and especially those with palmoplantar pustular psoriasis. Prospective clinical studies are needed to see whether stopping smoking makes any difference to the course of established psoriasis. Quite possibly people might be more willing to change their habits because of a current and socially debilitating skin disorder than because of long term risks of cancer and ischaemic heart disease.

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Palliative chemotherapy for advanced non-small cell lung cancer

Time to reappraise its role

Lung cancer was one of the first cancers to be treated with chemotherapy, back in the late 1940s.¹ Yet today lung cancer (other than small cell tumours) remains the Cinderella of cancer medicine, left behind as chemotherapy is increasingly used for other neoplasms. Palliative radiotherapy can provide good relief of localised symptoms for patients with inoperable disease.² Sooner or later, however, most patients develop metastatic disease, and the message they receive remains, "I'm sorry, there's nothing further we can do." A recent survey of chest physicians, surgeons, and oncologists in Britain showed chemotherapy was offered to only 8% of patients with non-small cell lung cancer and actually given to only 5% (Cancer Research Campaign, data on file, 1991). Is this nihilism justified?

Advanced non-small cell lung cancer certainly lacks the chemosensitivity—sometimes dramatic—of the small cell type, but it is by no means completely resistant to drugs. Response rates of 30-40% are consistently reported with modern chemotherapy regimens,³ and more intensive schedules have achieved responses in over half of patients.⁴ These results may seem modest, but they are beginning to approach the response rates seen in advanced breast cancer, where for many years palliative chemotherapy has been widely accepted as having a place. Preoperative chemotherapy for marginally operable non-small cell lung cancer provides a similar comparison. Here response rates of almost 70% have been reported, with complete resolution of histological changes in 14-19% of patients who had subsequent surgery⁵; these results are again similar to those of preoperative chemotherapy for early breast cancer, both in our own experience and elsewhere,⁷ and argue against non-small cell lung cancer being considered resistant to drugs.

The impact of chemotherapy on survival in patients with advanced non-small cell lung cancer has been better studied than that for many other common cancers. In an overview of seven randomised trials comparing chemotherapy with best supportive care three showed a survival benefit in favour of chemotherapy, with a similar but non-significant trend in survival in all the others; the overview analysis confirmed a benefit in favour of chemotherapy.⁸ The effect was not large—the average improvement was around three months—but even this is more than has been shown for some "standard" treatments such as chemotherapy for advanced breast cancer and palliative radiotherapy in non-small cell lung cancer.

In this disease, which is so difficult to treat, neither encouraging response rates nor even improved survival necessarily imply real clinical benefit. The key question is whether chemotherapy makes patients with lung cancer feel better. Cancer specialists have taken far too long to start asking that question, which may partly explain why attitudes to chemotherapy for this disease remain so negative in Britain. A few years ago our unit began—belatedly—to measure not just the objective response seen on the x ray film but the subjective symptomatic response. The results surprised us. We found that around 70% of patients treated with a simple schedule of moderate dose chemotherapy reported relief of symptoms including malaise, dyspnoea, cough, and pain.⁹ We have subsequently confirmed our results in a much larger series of patients, and others have reported similar findings.¹⁰

I suspect there is another problem too—unease at the perceived high costs of palliative chemotherapy in so common a cancer. Such concern is understandable, but it may well be based on a false premise. Chemotherapy represents only a small fraction of the total cost of care for a patient with advanced cancer; in one study of patients with breast cancer it was less than 10%.¹¹ A trial in Canada showed that chemotherapy in non-small cell lung cancer not only prolonged survival compared with best supportive care alone but actually reduced the overall costs of care.¹² This was achieved because chemotherapy (which is relatively cheap) reduced the number of inpatient days (which are very expensive) required for control of symptoms. Too much is said about the allegedly high costs of palliative chemotherapy, and not enough careful research is done into the overall cost effectiveness of such treatment.

Chemotherapy still has a long way to go in non-small cell lung cancer. Its value as adjuvant treatment after surgery and as primary treatment for locally advanced disease before radiotherapy is being investigated.^{13 14} For patients with advanced and metastatic disease the best way forward is through further clinical trials looking at new drug schedules and using as end points cost effectiveness and validated quality of life measures (such as the quality of life questionnaire developed by the European Organisation for Research on the Treatment of Cancer).

Clinicians must continue to use their common sense: chemotherapy is inappropriate for frail or chronically ill patients with low performance status. But there is now good

evidence for its place in the control of symptoms and the prolongation of survival. Palliative chemotherapy, carefully supervised by accredited cancer specialists, should no longer be denied to selected patients with inoperable non-small cell lung cancer.

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The European Medicines Evaluation Agency

The new agency can be an important catalyst for drug innovation in Europe

The European Medicines Evaluation Agency (EMA) is to be set up in London—a decision that has been wanted and welcomed by the pharmaceutical industry. Many companies are tired of the long delays and the extra work required in submitting applications to 12 or more different regulatory agencies in the separate states of the European Union. As the life cycle of new drugs becomes steadily shorter, long delays—a year or more has been common in Germany—have become burdensome. A single registration procedure could lead to new products being introduced simultaneously in the 12 different European markets.^{1,2}

The agency will have a twin track procedure: one for centralised community licensing of biotech and innovative drugs and the other for mutual recognition licenses from member states with binding arbitration. The centralised system will have economic as well as health advantages by promoting the free circulation of medicinal products as well as reinforcing the protection of public health.

There could be other gains, too. Patients should benefit from the setting of clearer and higher standards in clinical trials and on the definitions of risk. They should also get quicker access to new and effective drugs. Doctors could benefit in terms of improved ability to deliver patient care and opportunity to take part in the development of new drugs. Above all the agency could give a clear signal that the industry in Europe should be trying to do more in terms of innovation.

The EMA could be a success, but it will need to face some problems. In reviewing some applications itself and also working with regulatory agencies it will have to develop a uniform approach with common standards. Unless it has the staff and the executive drive to make high quality decisions coherently and quickly, much of the initial goodwill might be dissipated. It will have to establish its authority early if the 12 member states are to accept its decisions without questioning them.

One high risk topic will be exclusive to the agency: the approval of biotech drugs. It will need to set procedures not only for their initial approval but also for continuing review and surveillance once the drugs come into general use. Evidence may be needed on precisely how the drugs are actually used—some approved for one indication may come to be used for others, with unexpected side effects. The agency might also work closely with the United States Food and Drug

Administration to agree a common framework for the evaluation of biotech drugs.

Some decisions should be made very soon. For example, there is a strong case for appointing the chief executive and some core staff so that they can have time to develop procedures based on a review of past experience in other agencies. There would then be time for consultation with existing national agencies and the industry in building a new consensus. The likely future economic impact of the agency is also uncertain; it may have a part to play in promoting competition and in reviewing market developments. Possibly the clinical licensing function might be developed across the European Union while economic and reimbursement issues could still be concentrated at the national level. The agency has been given no explicit role in terms of reviewing the costs and effectiveness of drugs but it will need to ensure that reimbursement issues are not used as ways of impeding the introduction of new and innovative drugs.

If, as we hope, the European Medicines Evaluation Agency succeeds it will provide a powerful new stimulus to the location of drug development within Europe. It starts with goodwill and with logic on its side: but success will come only if the agency is seen to be willing to identify the contentious issues and to take effective action to deal with them.

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- 2 Huttin C, Bosanquet N, eds. *The prescription drug market*. Amsterdam: Elsevier/North Holland, 1992.

Blank pages in the international edition of the *BMJ*

Some copies of the international edition of the *BMJ* for 8 January were printed with blank pages. Any reader who has one of these journals and would like a replacement should contact the journal sales department, *BMJ*, BMA House, Tavistock Square, London WC1H 9JR (phone: 071 383 6055, fax: 071 383 6402). We apologise for this lapse, caused by a fault on the printing press.