Response to the appraisal consultation document
Pixantrone monotherapy for treating relapsed or refractory aggressive non-Hodgkin lymphoma

The Lymphoma Association notes the conclusions drawn by the Appraisal Committee not to recommend pixantrone within its marketing authorisation.

This decision will no doubt be a disappointment to people who don't respond well to, or relapse after, two standard courses of lymphoma treatment. People in this situation, as the committee acknowledged, face an incredibly difficult future. The treatment options currently used in England and Wales have no stronger or more conclusive evidence to support their use than the technology under review. . This makes it difficult to draw any useful conclusions, including the conclusion not to approve pixantrone, which may still be a useful drug and does appear to be quite well tolerated and acceptable to patients.

Specific comments and observations

3.44 The difficulty in finding appropriate utility weights for this multiply treated group of patients emphasises the need for manufacturers and researchers to include QoL data in study design. Patients should not be left feeling that decisions that potentially affect their treatment at such a difficult stage of their lives are being based on assumptions, divided opinions and lack of evidence.

3.47 Although it may not make much difference to the ICER, the manufacturer's exclusion of costs associated with treating leukopenia and thrombocytopenia seems appropriate as costs for febrile neutropenia and neutropenia not causing fever are included and it is unlikely that additional costs would be incurred for patients having reductions in their other white blood cell counts. It is also very unlikely that patients with thrombocytopenia would need a platelet transfusion.

4.8 Clearly it is important to complete this trial to confirm benefit in patients previously treated with rituximab as soon as possible as this is an important consideration and highly relevant to current UK clinical practice.

4.11 and 4.15 We are very concerned at the decision that "the sub group with aggressive B-cell lymphoma confirmed by central independent review was the most appropriate for decision-making" rather than restricting the assessment to third- and fourth-line treatment. The marketing authorisation excludes treatment at fifth-line and it is unlikely that patients who have been so heavily pre-treated would achieve a

meaningful response. It would be more reflective of clinical practice to exclude treatment at fifth and subsequent line from the sub-group for decision-making.

Conclusion

The Lymphoma Association fully supports evidence-based practice. At the same time, we are aware that there is a huge unmet need for this patient population and that clinicians and their patients are currently making difficult treatment decisions based on limited and scant clinical evidence. We had therefore hoped that the only licensed treatment currently available for this difficult and badly served patient population would gain NICE approval.

It is regrettable that PIX301 does not more closely match current clinical practice in England and Wales where all patients receive rituximab as part of their first and second line therapy, and that the appraisal committee did not feel that the trial results were sufficiently powered to enable approval.

There is a clear and pressing need for further research to assess whether pixantrone would be effective for patients who have already received the standard NHS treatments. While it is encouraging that the manufacturer is continuing with research as required as part of the marketing authorisation, it may not prove easy to recruit the number of patients needed to achieve sufficiently powered trials to demonstrate positive effect clearly enough to achieve NICE approval.

Taking a pragmatic viewpoint, it is therefore disappointing that a series of weaknesses in PIX301 have undermined the validity of what had appeared to be promising data. This means that the only licensed treatment for this patient population will not be available and leaves a large unmet need, with patients either receiving treatments for which there is no clinical evidence or palliative care.

We urge the manufacturer and NICE to seek a pragmatic way forward to improve the treatment options for this badly served group of patients.

Lymphoma Association
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