Rituximab for the maintenance treatment of follicular non-Hodgkin lymphoma following response to first-line chemotherapy

Response from the Lymphoma Association, Leukaemia CARE and Leukaemia & Lymphoma Research to the ACD

On behalf of the patients likely to be adversely affected by any decision not to approve first line maintenance treatment, we wish to express our strong concern at the committee's change of position. We understand the need to seek additional information from the manufacturer and are grateful to have the opportunity to comment on the ACD. However, we are surprised that this has resulted in a reversal of a previously held position, particularly as the input from three commissioning bodies seems to have tipped the balance and outweighed the views of clinical experts and patients.

Government policy to improve cancer outcomes in England
At a time when the government has a clear policy to save 5,000 lives from cancer and acknowledges that this country's survival rates are worse than other European countries, with less spending on cancer drugs, it is important that NICE makes decisions that support the overall commitment to improving outcomes.

This treatment has been approved and is funded in the US, Canada, Germany, Spain, Israel and Scotland. If it is not funded, patients in England and Wales will be disadvantaged and England will be out of step with common practice in other countries.

Choice
By refusing to fund the treatment, NICE would be depriving clinicians and their patients of choice based on clinical judgement, personal circumstances and preferences.

Not all patients will want to have maintenance therapy after first line treatment but many will as it is very hard for people to live with a life-threatening disease that they know will return, possibly within 18 months to two years. The significant extension of time to next treatment is a huge plus for patients. As has been acknowledged, maintenance rituximab is much easier to tolerate than chemotherapy and delivers much longer periods free from debilitating and toxic treatment regimens.

There may be family circumstances that make it imperative for a patient to know they will remain disease free for as long as possible – for example, a woman with follicular lymphoma in her late sixties who is the main carer for her husband. Or a parent who has children taking important exams and who needs to remain well.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
We do not believe that the provisional recommendations are a suitable basis for guidance to the NHS. For more mature data to be available, patients would have to wait

years. When there is so much positive evidence of the benefit to patients, it is unethical to delay implementation. The equitable solution would be to authorise the use of the drug immediately with a condition that data on long-term survival is accrued. NICE should set a date for review of the drug at the earliest point at which there is sufficient data.

There are several references, notably in the PCT comments, to the PRIMA trial having closed early and suggesting that there is a shortage of long-term data proving an ongoing benefit. We understand from the manufacturer's submission that "the study was stopped because the independent DSMC (in Sept 2009) declared that the study had reached its primary endpoint at the pre-specified interim analysis." It would have been unethical, and a violation of patients' consent, to have continued the trial beyond this endpoint. This issue has highlighted a disparity between two regulatory bodies which in effect amounts to the moving of goalposts. It is not acceptable that patients should suffer as a result of an inconsistent approach between two regulators.

We also question the focus on overall survival. In our view this is not as important as progression free survival in this condition and is difficult to assess because of the relapsing and remitting course of the disease. The key factor for patients with follicular lymphoma is to delay the time before they will need to have more chemotherapy because the chemotherapy is a more toxic treatment and also becomes less effective with each successive treatment. For older patients in particular, the ability to tolerate successive regimes of chemotherapy reduces and therefore time gained through longer remissions is extremely important. This is particularly the case for patients not eligible for high dose therapy and transplant which may be a treatment option for younger patients.

Conclusion

We recognise that NICE has a difficult role and that the issues are complex. In an ideal world, there would be longer-term data but it would be highly unethical to deny patients access to first line maintenance rituximab when the evidence for its positive benefit in giving patients longer progression free survival is so clear. Pending longer-term data, we urge NICE to approve funding and to review this decision in a few years time.

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