31 July 2005

Health Technology Appraisal
Pemetrexed disodium for the treatment of malignant pleural mesothelioma

General comment:

It is vital to remember that malignant pleural mesothelioma is a fatal, occupational disease that is increasing in incidence in the UK. Until recently there was little interest in the disease and very few patients were offered any active treatment. The current MSO1 trial compares ASC (active symptom control) vs navelbine + ASC vs MVP + ASC. The choice of the 2 chemotherapy regimes was based on the results of 2 very small Phase II studies. However, the fairly recently published Phase III International randomised trial of cisplatin and pemetrexed vs cisplatin alone (450+ patients) demonstrated a significant benefit for the combination therapy. Pemetrexed is now the only licensed drug for this tumour type. The median survival advantage of approximately 3 months is similar to the results for non small cell lung cancer which have led to the widespread introduction of palliative chemotherapy for that disease.

Comments on the Final scope:

In "Background" the scope mentions that surgery may be indicated for a small proportion of patients whose disease is at stage I or II. It then mentions that such patients have a much longer survival rate. This may well reflect the fact that the patients chosen for surgery are fitter, and with good prognostic factors, and would have survived longer anyway. Invariably those patients also received other treatments, e.g. chemotherapy or radiotherapy or both. There is no evidence that supports the use of surgery as a single treatment modality in malignant pleural mesothelioma. Surgery is a palliative treatment with the potential for significant toxicity.

In "Standard comparators", vinorelbine and MVP are included as they are the chemotherapy arms in the current MSO1 trial which examines the effect of chemotherapy vs active symptom control. It is worth remembering, as mentioned above, that these chemotherapy regimes were selected on the back of small Phase II clinical trials – patient numbers were much smaller than the number who received single agent cisplatin in the randomised Phase III trial.

Comments on the Technology Assessment report (final version 6 June 2005):

Unfortunately there are some inaccuracies in this report.

In Section IV (Background) on page 12, it mentions that the number of people diagnosed with mesothelioma each year will increase over the next 20 years to more than 3000 cases per year in Britain (ref 8). A very recent publication (Hodgson et al, British Journal of Cancer 2005) predicts a peak in the UK of between 1950-2450 annual cases sometime during 2011-2015. The authors then predict a rapid decline. This paragraph should be updated.

On page 13, in the section entitled "The Technology", the original Phase III paper published by Vogelzang should be quoted with regards the survival benefit of 3 months for cisplatin and pemetrexed vs cisplatin alone (Vogelzang et al, Journal of Clinical Oncology Vol 21, No 14, 2003, pages 2636-2644).

Further down there are important inaccuracies. Vitamin B12 is administered intramuscularly, NOT intravenously, and the injection is only necessary every 9 weeks whilst on pemetrexed chemotherapy. The sentence on corticosteroids could be simplified to "dexamethasone premedication is administered orally for 3 days with each cycle, commencing the day before treatment."

I am not convinced that dyspnoea (shortness of breath) is a common side effect of the chemotherapy – this is more likely to represent progression of the disease rather than an adverse effect of the drugs.

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