Additional analysis

1. Overview of the manufacturer submission

Following the FAD, the MS submitted a third version of the cost-effectiveness model. The model was modified to incorporate the proposed patient access scheme (PAS), i.e, that the cost for the drug for the first 5 cycles are financed by the NHS and the drug is then free of charge from cycle 6 onwards.

The PAS has been incorporated into the cost-effectiveness model by assigning a lower cost for cycle 6 onwards (only the cost associated with the administration of the drug and the cost of dexamethasone). A specific cost associated with the PAS was also included in terms of administration of claims forms (£8 per cycle) and staff training to the scheme (£12.30 per patient).

The base case submitted by the MS assumed that utility for the progressive free and progressed disease state is equal. The base case reported by the MS with and without PAS is presented below in Table 1 and Table 2 (Tables 5 and 6 in the MS, page 9 in the MS of the 1st October 2009).

Table 1: Base case incremental results without PAS

Technologies	Total costs (£)	Total LYG	Total QALY	Inc. costs (£)	Inc. LYG	Inc. QALY	ICER vs baseline (QALYs)	ICER inc. (QALYs)
Yondelis	[redacted]	1.529	0.98	[redacted]	0.819	0.535	50,747	50,845
Best Supportive care	1,965	0.710	0.449					

Table 2: Base case incremental results with PAS

Technologies	Total costs (£)	Total LYG	Total QALY	Inc. costs (£)	Inc. LYG	Inc. QALY	ICER vs baseline (QALYs)	ICER inc. (QALYs)
Yondelis	[redacted]	1.529	0.98	[redacted]	0.819	0.535	28,712	28,712
Best Supportive care	1,965	0.710	0.449					

Probabilistic Sensitivity Analysis (PSA) was conducted by the manufacturers to explore the uncertainty in the cost per QALY ratio. The cost-effectiveness acceptability curve (CEAC) for the base case is provided in Figure 1 (Figure 6, page 11 in the MS of the 1st October 2009). The Net benefit analysis is also presented in Table 3 (Table 8 in the MS, 1 October 2009)

The CEAC and net benefit analysis showed that trabectedin has a high probability of being cost-effective at a threshold of £30,000 per QALY gained.

Figure 1: Cost effectiveness acceptability curve

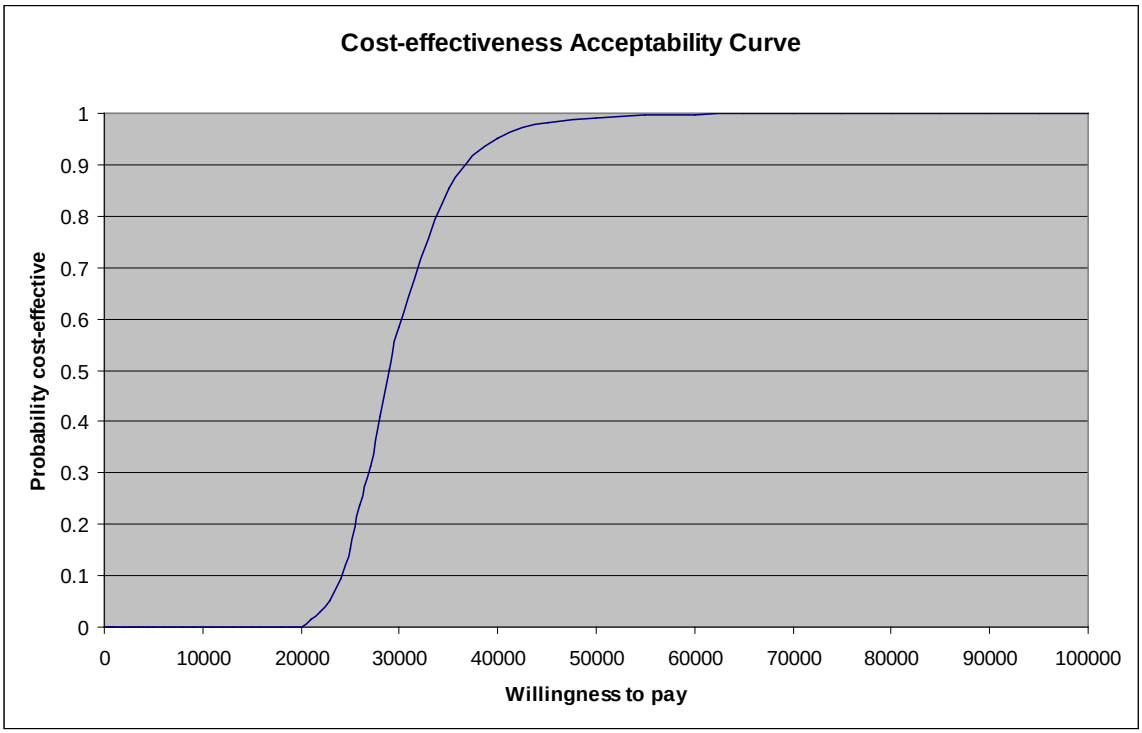

Table 3: Net Benefit Analysis

	Willingness to pay = £20,000		Willingness to pay = £30,000	
	Expected net benefit	**Probability CE**	**Expected net benefit**	**Probability CE**
Yondelis	£2,250.70	0.001	£12,030	0.585
Best Supportive Care	£6,988.47	0.999	£11,464	0.415

Other scenarios were also presented by the MS as described in previous submission. Results for these scenarios are shown in Table 4 (Table 9 in the MS, page 12 – 1 October 2009).

Table 4: Results of scenario analysis

Scenario	Without PAS	With PAS
Base case	£50,747	£28,712
Differential utility estimates for progression free and progressed disease	£56,884	£32,184
Differential utility estimate with linear decline in Best Supportive Care arm	£60,948	£34,484
Pooled analysis of non comparative phase II studies that include non-L-sarcoma patients.[1]	£45,646	£35,524

2. **Critique of the approach used**

The ERG judged that the analyses undertaken by the manufacturer to incorporate the PAS were appropriate.
Minor errors were also corrected as found in previous version of the cost-effectiveness model but had a minimal impact on the ICER:

- half cycle correction
- adverse event rate

The MS assumed for the base case that the utility for both progression free and progressed disease state were equal. Alternative scenarios were also presented. The ERG believed that the analysis with a differential utility for progression free and progressed disease state, adjusted for differences in the utility at baseline (i.e linear decline in the BSC arm) was a more appropriate base case.

The base case calculated by the ERG after revision of small errors in the model and assuming a differential utility for the progression free and progressed disease state (adjusted for BSC) is presented below in table 5.

Table 5: ICER calculated by the ERG

	Without PAS	With PAS
Base case	***£61,020***	***£34,538***
Pool analysis	***£55,343***	***£43,078***

[1] This do not include the adjustment for utility at baseline

The CEAC and net benefit analysis for the base case, with PAS are presented below. This analysis showed that trabectedin has a high probability of being cost-effective at a threshold of £40,000 per QALY gained.

Figure 2: Cost effectiveness acceptability curve

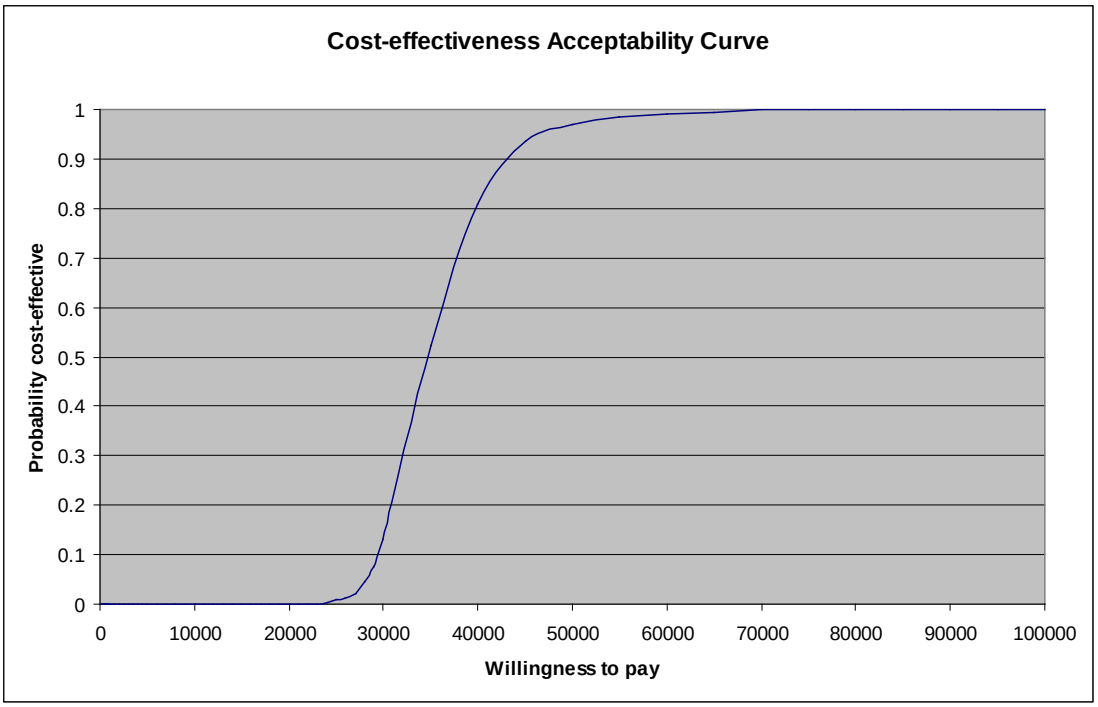

Table 6: Net Benefit Analysis

	Willingness to pay = £20,000		Willingness to pay = £30,000		Willingness to pay = £40,000	
	Expected net benefit	**Probability CE**	**Expected net benefit**	**Probability CE**	**Expected net benefit**	**Probability CE**
Trabectedin	-£1,139.44	0.000	£6,944	0.131	£15,028	0.807
Best Supportive Care	£5,396.60	1.000	£9,073	0.869	£12,750	0.193

3. Conclusion

The ERG found the method to incorporate the PAS appropriate, however believed that the base case selected by the manufacturer was inappropriate. The ERG believed a more realistic base case was the analysis with a differential utility for progression free and progressed disease state, adjusted for differences in the utility at baseline (i.e linear decline in the BSC arm) which corresponds to a cost per QALY ratio of £34,538. Results of the PSA indicate that trabectedin has a very high probability of being cost-effective at a threshold of £40,000.