Comments on NICE appraisal consultation document:

Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia

[redacted]

Has all of the relevant evidence been taken into account?

The relevant evidence at the date of publication of the appraisal has been taken into account. However there are of course current studies being undertaken which will report in the next few months.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

The complex interpretations by the ERG regarding cost effectiveness are outside my area of knowledge. With regard to the clinical effectiveness, I believe that the REACH trial demonstrated an advantage of Rituximab, Fludarabine and Cyclophosphomide (FCR) over FC (and in fact the Committee has accepted this – para4.5, p17). In general, on reading results from many clinical trials, Rituximab is seen as 'adding value' to existing chemotherapy combinations.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

Para1.1 I am pleased that the use of Rituximab with FC is being recommended for relapsed CLL patients. It might be reasonable with the current state of knowledge to withhold R if refractory to F (although it is worth pointing out that in the REACH trial even those with p53 deletion did better with FCR than those on FC alone) or relapsed within 6 months.

However restricting the use of Rituximab for those who had prior treatment with the antibody seems bizarre and flies in the face of general medical consensus as I understand it, whereby if you have a reasonable period remission with one drug regimen then usually that regimen will be repeated a second time.

As is pointed out in the document, treatment with FCR for first line has only really begun this year. In general patients will not require 2nd line treatment for the next 2 – 3 years. At that point (unless the Committee reconsiders the evidence) there will be a bizarre situation whereby patients will be only able to consider FC, chlorambucil, going on a clinical trial or stem cell transplant. Campath (alemtuzumab) is not approved in England by NICE and in the current economic climate it may prove more difficult to access this drug.

Para 1.2 I feel the evidence for the use of Rituximab in combination with other chemotherapy agents is somewhat weaker, although I understand that some studies will be reported at the end of this year(2009) at ASH conference. I hope that NICE will be considering the use of Rituximab with other chemotherapy combinations in the near future.

Para 1.3 I am concerned at the possiblity of suddenly withdrawing Rituximab from a patient who is in the process of a cycle of treatment. There will be guidance on this from clinicians, but I am certainly aware that not continuing with a particular sequence of treatment (unless there were serious side effects or the patient was not responding) can be very deleterious to the patient, causing future refractory disease or the disease accelerating. It would be invidious if a patient was having an excellent response after say 4 cycles of treatment, the consultant deciding that two more cycles would be worthwhile and having to stop that successful treatment because of the NICE recommendations.

Aspects of the recommendation that need particular consideration to ensure avoid unlawful discrimination against any group of people on the grounds of gender, race disability, age, sexual orientation, religion or belief.

As CLL is a disease that predominantly affects those over 65 this age group may perceive that the guidance denying them access to Rituximab as being related to their age. In general as CLL is a rarer cancer it is quite difficult for this group of patients to have a powerful lobby promoting their needs.

Proposed date for review of guidance

I would hope that the review of this technology takes place before Oct 2012. If new studies concerning the technology are published then the review date should be brought forward.