



Title	Pemetrexed Disodium for the Treatment of Malignant Pleural Mesothelioma: A Systematic Review and Economic Evaluation
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Aim

To assess the clinical and cost effectiveness of pemetrexed disodium combined with cisplatin in treating unresectable pleural mesothelioma in chemotherapy-naïve patients.

Conclusions and results

One randomized controlled trial (448 patients) comparing pemetrexed and cisplatin to cisplatin alone met the inclusion criteria. Pemetrexed combined with cisplatin showed a 2.8-month gain in median survival compared with cisplatin alone in an intention-to-treat (ITT) population. During the trial, increased reporting of severe toxicity in the pemetrexed arm led to a change in the protocol to add folic acid and vitamin B12 supplementation to therapy. For fully supplemented patients (n=331), the hazard ratio for median survival in favor of pemetrexed plus cisplatin was comparable (0.75), but of borderline significance between treatment arms (p=0.051). The inclusion criteria restricted recruitment to those with a Karnofsky performance status of 70 or greater (equivalent to ECOG/WHO 0 or 1 scales more widely used in the UK). Quality of life scores using the Lung Cancer Symptom Scale demonstrated significantly greater improvement for pain and dyspnea for patients in the combination group compared with those in the cisplatin group. In the ITT population, the incidence of serious toxicities with pemetrexed plus cisplatin was higher compared with cisplatin alone. However, the grade 3/4 toxicities of the combination arm, particularly leucopenia, neutropenia, and diarrhea, were found to improve with the addition of vitamin B12 and folic acid. Published economic literature was limited. The economic evaluation conducted by the study (and that submitted by the manufacturer) suggested that pemetrexed is unlikely to be considered cost effective at conventionally accepted thresholds in the UK for all patients, mainly due to the high cost of pemetrexed compared with cisplatin. These findings were better for some patient subgroups, eg, especially for fully supplemented (FS) patients with good performance status

(o/1) and advanced disease (AD). The findings seem robust. The estimated cost-effectiveness results were for the FS population, incremental cost-effectiveness ratio (ICER) per quality-adjusted life-year (QALY) gained = GBP 59 600; for the FS with AD population, ICER per QALY = GBP 47 600; for the FS with performance status o/1 population, ICER per QALY = GBP 49 800; and for the FS with performance status o/1 and AD population, ICER per QALY = GBP 36 700.

Recommendations

The new therapy addressed here demonstrates extended life expectancy and palliation. The small gain in absolute benefit must be weighed against the benefits of effective palliative care. Also, the limited benefit was at the expense of considerable toxicity. Economic evaluations suggest that pemetrexed is not cost effective at conventional thresholds in all patients. Cost effectiveness was better in some patient subgroups, eg, patients with good performance status and advanced diseases, where ICER per QALY is estimated at GBP 36 700. Given the few patients with mesothelioma, the budget impact of pemetrexed is unlikely to exceed GBP 5 million per year.

Methods

Electronic databases were searched up to May 2005. The systematic review followed accepted guidelines. Economic information from the manufacturer of pemetrexed was also assessed. This comprised 2 sections, each using an economic model. One of the models was reformulated to separately explore economic performance.

Further research/reviews required

Research is needed into the optimum chemotherapy for patients with mesothelioma and a clear definition of what constitutes best supportive care.