

Dear Chris

Thank you for sending the systematic review and economic evaluation assessment report for treatments for advanced renal cell carcinoma (RCC). Overall, we felt the report was a fair assessment of the technologies when based on the reference case outlined in the "Guide to the methods of technology appraisal" issued by NICE. Below are our comments on the report.

The economic model prediction for progression free survival (PFS) for sorafenib is higher than that shown in the TARGET study (Figure 32 versus Figure 2d in Escudier et al. NEJM 2007). Although the predicted median PFS is similar to that of the trial (180 days compared to 167 days, respectively), the overestimation of PFS post the 50th percentile results in an approximate overall mean PFS of 280 days compared to 220 days from the trial. You may want to check whether the application of a constant hazard ratio to the best supportive care arm is appropriate in this instance.

The researchers did not consider that patients without prior cytokine use as being unsuitable for cytokine therapy. However, TARGET was a randomised, placebo controlled trial; if a patient were deemed to be suitable for cytokine therapy, which was standard of care at the time of study commencement, it would have been unethical of doctors to risk their patient being randomised into a placebo arm. We acknowledge, however, your comments about these two sub groups not being defined a priori and the relatively low sample size of the no prior cytokine treatment sub group.

The report states that the primary objectives of medical interventions in advanced RCC is the relief of physical symptoms and maintenance of function as no treatments are currently available to cure advanced RCC (page 26). However, the attainment of increased progression free survival and life remains a primary objective of medical management.

For page 85, we can confirm that all overall survival analyses were on an intention to treat basis.

On page 140, you refer to Wyeth as the manufacturer submission. It should be Bayer plc.

Table 38 (page 144). A six week course of sorafenib would cost £3,757 rather than £3,767 as reported.

Kind Regards