NICE HEALTH TECHNOLOGY APPRAISAL:
Pemetrexed disodium for the treatment of malignant pleural mesothelioma

Comments on behalf of the Royal College of Physicians, Royal College of Radiologists, the Association of Cancer Physicians and the Joint Collegiate Council for Oncology

The benefit of Pemetrexed in mesothelioma and presumably its licensing authorisation is primarily based on one randomised trial.

In this study 456 patients with malignant mesothelioma were randomised to treatment with either cisplatin alone or cisplatin combined with Pemetrexed (1). The patients treated with the combination had a median survival of 12 months versus 9.3 months for patients treated with cisplatin alone. This result was statistically significant p=0.02.

However, before this treatment is widely adopted as the standard and recommended treatment for the palliation of advanced malignant pleural mesothelioma, we would make the following observations:

1. The effect on quality of life of the Pemetrexed / cisplatin combination has so far only been reported orally and published in abstract form.

   Data from a UK pilot study conducted by the MRC in which patients with mesothelioma were randomized to Active Symptom Control (ASC) with or without chemotherapy have shown that palliation of chest pain, breathlessness anorexia and sweating attacks can be obtained in 28%, 11%, 44% and 67% respectively with ASC alone compared with 52%, 28%, 51% and 63% with ASC plus chemotherapy (2).

   These data have led UK investigators to continue recruitment of patients with malignant mesothelioma into the MSO1 study; a trial that randomises patients between ASC alone, and ASC with chemotherapy. Chemotherapy is either with vinorelbine or the mitomycin, vinblastine, cisplatin (MVP) combination.

2. The comparator of single agent cisplatin used in the Pemetrexed trial referred to above, would not be considered as a standard treatment in the UK; in the ongoing MSO1 trial the chemotherapy options are single agent Vinorelbine or the MVP combination based on Phase II trials of these regimes (3, 4).

3. It is conceivable that any improvement in quality (and even quantity) of life, seen in the Pemetrexed cisplatin study may be due in part to avoiding the excess toxicity which can arise when cisplatin is used in higher doses as single agent.

   The overall mortality whilst on treatment for patients receiving the combination treatment was 6.2% versus 3.6% for single agent cisplatin. It was however shown that

the toxicity and the death rate for the Pemetrexed combination could be reduced by vitamin supplementation.

4. The Pemetrexed / cisplatin combination has not been compared with other standard platinum containing combinations including drugs such as gemcitabine, mitomycin vinorelbine, or doxorubicin, all of which have documented activity in mesothelioma.
5. The improvement in median survival of 2.8 months is lower than has been shown to be acceptable to most patients with non-small-cell lung cancer when considered against the toxicity of cisplatin based chemotherapy (5).
6. Pemetrexed is expensive at around £1,800 a cycle; patients in the study received a median of 6 cycles. This is considerably more expensive than MVP, vinorelbine, gemcitabine with cisplatin or doxorubicin with cisplatin. To our knowledge no cost effectiveness data have been reported for the Pemetrexed combination or any other chemotherapy regimen.

Conclusions

Therefore, before the Pemetrexed / platinum combination is recommended we feel that the following information would be required.

1. Detailed Quality of Life data from the randomised trial.
2. Cost benefit analysis of Pemetrexed / cisplatin, “MVP” and single agent vinorelbine in the treatment of Mesothelioma.
3. Ideally results of the MSO1 trial though data from this study is unlikely to be available during the time course envisaged.
4. Canvassing the views of patients and carers.

References:

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