model to estimate the cost-effectiveness of the patient access scheme.

All costs are discounted at an annual rate of 3.5%.

Utility assumptions

Utility values were assumed to be the same as those used in the PenTAG base case analysis for second line treatments.

Table 5: Utility values

Utility values	PenTAG values
PF	0.76
PD	0.68
Death	0.00

All QALYs are discounted at an annual rate of 3.5%.

Results

Overall group

The modelling of the overall TARGET group data, using curve fits to both placebo and Nexavar groups, estimates that Nexavar provides an additional 5.1 months of life compared to best supportive care, and an associated 0.280 QALYs. The mean number of packs of Nexavar is estimated at 7.4.

The tables below show the cost-effectiveness of Nexavar for the overall TARGET patient group. They include the cost-effectiveness estimates and the drug cost with and without the patient access scheme.

Table 6: Results for overall TARGET group (no patient access scheme)

	Nexavar	BSC	Difference	ICER
Costs (discounted)	£27,183	£3,919	£23,264	-
Drug cost (undiscounted)	£22,020	NA	-	-
QALYS (disc)	1.215	0.935	0.280	£83,206
Life years (undiscounted)	1.798	1.377	0.421	£55,272
PFS	0.568	0.371	0.197	
PD	1.230	1.006	0.224	

Table 7: Results for overall TARGET group (with patient access scheme)

	Nexavar	BSC	Difference	ICER
Costs (discounted)	£24,203	£3,919	£20,283	-
Drug cost (undiscounted)	£19,039	NA	-	-
QALYS (disc)	1.215	0.935	0.280	£72,546
Life years (undiscounted)	1.798	1.377	0.421	£48,191
PFS	0.568	0.371	0.197	
PD	1.230	1.006	0.224	

Prior cytokine group

The modelling of the post cytokine group data estimates that Nexavar provides an additional [redacted] months of life compared to best supportive care, and an associated [redacted]QALYs. The mean number of packs of Nexavar is estimated at [redacted].

The tables below show the cost-effectiveness of Nexavar for patients who have had prior cytokine therapy. They include the cost-effectiveness estimates and the drug cost with and without the patient access scheme.

Table 8: Results for prior cytokine group (no patient access scheme)

	Nexavar	BSC	Difference	ICER
Costs (discounted)	£27,070	£3,835	£23,235	-
Drug cost (undiscounted)	£21,736	NA	-	-
QALYS (disc)	[redacted]	[redacted]	0.325	£71,417
Life years (undiscounted)	[redacted]	[redacted]	0.496	£46,861
PFS	[redacted]	[redacted]	[redacted]	
PD	[redacted]	[redacted]	[redacted]	

Table 9: Results for prior cytokine group (with patient access scheme)

	Nexavar	BSC	Difference	ICER
Costs (discounted)	£24,089	£3,835	£20,254	-
Drug cost (undiscounted)	£18,756	NA	-	-
QALYS (disc)	[redacted]	[redacted]	0.325	£62,256
Life years (undiscounted)	[redacted]	[redacted]	0.496	£40,850
PFS	[redacted]	[redacted]	[redacted]	
PD	[redacted]	[redacted]	[redacted]	

Treatment pathway cost consequence analysis

Cost-effectiveness analyses of a new technology will typically look at a comparison against the most routinely available treatment practice it is likely to replace (e.g. Nexavar versus BSC in a second line setting). However, when considering several technologies which have different treatment line indications (as in a multiple technology appraisal) it may also be beneficial to the decision maker to examine overall treatment pathway costs and outcomes.

The analysis below presents a potential cost consequence analysis of different treatment pathways under consideration in the MTA. It specifically examines the following pathways from a first line advanced setting:

1. Current practice: cytokine therapy followed by BSC
2. Sunitinib as an alternative to cytokine therapy followed by BSC
3. Cytokine therapy followed by Nexavar followed by BSC.

As discussed in the second appraisal committee meeting, pathways 1 and 2 were examined closely, with particular attention applied to the overall survival of the cytokine only and sunitinib only groups. The cost consequence analysis below is based on:

1. The analyses undertaken by the NICE Decision Support Unit in their analysis of the appraisal committee's preferred assumptions for the sunitinib new data
    a. Overall survival and costs of a sunitinib only treatment pathway
    b. Overall survival and costs of a cytokine only treatment pathway
    c. Progression free survival and costs of cytokine therapy before progression
2. The analysis provided in this submission to estimate the additional survival and costs associated with Nexavar for patients progressing after cytokine therapy, including the patient access scheme.

Table 10: Overview of outcomes (in years) and costs of a single versus sequential treatment pathway

Treatment	Outcome (mean, years)	Cost
Sunitinib alone	3.13* (max est.)	£54,220^
IFN-α alone	2.29** (1.06 years as progression free)	£22,547^
IFN-α followed by Nexavar		
IFN-α component	1.06 progression free years***	£10,789^^
Nexavar component	[redacted] (prior cytokine group)	£24,089
Combined effect	[redacted]	£34,878

*DSU report that this could be an overestimate as it includes patients who receive subsequent therapies (Table 4, pg 58).
**DSU estimate of IFN-α (Table 4, pg 58).
*** DSU estimate of IFN-α progression free years (Table 4, pg 58)
^DSU estimate of total costs of sunitinib and IFN-α (no subsequent treatments, including BSC PD costs) (pg. 58)
^^DSU estimate of IFN-α prior to BSC (progressive disease) (pg. 58)

This cost-consequence analysis shows that similar outcomes may be achieved at lower cost using pathway three (cytokine therapy followed by Nexavar) than a sunitinib alone pathway (pathway 2).

Summary

There are less than 7,000 new patients per annum who are diagnosed with RCC each year. Those diagnosed with advanced RCC have a poor survival prognosis, with a median survival of between 6 and 12 months. Nexavar has been shown to substantially increase both progression free and overall survival in patients with RCC who have failed prior cytokine therapy. The economic analysis presented indicates that the mean increase in life is between 30% and 37% (equivalent to at least an additional 5 months of life). As a consequence, Nexavar should be considered by the Appraisal Committee as a medicine that meets the proposed NICE criteria for evaluating medicines for the end of life.

Considering the issues relating to the academic modelling assumptions, the new clinical data, and the patient access scheme, this revised reanalysis and new clinical data analysis shows that Nexavar's incremental cost per QALY is between £62,256 (for the prior cytokine group) and £72,546 (for the overall TARGET group).

The patient access scheme is currently being formalised and agreed with the Department of Health. In the UK, Nexavar currently has one of the lowest list prices in Europe. The patient access scheme, which provides the first pack free for patients with RCC commencing a course of Nexavar, confirms Bayer's commitment to ensuring that patients have access to the most innovative drugs.

Bayer are committed to both patients and clinicians having a choice in the management and treatment of renal cell carcinoma. The cost consequence analysis not only highlights that Nexavar at second line is a clinically relevant pathway for patients and clinicians, it also shows it provides a viable option to funders.

Appendices

[redacted]
Weibull fit results – overall group

[redacted]
28 day survival data – overall group

[redacted]

1 calendar month survival data – overall group

[redacted]

[redacted]

[redacted]

Weibull fits: overall TARGET group, progression free survival (based on a 28 day cycle translated into yearly equivalent)

BSC: PFS Estimate start at month 2

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9964
R Square	0.9928
Adjusted R Square	0.9923
Standard Error	0.0481
Observations	16.0000

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1.0000	4.4536	4.4536	1924.4244	0.0000
Residual	14.0000	0.0324	0.0023		
Total	15.0000	4.4860			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	0.9275	0.0152	61.0110	0.0000	0.8949	0.9601	0.8949	0.9601
X Variable 1	0.8612	0.0196	43.8683	0.0000	0.8191	0.9033	0.8191	0.9033

Nex: PFS Estimate start at month 2

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9973
R Square	0.9945
Adjusted R Square	0.9941
Standard Error	0.0657
Observations	16.0000

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1.0000	10.9528	10.9528	2539.3699	0.0000
Residual	14.0000	0.0604	0.0043		
Total	15.0000	11.0131			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	0.6502	0.0208	31.3296	0.0000	0.6057	0.6947	0.6057	0.6947
X Variable 1	1.3506	0.0268	50.3922	0.0000	1.2931	1.4081	1.2931	1.4081

Weibull fits: overall TARGET group, overall survival (based on a 28 day cycle translated into yearly equivalent)

BSC: Estimate start at month 4

Regression Statistics	
Multiple R	0.9962
R Square	0.9925
Adjusted R Square	0.9920
SE	0.0641
Observations	17.0000

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1.0000	8.1331	8.1331	1980.8857	0.0000
Residual	15.0000	0.0616	0.0041		
Total	16.0000	8.1947			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	-0.6112	0.0167	-36.6700	0.0000	-0.6467	-0.5756	-0.6467	-0.5756
X Variable 1	1.4663	0.0329	44.5071	0.0000	1.3960	1.5365	1.3960	1.5365

Nex: Estimate start at month 4

Regression Statistics	
Multiple R	0.9957
R Square	0.9915
Adjusted R Square	0.9912
SE	0.0793
Observations	31.0000

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1.0000	21.1870	21.1870	3369.9778	0.0000
Residual	29.0000	0.1823	0.0063		
Total	30.0000	21.3693			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	-0.9655	0.0153	-63.0101	0.0000	-0.9969	-0.9342	-0.9969	-0.9342
X Variable 1	1.4160	0.0244	58.0515	0.0000	1.3661	1.4659	1.3661	1.4659

Weibull fits: prior cytokine group, progression free survival (based on a 28 day cycle translated into yearly equivalent)

BSC: PFS Estimate start at month 2

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9961
R Square	0.9922
Adjusted R Square	0.9916
Standard Error	0.0495
Observations	16.0000

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1.0000	4.3399	4.3399	1771.4173	0.0000
Residual	14.0000	0.0343	0.0024		
Total	15.0000	4.3742			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	[redacted]							
X Variable 1								

Nex: PFS Estimate start at month 2

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9972
R Square	0.9944
Adjusted R Square	0.9940
Standard Error	0.0692
Observations	17.0000

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1.0000	12.6674	12.6674	2647.0540	0.0000
Residual	15.0000	0.0718	0.0048		
Total	16.0000	12.7392			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	[redacted]							
X Variable 1								

Weibull fits: prior cytokine group, overall survival (based on a 28 day cycle translated into yearly equivalent)

BSC: OS Estimate start at month 3

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9964
R Square	0.9928
Adjusted R Square	0.9924
Standard Error	0.0777
Observations	18.0000

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1.0000	13.3867	13.3867	2216.4611	0.0000
Residual	16.0000	0.0966	0.0060		
Total	17.0000	13.4834			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	[redacted]							
X Variable 1								

Nex: OS Estimate start at month 4

SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9965
R Square	0.9930
Adjusted R Square	0.9927
Standard Error	0.0713
Observations	31.0000

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1.0000	20.8274	20.8274	4099.3966	0.0000
Residual	29.0000	0.1473	0.0051		
Total	30.0000	20.9747			

	Coefficients	*SE*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	[redacted]							
X Variable 1								

28 day survival data – overall group

		PFS		OS	
Days	**Year**	**Placebo**	**Nexavar**	**Placebo**	**Nexavar**
0	0.0000	1.0000	1.0000	1.0000	1.0000
28	0.0767	0.9956	0.9956	0.9907	0.9954
56	0.1534	0.6105	0.8650	0.9838	0.9838
84	0.2301	0.4777	0.7570	0.9514	0.9768
112	0.3068	0.4147	0.6895	0.9167	0.9467
140	0.3836	0.3179	0.5814	0.8844	0.9121
168	0.4603	0.2774	0.5117	0.8404	0.8889
196	0.5370	0.2167	0.4307	0.7827	0.8473
224	0.6137	0.2032	0.3879	0.7480	0.8196
252	0.6904	0.1448	0.2866	0.7133	0.7849
280	0.7671	0.1358	0.2484	0.6902	0.7410
308	0.8438	0.1134	0.1944	0.6370	0.7179
336	0.9205	0.1022	0.1855	0.6116	0.6924
364	0.9973	0.0752	0.1563	0.5792	0.6624
392	1.0740	0.0730	0.1474	0.5561	0.6438
420	1.1507	0.0686	0.1114	0.5422	0.6184
448	1.2274	0.0574	0.0979	0.4960	0.5883
476	1.3041	0.0282	0.0439	0.4636	0.5652
504	1.3808	0.0260		0.4174	0.5513
532	1.4575			0.3781	0.5259
560	1.5342			0.3757	0.4819
588	1.6110				0.4657
616	1.6877				0.4380
644	1.7644				0.4218
672	1.8411				0.4010
700	1.9178				0.3825
728	1.9945				0.3663
756	2.0712				0.3385
784	2.1479				0.3269
812	2.2247				0.3084
840	2.3014				0.3015
868	2.3781				0.2991
896	2.4548				0.2944
924	2.5315				0.2875
952	2.6082				0.2528
980	2.6849				0.2528
1008	2.7616				0.2527

[redacted]

		PFS		OS	
Days	Year	Placebo	Nexavar	Placebo	Nexavar
0	0.0000	[redacted]	[redacted]	[redacted]	[redacted]
28	0.0767	[redacted]	[redacted]	[redacted]	[redacted]
56	0.1534	[redacted]	[redacted]	[redacted]	[redacted]
84	0.2301	[redacted]	[redacted]	[redacted]	[redacted]
112	0.3068	[redacted]	[redacted]	[redacted]	[redacted]
140	0.3836	[redacted]	[redacted]	[redacted]	[redacted]
168	0.4603	[redacted]	[redacted]	[redacted]	[redacted]
196	0.5370	[redacted]	[redacted]	[redacted]	[redacted]
224	0.6137	[redacted]	[redacted]	[redacted]	[redacted]
252	0.6904	[redacted]	[redacted]	[redacted]	[redacted]
280	0.7671	[redacted]	[redacted]	[redacted]	[redacted]
308	0.8438	[redacted]	[redacted]	[redacted]	[redacted]
336	0.9205	[redacted]	[redacted]	[redacted]	[redacted]
364	0.9973	[redacted]	[redacted]	[redacted]	[redacted]
392	1.0740	[redacted]	[redacted]	[redacted]	[redacted]
420	1.1507	[redacted]	[redacted]	[redacted]	[redacted]
448	1.2274	[redacted]	[redacted]	[redacted]	[redacted]
476	1.3041	[redacted]	[redacted]	[redacted]	[redacted]
504	1.3808		[redacted]	[redacted]	[redacted]
532	1.4575			[redacted]	[redacted]
560	1.5342			[redacted]	[redacted]
588	1.6110				[redacted]
616	1.6877				[redacted]
644	1.7644				[redacted]
672	1.8411				[redacted]
700	1.9178				[redacted]
728	1.9945				[redacted]
756	2.0712				[redacted]
784	2.1479				[redacted]
812	2.2247				[redacted]
840	2.3014				[redacted]
868	2.3781				[redacted]
896	2.4548				[redacted]
924	2.5315				[redacted]
952	2.6082				[redacted]
980	2.6849				[redacted]
1008	2.7616				[redacted]

1 calendar month (30.4 days) survival data – overall group

		PFS		OS	
Days	**Month**	**Placebo**	**Nexavar**	**Placebo**	**Nexavar**
0	0	1.0000	1.0000	1.0000	1.0000
30.4	1	0.9956	0.9956	0.9884	0.9954
60.8	2	0.5902	0.8650	0.9722	0.9838
91.2	3	0.4507	0.7164	0.9514	0.9676
121.6	4	0.4102	0.6827	0.9167	0.9306
152	5	0.2796	0.5792	0.8659	0.9051
182.4	6	0.2302	0.4599	0.8173	0.8797
212.8	7	0.2145	0.4262	0.7595	0.8311
243.2	8	0.1537	0.2889	0.7295	0.7965
273.6	9	0.1358	0.2664	0.6902	0.7525
304	10	0.1134	0.1944	0.6532	0.7179
334.4	11	0.1022	0.1855	0.6116	0.6924
364.8	12	0.0752	0.1563	0.5792	0.6624
395.2	13	0.0730	0.1474	0.5561	0.6277
425.6	14	0.0686	0.1114	0.5422	0.6045
456	15	0.0349	0.0462	0.4867	0.5722
486.4	16	0.0282	0.0439	0.4382	0.5606
516.8	17	0.0260		0.3827	0.5374
547.2	18			0.3781	0.5097
577.6	19			0.3757	0.4750
608	20				0.4519
638.4	21				0.4264
668.8	22				0.4079
699.2	23				0.3825
729.6	24				0.3547
760	25				0.3385
790.4	26				0.3269
820.8	27				0.3084
851.2	28				0.3015
881.6	29				0.2991
912	30				0.2944
942.4	31				0.2551
972.8	32				0.2528
1003.2	33				0.2527

[redacted]

		PFS		OS	
Days	**Month**	**Placebo**	**Nexavar**	**Placebo**	**Nexavar**
0	0	[redacted]	[redacted]	[redacted]	[redacted]
30.4	1	[redacted]	[redacted]	[redacted]	[redacted]
60.8	2	[redacted]	[redacted]	[redacted]	[redacted]
91.2	3	[redacted]	[redacted]	[redacted]	[redacted]
121.6	4	[redacted]	[redacted]	[redacted]	[redacted]
152	5	[redacted]	[redacted]	[redacted]	[redacted]
182.4	6	[redacted]	[redacted]	[redacted]	[redacted]
212.8	7	[redacted]	[redacted]	[redacted]	[redacted]
243.2	8	[redacted]	[redacted]	[redacted]	[redacted]
273.6	9	[redacted]	[redacted]	[redacted]	[redacted]
304	10	[redacted]	[redacted]	[redacted]	[redacted]
334.4	11	[redacted]	[redacted]	[redacted]	[redacted]
364.8	12	[redacted]	[redacted]	[redacted]	[redacted]
395.2	13	[redacted]	[redacted]	[redacted]	[redacted]
425.6	14	[redacted]	[redacted]	[redacted]	[redacted]
456	15	[redacted]	[redacted]	[redacted]	[redacted]
486.4	16	[redacted]	[redacted]	[redacted]	[redacted]
516.8	17	[redacted]	[redacted]	[redacted]	[redacted]
547.2	18		[redacted]	[redacted]	[redacted]
577.6	19			[redacted]	[redacted]
608	20			[redacted]	[redacted]
638.4	21				[redacted]
668.8	22				[redacted]
699.2	23				[redacted]
729.6	24				[redacted]
760	25				[redacted]
790.4	26				[redacted]
820.8	27				[redacted]
851.2	28				[redacted]
881.6	29				[redacted]
912	30				[redacted]
942.4	31				[redacted]