Appendix D – Clinical specialist statement template

Rituximab for first line maintenance treatment of follicular non-Hodgkin's lymphoma

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Dr Helen McCarthy

Name of your organisation: Royal College Pathologists

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? √
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? √
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- other? (please specify)

What is the expected place of the technology in current practice?

Approximately 80 % follicular lymphoma patients present with stage III or IV disease. Previous studies have demonstrated no survival benefit in treating asymptomatic patients with advanced disease. Patients are therefore managed with an expectant approach with active surveillance until they develop symptoms requiring treatment. The prognosis and management also varies with histological grade (WHO classification grades I, II, IIIA and IIIB).

For those patients with advanced disease (clinical stage II-IV) requiring treatment, immune-chemotherapy (Rituximab-chemotherapy) is the standard of care. Rituximab has been successfully combined with CVP, CHOP and fludarabine based combinations (Marcus, Blood 2005, Hiddenmann Blood 2005, Forstpointner Blood 2004, Zinzani JCO 2004). R-CVP (Rituximab, cyclophosphamide, vincristine, prednisolone) is recommended in NICE guidance TA110 (September 2006) as a front line treatment and is therefore the combination routinely given in the UK. An NCRI study (PACIFICO) has recently opened for older patients comparing first line induction with R-CVP to attenuated FCR (fludarabine, cyclophosphamide and rituximab) followed by rituximab maintenance. This represents an alternative treatment option for eligible patients.

Although follicular lymphoma is readily treatable it is characterised by a recurring and remitting course. At first relapse the standard treatment in the UK is R-chemotherapy followed by rituximab maintenance for two years as recommended in NICE guidance TA137 (February 2008)

Rituximab should generally be administered in the secondary care setting particularly during initial treatment. This should be in a day ward or in-patient setting where nursing staff are familiar with administration and managing infusion reactions.

The advantages and disadvantages of the technology

Following the publication of the NICE guidance TA137, 2nd line maintenance rituximab has been widely used in the UK. It is well tolerated in all patient groups. The most common side effects are a minor increase in infections. Other reported rare side effects include late onset neutropenia and progressive multifocal leukoencephalopathy.

The phase III International PRIMA trial, comparing 2 years of Rituximab maintenance versus observation following R-chemo, showed that disease progression occurred in 18 % rituximab group compared to 34 % observation group after a median follow up of 25 months. These findings were presented at the American Society of Clinical Oncology in June 2010 by Dr Gilles Salles and form the basis for this NICE application. Progression free survival is an appropriate outcome to consider as the follow up is currently too short to assess differences in overall survival.

The UK population is an aging population and the incidence of follicular lymphoma increases with age. Older patients, particularly those with co-morbidities are under-represented in clinical trials and less likely to tolerate the more intensive salvage combination chemotherapy regimens. Maintenance rituximab is well tolerated in older patients (>70 years).

In considering the cost benefit of rituximab maintenance it is important to factor in the cost saving of avoiding other salvage treatments and associated costs such as repeat biopsies and hospital admissions etc.

Any additional sources of evidence

ASCO PRIMA presentation as above

Implementation issues

Maintenance rituximab in second remission is already widely used and chemotherapy centres throughout the UK are experienced in administration and have adequate facilities. If maintenance rituximab is approved for earlier use in the disease history i.e. in first remission there may be a modest overall increase in patient numbers but those receiving rituximab in second remission will also reduce.