DSU responses to the consultation renal cell

Consultee	Comments	DSU repsonse
Wyeth		No responses from DSU
Royal College of Nursing		No responses from DSU
Novartis		No responses from DSU
RCP		No responses from DSU
Pfizer	No provision of the DSU model	There is no DSU model. The analyses referred to are based on Pfizer's own model
	In the detailed cost-effectiveness analysis (table 2), the IFN-a estimate of PFS is written as 0.62 years. Does this refer to a capped treatment duration as in PenTAG's original analysis or the total PFS time? This distinction is important as the table could be considered misleading if this time is actually the treatment duration.	The DSU have only made changes to the PenTAG model as documented.
	The DSU argue that "*…the use of second line therapies in the UK NHS must be considered in order to identify the appropriate subgroups of patients."* Ordinarily, Pfizer would agree with this statement, however in the current context this position is problematic.	
	In challenging the use of the NPST analysis, the DSU also argue that excluding patients who receive a second line therapy will *"almost certainly produce inappropriate results since their reason for exclusion is inextricably linked to outcome i.e. death."* The validity of the NPST analysis could be questioned if the sub-group was not representative of the ITT population. However, a comparison of the demographics and patient characteristics between the NPST and ITT analysis has shown no systemic difference between the two analysis groups. In addition, the empirical PFS curves for the NPST analysis is comparable to the empirical PFS curves for the ITT population.	The apparent similarities in patient groups presented by Pfizer only allow conclusions to be drawn on the specific characteristics presented. This does not rule out the potential for systematic differences between the groups.Groups are being excluded on the basis of outcome i.e. conditioning on future events
	In their report the DSU present a cost effectiveness analysis based on the Committee's preferred assumptions using the Pfizer model and resulted in a cost per QALY of £49,304. The DSU regarded this result to be an underestimate of the ICER since the mean overall survival estimate used for sunitinib was based on the results from the overall ITT population.	

	The certainty with which this estimate is presented must be challenged. The DSU are using in their analysis a value of 2.29 years for IFN-a extracted from a modelled curve of the NPST analysis. When this curve is used to derive an estimate for sunitinib with in the Pfizer model, this data is challenged by the DSU for its 'lack of fit' to the empirical data. It would therefore appear to be adopting significant double standards to use without question the IFN-a curve in deriving the 'definitive' estimate of cost-effectiveness. Second, the calculation of ICERs is producing results which appear all over the place. For instance, in the comparisons between sunitinib and interferon, ICERs per QALY range from £28 546 all the way up to £104 715. Even just within Pfizer's calculations, the ICERs range from £28 546 to £72 003; and within those made by the DSU, using the PenTAG model, the range is from £49 304 to £104 715. Huge differences like this appear to be generated by what seem to be relatively small changes in the parameters of the underlying model. The results are anything but robust and are highly sensitive to variations in a number of factors. This does not inspire confidence in the results, especially since little is offered by way of explanation for the differences.	This DSU does not present this estimate as the "definitive" estimate. This is simply the result of applying the parameter values that the committee felt were preferred.
Kidney Cancer UK	No comment	
Roche	Table 1 (Baseline characteristics of censored patients) of Roche's ACD response appears to have been misinterpreted, as the DSU describes this population as patients that had <u>not</u> received post-protocol treatments. In fact, this population <u>did</u> receive post-protocol systemic treatments. Therefore to clarify, all patients were included to inform the PFS analysis and 269 patients (325 minus 56) contributed towards post-progression survival in the bevacizumab arm and 225 patients (316 minus 91) contributed towards post-progression survival in the placebo arm. Appropriateness of basing the analysis on the safety population	Noted

	The DSU commented that censoring within the trial would cause the mean observed dose to be an under estimate of the expected dose. This was based on the fact that not all patients had progressed at the point of un-blinding However a large proportion of patients had completed treatment by the point of un-blinding, hence we assumed the dosing data was sufficiently complete to provide a reliable estimate of the expected dose. We acknowledge though that due to censoring of some patients prior to completion of treatment this may underestimate the expected dose.	Noted
	However as acknowledged by the DSU, given the definition of the dose intensity figure of 88% quoted in the study paper (see section 1.2) the current AG model will be overestimating drug acquisition cost.	
	Estimated mean number of treatments and cumulative dose	Noted
BUG		No responses from DSU
Bill Savage		No responses from DSU
Bayer		No responses from DSU
Royal College of Pathologists		No responses from DSU