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Efficacy and tolerability of vindesine in the treatment of small-cell lung cancer

A phase II study

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Summary. Eighteen patients suffering from small-cell lung cancer, all with measurable lesions, were treated with vindesine (3 mg/m^2 i.v. on days 1 and 8 of a 21-day cycle). Partial responses (PR) were seen in six patients (three of whom had been previously heavily treated). Most patients tolerated the drug extremely well, an important consideration when expected cure rates are very poor.

Introduction

Despite the improvements in response rates and median survival that combination chemotherapy has achieved in the treatment of small-cell lung cancer (SCLC), the great majority of patients still die of the disease, and at present improved cure rates appear a remote goal. Since most chemotherapy regimens entail unpleasant side-effects, the value of such treatments for the incurable majority of patients remains a matter of some debate. A need clearly exists to identify treatments that are effective in terms of response rates but are acceptable to patients in terms of side-effects.

Having found vindesine to be a well-tolerated drug when used in other malignancies, it was decided to assess its use as a single agent in the treatment of advanced SCLC.

Patients and methods

Eighteen patients with histologically proven SCLC were treated, all of whom had disease measurable in two dimensions. Fourteen had relapsed following previous treatment with vincristine, doxorubicin and cyclophosphamide; 4 were hitherto untreated but had been assessed on physical and/or psychological grounds as being unsuitable for such aggressive therapy. Of these previously untreated patients, 2 had limited-stage disease and 2 extensive.

Vindesine was given by intravenous bolus in doses of 3 mg/m^2 on days 1 and 8 of a 21-day cycle. Treatment was discontinued if there was evidence of disease progression, or after three cycles if there was no evidence of response. Partial response (PR) was assessed by World Health Organization criteria [3]; responding patients were given further treatment at the same dosage once every 3 weeks, discontinuing at disease progression.

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Results

Of the 18 patients, 6 showed PR; 3 of these had received prior chemotherapy and 3 were previously untreated. (These responses were all assessed in terms of the two-dimensionally measurable lesions.) Responses were thus seen in 3 of 14 pre-treated patients, and 3 of 4 who had received no previous treatment. In all cases except 1, the sites of response were the primary tumour and/or regional nodes, the exception being 1 patient whose sole clinically detectable site of relapse at the time of starting vindesine was an enlarged inguinal node, shown histologically to be metastatic. This node showed a considerable regression.

Of the 3 pre-treated patients who responded, only 1 had shown signs of progression whilst receiving other chemotherapy (etoposide); the other 2 had initially responded to short courses of combination chemotherapy and had relapsed at, respectively, 5 and 8 months off treatment. All responses to vindesine were of short duration, ranging from 5 to 13 weeks (median 8 weeks): these figures were very similar for both the untreated and the previously treated responders.

Symptomatic side-effects were seldom troublesome. Out of a total of 91 actual occasions of drug administration, only 27 (30%) were followed by grade 1–2 gastrointestinal toxicity (WHO scale [3]). Four patients developed grade 1 peripheral neuropathy, and one grade 2. Four patients developed moderate alopecia, but none required a hair-piece. Two patients required blood transfusions during their courses of treatment; neutropenia necessitated a delay of tretment on one occasion; thrombocytopenia was never a problem.

Discussion

Previous workers have demonstrated a useful level of activity of vindesine as a single agent in the treatment of SCLC [2]. This is confirmed by the objective response rate of 6 of 18 patients (33%, with 95% confidence limits of 11% and 54%) in this series, meeting the requirements of Lee et al. [1] for the identification in a phase II study of a drug likely to give responses in at least 20% of treated patients. It should also be noted that the majority of these patients had been heavily pre-treated, although only one of the responding patients had clear evidence of drug resistance.

Assessment of side-effects, particulary the symptomatic ones that are noticed by patients, is less precise, but it

does appear that this drug is better tolerated than many chemotherapeutic agents, both from the data here presented and from informal observation.

The low rate of alopecia in this study, perhaps lower than anticipated, is worthy of comment. There are probably two contributing factors: firstly, very few patients received more than three cycles of drug because of disease progression; secondly, during treatment, no other cytotoxic drugs were administered.

The results presented here suggest that vindesine is an active agent against SCLC and one that is well tolerated: it might be useful to investigate it in combination with other active and well-tolerated drugs as treatment for patients with a low expectancy of cure.

References

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