Submission from CancerBACUP to NICE Appraisal Committee on pemetrexed disodium for the treatment of malignant pleural mesothelioma

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CancerBACUP welcomes the opportunity to contribute to the appraisal of pemetrexed disodium for the treatment of malignant pleural mesothelioma. As the leading specialist provider of independent information on all types of cancer, CancerBACUP has regular contact with people living with mesothelioma and those caring for them.

CancerBACUP received 389 enquiries between 2003 and 2004 about mesothelioma and its treatment.

CancerBACUP believes that everyone with cancer should be offered the most effective and appropriate treatment, based on the available evidence and the patient's own wishes and preferences. We believe that:

- Patients should have access to the most effective treatments appropriate to them as individuals;
- Patients should be able to choose – in partnership with their oncologist – the treatment that is likely to suit them best in terms of relative benefits and side-effects;
- The impact of treatments on patient's quality of life, as well as length of life, should be given full consideration by the Appraisal Committee.

We urge the Appraisal Committee to recommend that pemetrexed disodium should be made available for patients for the treatment of malignant pleural mesothelioma.

Living with mesothelioma

An estimated 1,700 people in the UK are diagnosed with mesothelioma each year. Mesothelioma is a cancer of the mesothelium. The mesothelium is a thin membrane that lines the chest and abdomen and surrounds the organs in these areas. The lining around the lungs is called the pleura and in the abdomen it is known as the peritoneum.

Mesothelioma of the lining of the lungs (pleural mesothelioma) is much more common than mesothelioma in the peritoneum, and for every person with peritoneal mesothelioma there will be about 12 people who have pleural mesothelioma.

Pleural mesothelioma

The pleura has two layers: the inner (visceral) layer, which is next to the lung and the outer (parietal) layer, which lines the chest wall. The two layers of the pleura are usually in contact and slide over each other as we breathe. The membranes produce fluid, which allows them to slide over each other easily.

When a mesothelioma develops in the pleura (pleural mesothelioma), the delicate membranes thicken and may press inwards on the lung. Fluid may also collect between the two layers of the pleura and this is known as pleural effusion.

Causes

Up to 9 out of 10 cases of mesothelioma are caused by exposure to asbestos. When asbestos is disturbed or damaged, it releases tiny fibres that can be breathed into the lungs and cause inflammation, a build up of scar tissue and sometimes cancer.

Mesothelioma does not usually develop until 10-60 years after exposure to asbestos and for this reason it is often difficult to discover the exact cause. As mesothelioma develops so slowly it is estimated that by 2020 approximately 3,000 people will be diagnosed with mesothelioma each year. The number of people who develop the disease will then start to reduce each year.

Symptoms

Mesothelioma often starts as many tiny lumps (nodules) in the pleura, which may not show up on scans or x-rays until they are quite large. The main symptoms of pleural mesothelioma are pain in the chest and breathlessness. Some people also notice their voice becomes hoarse and they have a cough that does not go away.

Pleural mesothelioma can cause other general symptoms such as loss of appetite, weight loss and tiredness.

Staging of mesothelioma

There are several staging systems for pleural mesothelioma. An outline of a commonly used system is described below:

Localised malignant mesothelioma

Stage 1 *– The cancer cells are found in the pleura near the lung and heart or in the diaphragm or the lung*

Advanced malignant mesothelioma

Stage 2 *– The cancer has spread beyond the pleura to lymph nodes in the chest*
Stage 3 *– The cancer has spread into the chest wall, the centre of the chest, the heart, through the diaphragm or abdominal lining and in some cases into nearby lymph nodes*
Stage 4 *– The cancer has spread to distant organs or tissues*

Treatment

Surgical resection is possible in a minority of patients but fewer than 15 percent of these patients live beyond five years. For those who are not treated with curative resection, the median survival duration when receiving best supportive care alone has been reported as six months, whereas the median survival time of 337 patients in 11 multicentre chemotherapy trials was seven months. Treatment with radiation therapy has been equally disappointing, in part because of difficulties in irradiating disease while avoiding toxicity to normal lung, cardiac and spinal cord tissues.

Pemetrexed disodium

Pemetrexed is a multitargeted antifolate and works by slowing the growth of tumours.

CancerBACUP argues strongly that NICE should recommend that pemetrexed disodium in combination with cisplatin are available on the NHS for the treatment of patients with mesothelioma in accordance with their licences as it can extend survival.

A phase III study in malignant pleural mesothelioma compared treatment with cisplatin and pemetrexed with cisplatin alone. Median survival time was at 12.1 months for the combination arm compared to 9.3 months for cisplatin alone. This was a statistically significant difference[1]

As with survival duration, the median time to progressive disease was significantly longer for patients who received pemetrexed and cisplatin as compared with patients who received cisplatin alone (5.7months compared to 3.9 months). [2]

The median time to treatment failure was also significantly longer in the pemetrexed/ cisplatin arm than in the control arm.[3]

[1] Journal of Clinical Oncology, Vol 21, No 14 (July 15), 2003: pp 2636-2644
[2] Ibid
[3] Ibid

Adverse effects experienced with pemetrexed

Although pemetrexed can improve survival, trial data suggests that patients receiving pemetrexed in combination with cisplatin can experience severe toxicity. [4]

In patients receiving cisplatin as a single agent, severe toxicity was uncommon. In the pemetrexed/cisplatin arm grade 3/4 neutropenia and grade 3/4 leukopenia were the most common haematologic toxicities.

However, patients who received vitamin supplementation had a notable reduction in haematologic toxicity, specifically grade 3/4 neutropenia and leukopenia. Overall improvement in severe toxicity has been observed in other pemetrexed studies because vitamin supplementation has become a standard of pemetrexed therapy. [5]

Declaration of interest

CancerBACUP has received sponsorship from Lilly, the manufacturer of pemetrexed disodium for several publications and projects.

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[4] Ibid
[5] Niyikiza C, Baker SD, Seitz DE, et al: Homocysteine and methylmalonic acid: markers to predict and avoid toxicity from pemetrexed therapy. Mol Cancer Ther 1:545-552, 2002