Cancer Research UK response to NICE's consultation on the Appraisal Consultation Document: Bevacizumab, sorafenib, sunitinib and temsirolimus for the treatment of advanced and/or metastatic renal cell carcinoma

Summary

Cancer Research UK welcomes the opportunity to respond to this consultation. We are very disappointed with NICE's decision to reject these four kidney cancer drugs.

We have outlined our major concerns in more detail below, briefly that:
- NICE's appraisal process is not appropriate for all types of cancer drugs;
- NICE needs to consider how it can reconcile making recommendations so clearly at odds with current clinical opinion;
- these decisions from NICE impact on the public's trust in the NHS and are a potential future threat to medical research in the UK.

We also asked the public to share their views on this decision with us. We believe that it is time now for a government-led public debate about how the NHS is funding treatment and how it can best serve patients' needs now and into the future. Failure to engage with the public could have serious consequences in terms of our ability to raise money and fund research within the UK in the future.

Our position

We are disappointed at NICE's view that although these drugs are clinically effective, their high price means that they are not considered to be value for money for the NHS. These drugs have shown a small but definite improvement in an illness where there are few alternative treatments. If this decision stands it will be very frustrating for cancer patients and their clinicians.

This decision once again raises questions about whether NICE's system of appraisal is appropriate for all types of drugs. It is often difficult to get unequivocal research data in rarer cancers, such as metastatic kidney cancer, which have a small patient population. Although we understand that NICE often has to make difficult decisions, in this case there is a clear separation between what NICE finds to be a valuable treatment and clinical opinion. Action is needed to bring these two positions closer together.

We believe that NICE needs to look at whether it is making appropriate allowances to compensate for the lack of uncontaminated large scale trials in these areas. However, we do accept that not all responsibility lies with NICE. We also need to look at the way that pharmaceutical companies are charging the NHS for drugs, and to ensure that further results are sought and that larger trials are carried out. If NICE is to do its job

properly then we need to consider what responsibility it should be taking for both of these related issues.

Specific concerns

The Appraisal Committee has asked us to respond to four specific questions:

i) Do you consider that all of the relevant evidence has been taken into account?

While we accept that all the relevant published data has been taken into account, we are concerned that NICE's methodology is not sufficiently flexible to provide recommendations based on the existing clinical evidence.

Metastatic renal cell carcinoma is one of the less common cancers. This low prevalence limits the number of people available for entry into clinical trials. This small population pool is further complicated by the fact that in the majority of cases there are no other treatment options for this type of cancer. Interferon is not considered by clinical colleagues to be an effective alternative treatment for advanced metastatic renal cancer—and in fact is only suitable for use in 30% of patients, leaving 70% untreated.

ii) Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?

The combination of the above factors leads to significant limitations in the trials presented to NICE. We do not consider that this evidence, which has played a major part in NICE's decision not to recommend the drugs for use in the NHS, is a basis from which reasonable interpretations of cost-effectiveness can be drawn. Where patients were crossed-over from the control into the treatment arm estimations about overall survival cannot be extrapolated effectively enough to make them suitable for NICE's cost-effectiveness calculations. For this reason we think NICE should reconsider whether a more appropriate approach is needed in this situation.

We also understand that the National Cancer Research Institute Clinical Study Group (CSG) on renal cancer has some significant concerns about comparisons with interferon (IFN) in this appraisal. We support the CSGs request that QALY analyses within the appraisal are redone using more appropriate comparative data for IFN with expert oncology input. We also call on NICE to give more consideration to two concerns outlined to us by the CSG that:

1. comparisons with IFN in the appraisal are not appropriate, as data taken from the control arm of the bevacizumab plus IFN vs. IFN alone are considered to over-estimate the effectiveness of IFN and are not in line with clinical experience;
2. emerging results presented at the American Society of Clinical Oncology (ASCO) meeting in June this year, provide evidence that the benefit for interferon in the sunitinib vs. interferon trial was inappropriately enhanced by the high number of patients receiving active second line treatments.

iii) Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

For the reasons given above, we do not consider the provisional recommendations sound or suitable for the preparation of guidance to the NHS.

We take the council of the renal CSG that bevacizumab, sorafenib, sunitinib and temsirolimus should be recommended for use in metastatic renal cell carcinoma patients on the NHS. We know that the CSG does not make such recommendations lightly.

iv) Are there any equality related issues that may need special consideration?

We strongly believe that the lack of a suitable alternative treatment for the majority of patients with metastatic renal cell carcinoma should mean that these patients in particular should not be denied treatments that have shown in trials to be clinically effective. The small patient population for this type of cancer also raises questions about equality, given the impact that this may have on the way these drugs are priced by the manufacturers under our current system of pricing—we think it unfair that these patients should be penalised because of this.

General comments

As proponents of the NHS, we understand that the reality of having a publicly-funded healthcare system that provides treatments for all members of the population who need it free at the point of delivery often means making difficult choices about those treatments that should be included in the NHS package of care. And we think that NICE is well placed to inform these difficult decisions.

NICE is well regarded globally, as a leader in the field of health technology assessment. NICE's methodology has developed over its lifetime to be responsive to the needs of society. However, we believe that cancer still challenges this methodology and that a more flexible approach needs to be developed to ensure that we continue to support innovation and give patients in the UK access to those drugs which we already see benefiting patients elsewhere in the world.

We also welcome recent efforts by NICE to reach agreements with the pharmaceutical industry which has resulted in otherwise unapproved drugs becoming available on the NHS. We would welcome a greater role for NICE in agreeing appropriate prices for new medicines. If, in the course of the appraisals, NICE consider a drug to be cost-ineffective at the current price, they should also be able to calculate at what price the drug would become cost-effective. This could then form the basis of negotiation with the manufacturers. We do hope that NICE is taking every opportunity to negotiate with manufacturers aimed at similar resolution in the case of these four kidney cancer drugs.

What the public think

Cancer Research UK received an significant response to our call for the public to share their views on this decision with us. Over 100 people submitted comments through our online science blog (http://scienceblog.cancerresearchuk.org/), to a prescribed email address , or alongside a Guardian online article (http://www.guardian.co.uk/commentisfree/2008/aug/07/cancer.health)

by Cancer Research UK's Chief Clinician, Professor Peter Johnson.

The responses were not wholly surprising. However some salient points outlined below should be of concern to NICE, the Department of Health, politicians and those with a desire to see the science base in the UK continue to prosper.

The need for public debate

It is clear that the public are bewildered by much of the current debate in the media about which drugs are available on the NHS, why, and how, these decisions are made. As expected with this sort of exercise, respondents were mostly unsupportive both of NICE's decision and the organisation as a whole. However, there is clearly sufficient understanding both of the need to manage the limited budget of the NHS and the role that the various stakeholders play in this process. More than ever we believe that it is both timely and essential that the Government, and NICE, engage the public in a debate about healthcare funding in the UK.

There was much comment about the following areas, in particular:

1. The role of NICE

Respondents expressed anger towards NICE in respect of this recent decision. It is clear that many people are confused about the extent of NICE's influence and their responsibilities and how independent they are of Government control. People feel powerless and frustrated.

2. The cost of cancer drugs in the UK

A number of respondents questioned why cancer drugs are too expensive to get through NICE's cost-effectiveness requirements. It appears that the public can't understand why the NHS doesn't have more negotiating power with the pharmaceutical companies. Many expressed the concern that the pharmaceutical companies are holding NICE to ransom.

3. Funding for cancer drugs in the UK

A clear message from the public is that they cannot understand why these cancer drugs are available and being successfully used in other European countries and not the UK. Reference was particularly made to those countries with a lower GDP, including new EU member states, and considered to be in a greater financial predicament than the UK.

The ABPI estimate that UK per capita spending on cancer medicine currently stands at just 60% of the European average. The figures advise that, by 2006 rates, additional investment of £403m a year would be necessary for the UK to have parity with the existing average per capita expenditure on cancer medicines in 11 comparable countries. In addition uptake of innovation is slow, with major cancer medicines still being prescribed in the UK at under two-thirds of the European average, five years after licensing.

Many respondents expressed strong opinions on how they considered the NHS should be better spending their money to ensure sufficient funding for cancer drugs.

Loss of public support for medical research

The UK is in an enviable and unique position of having a public that is enthusiastically supportive of medical research. Every year people donate in their millions to medical research charities across the UK. Cancer Research UK alone has over 2 million regular givers. Last year we raised £420 million, mostly from individual donors.

A report by the European Cancer Research Mangers Forum in 2006 found that public cancer research spend in Europe is evenly balanced between charitable and government organisations with 47% and 53% of spend, respectively. In comparison, USA government organisations are the dominant source of cancer research funding with 96% of all funds coming from ten federal funders.

We were therefore very concerned that a significant majority of those submitting comments raised questions about the point of giving money to research when the resulting medicines were not being made available to patients in the NHS. Loss of public support, both financially and in terms of willingness to participate in research, could be very serious for UK science.

Conclusion

We hope that NICE reconsiders its preliminary decision not to recommend bevacizumab, sorafenib, sunitinib and temsirolimus for use in metastatic renal cell carcinoma patients on the NHS. We also hope that NICE takes this opportunity to review whether its current process is suitable for all cancer drugs and how flexibility can be introduced into the appraisal process to ensure that patients can get access to drugs where they are likely to benefit.

This appraisal also clearly raises some broader questions relating to whether patients in the UK are getting fair and equal access to new medicines on the NHS. We will also be sharing these thoughts with the Secretary of State for Health and await his response on these important issues.