Kidney Cancer UK

Support for kidney cancer patients and carers

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Dr Margaret Helliwel
Chair, Appeal Committee
National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
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Dear Margaret,

Re: Final Appraisal Determination: Everolimus for the second-line treatment of advance renal cell carcinoma

Kidney Cancer UK (KCUK) would like to appeal against the above FAD on the following ground:

Ground Two The Institute has formulated guidance which cannot reasonably be justified in the light of the evidence submitted.

The decision not to recommend Everolimus is based on the premise that patients receiving only best supportive care, following failure on first-line Sunitinib, live for an average of 10.8 months. This is not consistent with the evidence submitted, especially that from clinical experts who have reported that patients who are on best supportive care alone survive for something between 4 and 5 months. It is also very much in conflict with the results of a study by Di Lorenzo et alia (*Journal of Clinical Oncology*, 2009) which showed that even when patients were treated with Sorafenib following failure on first-time Sunitinib, they only survived for a median of 7.4 months. Given this, it is highly unlikely that untreated patients, on best supportive care alone, would live for longer, certainly not to the average of 10.8 months assumed in the NICE appraisal.

The effect of making an optimistic assumption of survival for patients on best supportive care, as in the NICE appraisal, is to reduce the difference in overall survival times as between Everolimus and best supportive care alone from 8.2 to 5.9 months. In the arithmetic calculation of the ICER, giving the cost per QALY, this reduction is absolutely crucial. All this is recognised in the FAD document produced by the NICE Committee itself. Paragraph 4.10 of the FAD document reads:

> [The Committee]... agreed that the incremental difference in overall survival was a key factor in determining the cost effectiveness. The Committee acknowledged comments received that overall survival with best supportive care... in exploratory analyses using the Weibull distribution (10.8 months) was higher than that seen in clinical practice, and that the estimate in the manufacturer's analysis (7.9 months) was more likely to reflect clinical practice.

Despite this, the FAD document says that an incremental difference in overall survival for Everolimus versus best supportive care of 5.9 months is 'more plausible' than the one of 8.2 months derived in the manufacturer's analysis. But one looks in vain for some support for this assertion.

Elsewhere in the document (paragraph 3.30) it is reported that reducing the estimate of overall survival on best supportive care alone from 10.8 months to 6.0 months lowers the ICER to £39,724 per QALY, well below the upper-bound benchmark of £50,000 now used in the appraisal of clinically effective, end-of-life medicines such as Everolimus. In view of the extreme sensitivity of the ICER to differences in overall survival—over which there is much dispute—the fact that the mean probabilistic ICER of £51,700 is only slightly above the £50,000 might reasonably suggest that its estimation lies within a fairly narrow margin of error around the upper bound.

Conclusion

KCUK is strongly of the opinion that, for the purpose of second-line treatment of advanced renal cell carcinoma, Everolimus should be recognised, not just as clinically effective but cost effective as well. It wishes this appeal to proceed at an oral hearing.

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PS Could you please acknowledge receipt, to my home address given above.