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Letters

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Tropisetron (Navoban®) Compared With Alizapride in the Control of Emesis Induced by Cyclophosphamide-containing Regimens

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Traditional anti-emetic treatment consists of drug combinations, including high doses of metoclopramide or alizapride, which may cause extrapyramidal [1] or adverse cardiovascular reactions [2, 3]. Recently, anti-emetics of the 5-HT_3 receptor antagonists class, including tropisetron, have been synthetised [4–7].

This small, open, randomised study (15 + 15 patients with breast cancer) compared the efficacy of tropisetron and alizapride in preventing and controlling nausea and vomiting induced by chemotherapy regimens containing emetogenic doses of cyclophosphamide (CTX 500–600 mg/m^2 on a single day).

The patients fulfilled the following selection criteria: age ≥ 18 years; no severe cardiac, renal or hepatic dysfunction; no brain metastases; no severe constipation or diarrhoea, and no chemotherapy during the previous 3 months.

The chemotherapy consisted of cyclophosphamide, methotrexate, 5-fluorouracil (CMF) regimen in 25 patients, and of CTX plus 5-fluorouracil combined with mitoxantrone, vincristine or epirubicin in, respectively, 2, 1 and 2 patients.

Each patient received anti-emetic treatment during two consecutive courses of chemotherapy: tropisetron [5 mg by intravenous (i.v.) infusion over 15 min] or alizapride (100 mg by i.v. injection) immediately before chemotherapy; oral tropisetron (5–10 mg/day) or intramuscular alizapride (100–200 mg/day) on 2 subsequent days.

For 3 days after each course of chemotherapy, patients recorded nausea as absent, mild, moderate or severe and the number of vomiting episodes. The daily control of vomiting was expressed as complete (0 episodes), major (1–2 episodes), minor (3–4 episodes) and failure (≥ 5 episodes).

To evaluate the tolerability, we considered the side-effects reported by the patients, and the following parameters recorded before each chemotherapy course and at the end of the study: blood pressure, heart rate, body temperature, ECG results and routine haematological laboratory parameters. 2 patients of the alizapride group were withdrawn from the study due to anti-emetic treatment failure and disease progression.

Tropisetron was superior to alizapride in the 24 h following chemotherapy, with complete or major control of vomiting occurring in 93% of the patients in both courses versus 60% ($P = 0.04$) and 77% ($P = 0.06$) of the patients receiving alizapride (Table 1).

The analysis of vomiting episodes confirmed that on day 1 there was a statistically significant ($P < 0.05$) difference in favour of tropisetron.

These results compare well with those reported in the literature: complete or major control of acute emesis in 72–86% of the patients receiving ondansetron (8 mg three times daily) and in 76–81% of patients receiving granisetron (40 μ/kg/day) [8, 9].

There were no differences between tropisetron and alizapride

Table 1. Anti-emetic effect

			Tropisetron				Alizapride			
Course	Day	Administration route	Complete No. (%)	Major No. (%)	Minor No. (%)	Failure No. (%)	Complete No. (%)	Major No. (%)	Minor No. (%)	Failure No. (%)
1	1	i.v.	14	0	1	0	9	0	2	4
			(93)	(0)	(7)	(0)	(60)	(0)	(13)	(27)
	2	p.o./i.m.	13	0	1	1	7	5	2	0
			(86)	(0)	(7)	(7)	(50)	(36)	(14)	(0)
	3*	p.o./i.m.	7	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
2	1	i.v.	13	1	1	0	7	3	3	0
			(86)	(7)	(7)	(0)	(54)	(23)	(23)	(0)
	2	p.o./i.m.	11	3	0	1	9	2	1	0
			(73)	(20)	(0)	(7)	(75)	(17)	(8)	(0)†
	3*	p.o./i.m.	5	0	0	0	4	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

p.o., orally; i.m., intramuscularly; i.v., intravenously. * Only patients with nausea took the anti-emetic. † One patient refused the anti-emetic due to absence of nausea and vomiting.

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in preventing delayed emesis: complete or major control of vomiting in 86–100% of patients of both treatment groups (Table 1). There were no noteworthy changes in clinical and laboratory parameters. Headache, asthenia or sedation were reported by 6 patients receiving tropisetron and by 4 receiving alizapride.

In conclusion, our results confirm that tropisetron is a well-tolerated and manageable anti-emetic drug. Its efficacy is superior to that of alizapride, at least in the control of acute emesis.

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The Treatment of Progressive Ovarian Carcinoma With D-Trp-LHRH (Decapeptyl)

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Several authors [1–4] have shown the presence of follicle-stimulating hormone (FSH) and luteinising hormone (LH) receptors in malignant tumours of the ovary. Parmar [5] has shown gonadotropin level reduction in ovarian carcinomas with the administration of luteinising hormone releasing hormone (LHRH) agonists. Emons [4] postulates that LHRH analogues could act in epithelial ovarian carcinoma patients through two mechanisms: (a) suppressed FSH and LH secretion and removal of a possible proliferation stimulus, (b) direct inhibitory effect on tumour cells through LHRH receptors. These experimental data led us to investigate the use of a LHRH agonist for advanced ovarian carcinomas.

We treated 20 epithelial ovarian carcinoma patients, already submitted to surgery, with stable or progressive disease after lines I, II and III chemotherapy or relapsing within 6 months after line I chemotherapy. All patients were menopausal with an average age of 60 years.

Triptoreline (D-Trp-6-GnRh) at a dose of 3.75 mg was administered intramuscularly every 4 weeks until progression. 5 patients could not be assessed as they died within the first 8 weeks of observation due to rapid disease progression. 7 of the 15 assessable patients received line II chemotherapy, 3 also received line III and 5 only line I (Table 1).

No remission was observed; 14 stabilisations were achieved and only one progression occurred (the only Brenner tumour of the series). The longest stabilisations were observed in progression patients after complete remission following line I chemotherapy and not submitted to further treatment (patients 9 and 11). Drug tolerance was excellent, only three hot flushes and two not certainly drug-dependent gastrointestinal disturbances occurred.

Many attempts have been made to cure epithelial ovarian carcinomas with hormone therapy. Bruckner [6] treated 5 advanced ovarian carcinoma patients with leuprolide acetate (gonadotropin releasing hormone analogue) associated with megestrol acetate to minimise the potentially adverse effects of leuprolide acetate and reported one complete response, two partial responses and two stabilisations. Kavanagh [7] reported four partial responses (17%) and two stabilisations in a series of 18 assessable epithelial ovarian carcinoma patients treated with leuprolide acetate. Parmar [5] reported six partial remissions and five stabilisations with triptoreline administered to 39 advanced epithelial carcinoma patients. Jager [8] treated 19 advanced epithelial ovarian carcinomas with triptoreline and observed stabilisation for over 20 months in 12 patients (63%).

No responses were observed in our series but the large number of some long duration stabilisations should not be discounted. It should also be noted that prognosis for all our patients was extremely unfavourable for tumour stage or previous II or III line chemotherapy, residual tumour and grading; for this last factor, Kavanagh [7] postulated that LHRH analogues only have anti-tumoral effects in well-differentiated tumours.

Considering the negligible toxic action of triptoreline and low response percentage observed with chemotherapy regimes used as a second- or third-line at the expense of high toxicity levels, the use of this drug for ovarian advanced carcinoma patients after conventional treatment or the association of Decapeptyl with conventional cisplatin-containing line I chemotherapy as proposed by Emons in a randomised study [9] seems to be well-founded.

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