regimen of lomustine, etoposide and prednimustine (CEP). From 1983 to 1989 we administered CEP to 26 patients with advanced Hodgkin's disease who had been pretreated with two first-line regimens (COPP/ABVD) and had either reached no complete remission (CR) or relapsed early after the last course. CEP consisted of 4 week courses of lomustine (80 mg/m^2 on day 1), etoposide (100 mg/m^2 days 1–5) and prednimustine (60 mg/m^2 days 1–5), all orally.

16 patients responded and received five or more courses; in the other 10 patients, CEP was interrupted earlier because of progression. 5 responders showed partial remission (PR), 11 responders showed CR lasting 1+ to 72+ months. The median survival time for the 11 patients with CR is 33+ months. All patients who did not reach CR following CEP treatment had progressive disease, and no case could be brought into CR by subsequent chemotherapy and/or radiation therapy. Nevertheless, these patients showed survival times up to 61 months under palliative therapy with a median survival time of 11 months (Fig. 1).

Looking for predictive signs, we found that CEP was most effective when previous chemotherapies resulted in CR. After failure of primary chemotherapy CEP was ineffective, whereas in ineffectively treated relapses CEP still achieved a few CRs. Lack of B symptoms was possibly a favourable predictor, whereas metastatic spread did not correlate with efficacy. The CEP treatment had a modest toxicity—most of the patients had mild nausea and vomiting in the first 2 days of treatment.

By CEP treatment CRs with a median duration of 16+ months were reached in 42% and PRs in 19%. This is in line with the findings of Santoro *et al.* [2, 3]. Of those chemotherapy regimens which have been studied in patients resistant to MOPP/COPP and ABVD, only CEVD (lomustine/etoposide/vindesine/dexamethasone) [4] and lomustine/teniposide/methotrexate/epirubicin [5] had a similar efficacy to CEP. Other third-line protocols have a CR rate between 0 and 29%. Only high-dose chemotherapy followed by autologous or allogenic bone marrow transplantation achieves higher CR rates but is fraught with severe toxicity [6, 7]. The median duration of a complete remission after CEP mostly lasted longer than that achieved in previous primary or first relapse therapies.

Because of its high efficacy and its similarity to the conditioning chemotherapy with BCNU/etoposide, CEP may win time and may allow testing of sensitivity to conditioning chemotherapy before bone-marrow transplantation. The low toxicity of the CEP protocol makes outpatient treatment possible.

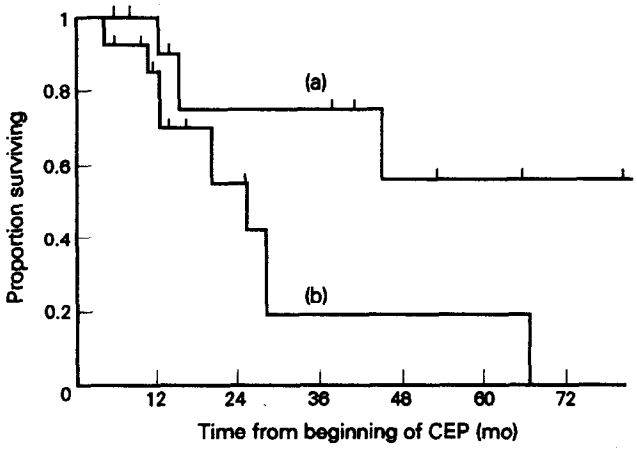

Fig. 1.

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Ondansetron in the Prophylaxis of Nausea and Vomiting Induced by Cisplatin

Peter A. van Liessum, Caroline Seynaeve, Pieter H. de Mulder, Stein Kaasa, Elizabeth Lane-Allman, Louk V. Beex and Jaap Verweij

WE HAVE evaluated the safety and efficacy of ondansetron [1–5] in the prophylaxis of acute and delayed nausea and vomiting induced by cisplatin (70–120 mg/m^2). Forty-five patients were entered. Nineteen had previously been treated with chemotherapy (cisplatin in nine). Three different dosage schedules administering a continuous infusion of ondansetron for 24 h were assessed. The initial dose for the first eight patients in each centre was 10 mg intravenously followed by a continuous infusion for 24 h of 2 mg/h. The dosage was increased (12 mg and 4 mg/h) or decreased (8 mg and 1 mg/h) depending on the response of these patients. Ondansetron was then given orally for 5 days (4 or 12 mg four times a day).

The timing and number of episodes of vomiting and retching were recorded and cross-checked with the patient. Nausea was assessed on a 100 mm visual analogue scale (VAS), 0 mm representing 'felt not at all sick' and 100 mm representing 'worst ever feeling of sickness'. One emetic episode was defined as any vomit productive of liquid or one to five retches within 5 min. On days 2–6, a single retch was considered as one emetic episode. A complete response (CR) was defined as no emetic episodes, a major response as (MR) zero to two episodes and a minor response (mR) as three to five episodes. Failure (F) was defined as more than five emetic episodes or that rescue therapy was necessary.

Forty-three patients were evaluable. During the acute phase (first 24 h) sixteen patients (37%) had a complete response, eleven (26%) a major response and six (14%) a minor response, ten patients (23%) failed. In the sixteen patients refractory to prior treatment the response was: CR in three patients, MR one, mR four and F in eight patients. Almost complete control of nausea (VAS $\leq$10 mm) was achieved in seventeen patients (40%). No dose–response with this broad dose range was detected.

In the delayed phase (days 2–6) twenty-eight patients were included. Nine (32%) patients had a complete response, six (21%) a major response and four (14%) a minor response. Nine patients (32%) failed. Diary cards on nausea were not completed for 1 or more days in nine patients. Therefore, these data were not analysed in detail.

Headache (22%) and constipation (16%) were the main side-effects reported and these were generally mild. No major sedative or extrapyramidal side-effects were observed. When questioned at follow up, twenty-two out of twenty-eight patients (79%) wanted ondansetron treatment if they were to receive chemotherapy again.

Ondansetron was effective and well tolerated over a broad dose range in the prevention of cisplatin-induced emesis. However, efficacy in the prevention of delayed emesis remains unclear.

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Octreotide and Bromocriptine in Patients with Stage D2 Prostate Cancer who Relapsed during Treatment with Flutamide and Castration

André Dupont, Hélène Boucher, Leonello Cusan, Yves Lacourciere, Jean Emond and Fernand Labrie

LUTEINISING-HORMONE releasing hormone (LHRH) analogues have an increased inhibitory effect on the growth of the Dunning prostate adenocarcinoma when combined with a somatostatin agonist [1]. Thus, 11 patients with progression of disseminated prostate cancer while receiving the LHRH agonist (D-Trp^6, des-Gly-NH$_2^{10}$)LHRH ethylamide (250 μg subcutaneously daily) or surgical castration in association with flutamide (250 gm, every 8 h orally) also received octreotide and bromocriptine. Octreotide was administered subcutaneously under constant infusion with a model AS-6C syringe pump (Travenol). The starting daily dose was 600 μg with a stepwise increase until a daily dose of 1350 μg was reached after 1 week. Bromocriptine was started on the second week and given at 2.5 mg every 12 h orally. The average duration of treatment for the 10 evaluable patients was 75.1 days (range 21–114).

None of the 10 evaluated patients had a positive objective response assessed by the NPCP criteria [2] after the addition of octreotide and bromocriptine. Three of the patients discontinued treatment because of rapid deterioration of disease after 21, 39 and 48 days, respectively; these patients died 58, 220 and 78 days later. All the other patients showed signs of deterioration at bone scintigraphy 3 months after starting treatment with octreotide and bromocriptine. Seven patients died at 58, 78, 90, 158, 164, 220 and 350 days after stopping octreotide and bromocriptine. The three surviving patients continued to progress despite the addition of aminoglutethimide and hydrocortisone.

The decrease in plasma growth hormone concentration was not significant during the daily administration of an average of 1350 μg octreotide and 5 mg bromocriptine. Serum prolactin and IgF, on the other hand, significantly decreased after 1 month of treatment and remained low for up to 3 months; insulin and glucagon levels changed similarly.

The early termination of this phase II trial, in which the sample size had been fixed at 19, was mainly caused by rapid evolution of disease during treatment with octreotide and bromocriptine. The number and/or size of bone lesions increased in all patients except one. In this patient disease progression was

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