Pergamon

European Journal of Cancer, Vol. 33, Suppl. 1, p. S1, 1997

Printed in Great Britain
0959–8049/97 $17.00+0.00

PII: S0959-8049(96)00323-1

Introduction

P.E. Postmus

Department of Pulmonology, Free University Hospital, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

MANY PEOPLE die from malignant disease and a large part of health care budgets is used for treatment and care of these patients.

There have been considerable improvements in treatment during the last two decades. The results of surgery have been improved, especially by better peri- and postoperative care. Technical facilities and new imaging techniques have resulted in better planning of radiotherapy and have led to use of higher doses without increased toxicity. A better insight into the mechanism of action of the available chemotherapeutic agents and their side-effects has led to the intensification of chemotherapy in many situations. Another step forward has come with the introduction of haematopoietic growth factors with initially a reduction of myelotoxicity, then subsequently a further intensification of chemotherapy. Also a better understanding of side-effects of combined modality treatment i.e. radiotherapy and chemotherapy, has resulted in improved survival in a number of tumours.

Despite this ongoing process of improved therapy and care, the currently available therapies fail in many patients. For these patients, it is necessary to find new options in the management of cancer. During the satellite meeting at ECCO8 in Paris, '*New Options in the Management of Cancer Patients: Experience with Gemcitabine and DAB_{389}-fusion Toxin*', results of such new approaches were demonstrated in a number of tumour types.

Jean Nichols reported on the first results of a novel approach. The team at Seragen has developed a fusion toxin targeted against interleukin-2 (IL-2) receptors. This was used in a phase I/II study in patients with IL-2 receptor expressing malignancies. Toxicity was rather mild, whereas the response rate in cutaneous T-cell lymphoma was impressive and warrants further evaluation in phase III studies (ongoing). Also, responses were reported in non-Hodgkin's lymphoma and phase II studies are planned.

The efficacy of the nucleoside analogue, gemcitabine, in one of the most common tumours, non-small cell lung cancer (NSCLC), is already proven. In the paper by Thatcher and Hopwood, studies with gemcitabine in NSCLC are reviewed and common findings are summarised. Dancey and le Chevalier review the difficult situation of treating NSCLC. After a long dispute, the time has now come to introduce wide-scale use of chemotherapy in all stages of NSCLC. For the higher stages (IIIb and IV), the main purpose still is palliation. However, with the introduction of new drugs such as gemcitabine, the balance between side-effects and quality of life has now shifted towards the use of chemotherapy. A new challenge is to improve the beneficial effects of gemcitabine further by combining it with other active drugs. In the report by Mosconi and associates, the combination of gemcitabine with cisplatin is evaluated. Both response rate and survival are high and look favourable in comparison with 'so-called' standard combination regimens. Application of this combination in earlier stage patients, in combination with radiotherapy and surgery, may open perspectives of prolonged survival and even cure. For palliative therapy, negation of the favourable toxicity profile of gemcitabine by the very toxic drug cisplatin should be avoided. Further attempts to combine it with less toxic drugs are needed to enhance its value for palliative use.

Another striking example of the value of gemcitabine for palliation is its effect in patients with pancreatic cancer. Despite a low objective response rate, the degree of symptomatic improvement ('clinical benefit') is much higher (see paper by Burris and Storniolo).

Bladder cancer is also frustrating to treat. Although standard combination chemotherapy produces a good response rate, long-term survival is disappointingly low. Stadler and associates demonstrated that gemcitabine has a response rate of $> 25\%$. Combining it with other new and active drugs, such as paclitaxel and ifosfamide, is a logical way to proceed.

For ovarian cancer and breast cancer, chemotherapy is standard treatment and most patients that are candidates for studies evaluating new drugs are heavily pretreated. Despite this, response rates around 20–25% with mild toxicity were reported with gemcitabine in both tumour types. Further studies of gemcitabine in combination with drugs with known activity are ongoing or planned.

In conclusion, gemcitabine has been evaluated in several solid tumours. The toxicity profile of the drug is favourable. It has activity in a number of chemo-resistant tumours. Furthermore, activity was demonstrated in tumours relapsing after first-line chemotherapy. The time has come to evaluate gemcitabine in combination chemotherapy regimens and, subsequently, in randomised studies as first-line treatment.

Correspondence to P.E. Postmus.