Introduction

Maurizio Tonato
Divisione di Oncologia Medica, Ospedale Policlinico, Monteluce, Perugia, Italy.

In the continuing search for new drugs active in cancer treatment, some new agents such as gemcitabine, paclitaxel, docetaxel, vinorelbine and the camptothecin derivatives represent a positive step forward. Gemcitabine, a nucleoside analogue with novel metabolic properties and mechanisms of action, was the subject of an international meeting at the 7th European Conference on Clinical Oncology (ECCO) in Jerusalem in November 1993. Information from that symposium is reported in this supplement.

Originally tested as part of the antiviral screening programme, gemcitabine demonstrated a therapeutic ratio better suited to the clinical needs of oncology, and was then screened as part of the Cancer Research Programme at Lilly Research Laboratories. Unlike other nucleoside analogues, gemcitabine showed extraordinary activity against murine solid tumours and human xenografts. Gemcitabine exerts its cytotoxic effect by (1) inhibiting ribonucleotide reductase, a key enzyme in the formation of nucleotides for normal DNA synthesis; and (2) competing with deoxycytidine triphosphate for incorporation into DNA which leads to DNA chain termination. This activity is enhanced by several unique and multiple mechanisms which may be responsible for the prolonged retention of the active metabolite seen in clinical trials.

The results of a number of phase II trials in different cancers are reported in which gemcitabine was administered at doses of 800–1250 mg/m^2 as a 30 min infusion, in a schedule once a week for 3 weeks followed by a week of rest. In particular, the experience with single-agent gemcitabine in non-small cell lung cancer (NSCLC) is reviewed. Response rate, confirmed by an independent Oncology Review Board, and low toxicity place gemcitabine among the most active drugs in this disease. In three multicentre studies involving over 300 patients, independently validated response rates were consistently 20% with a starting dose of gemcitabine of 900 mg/m^2/wk × 3. An experience evaluating the influence of gemcitabine on control of symptoms in NSCLC patients also appears encouraging, as is the role of gemcitabine in cisplatin-resistant ovarian cancer, and as second-line chemotherapy in breast cancer.

Phase I–II trials show a favourable side-effect profile, with a low incidence of adverse events usually associated with cytotoxic drugs, namely myelosuppression, nausea, vomiting and alopecia. Because of its unique mechanism of action and its non-overlapping toxicity with other active agents, gemcitabine is an attractive candidate for trial in combination with other cytotoxic agents and also with radiotherapy.

Particularly important is the value of the combination of gemcitabine with cisplatin in NSCLC, and the preliminary results of such a trial are presented. In addition, an economic assessment of gemcitabine monotherapy compared with a combination regimen in NSCLC makes gemcitabine valuable in reducing the costs of cancer treatment and of supportive care. Due to the importance of this point the issue deserves wider and thorough examination in pharmaco-economic studies.

Further investigation of this promising drug is required so that its role in cancer therapy can be fully defined and its efficacy optimized, both as a single agent and in combination therapy.

Correspondence to M Tonato
Divisione di Oncologia Medica
Ospedale Policlinico, Monteluce, Perugia, Italy
Tel: (+39) 75 5783456; Fax: (+39) 75 5720990