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Letter to the Editor

The Efficacy of GR38032F,* an Antagonist of 5-Hydroxytryptamine-3 (5-HT_3) in the Prophylaxis of Cisplatin (CDDP)-induced Nausea and Vomiting

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HIGH-DOSE metoclopramide, often combined with corticosteroids and/or benzodiazepines, is currently the treatment of choice in CDDP-induced emesis [1, 2]. Major drawbacks of these effective regimens are side-effects such as extrapyramidal symptoms and drowsiness.

GR38032F is a novel, highly selective 5-HT_3 antagonist, which is a potent inhibitor of CDDP-induced nausea and vomiting in ferrets [3]. Studies in healthy volunteers have shown that the compound is well tolerated up to 128 mcg/kg i.v. and up to 160 mcg/kg orally. The half-life of GR38032F was found to be 4.5 h. In non-CDDP containing regimens, very high efficacy was seen in patients refractory to other anti-emetic treatments [4].

In the present study we report on the results in 13 naive cisplatin-treated patients (70–120 mg/m^2). GR38032F was given i.v. at two dose levels. The first dose was given in 15 min just prior to the start of the 4 h CDDP infusion and repeated at half the initial dose 6 and 12 h later. Six patients were treated with a starting dose of 4 mg (level A) and 7 patients with 8 mg (level B).

Efficacy was scored after 24 h and the results are shown in Table 1. Complete prevention of emesis was seen in 45% and a major response (all patients with less than three vomiting episodes) was observed in 72%. Nausea was assessed using a 100 mm visual analogue scale with 0 mm representing no nausea. In case of, respectively, a complete response, major response or failure, patients scored: 7, 1–19 (n = 6), 53, 10–72 (n = 3) and 39.5, 13–89 (n = 4; median + range).

No correlation between plasma level and response was found. Thirteen of the 18 treatment courses with GR38032F were associated with adverse events such as mild sedation (six patients), flushing (five patients) and headache (two patients). Three

Table 1. *Antiemetic response of GR38032F at two dose levels in 13 CDDP-treated patients*

GR38032F	Number of patients	
	First course	Second course
Dose level A	6	4
No vomiting	4	1
≤2 vomiting periods	1	2
>2 vomiting periods	1	1
Dose level B	7	1
No vomiting	2	1
≤2 vomiting periods	2	
>2 vomiting periods	3	

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*1,2,3,9-Tetrahydro-9-methyl 3(2-methylimidazol-1-yl) methyl carbazol 4-one, hydrochloride, dihydrate.
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patients showed a slight, transient elevation of transaminases.

GR38032F is effective and well tolerated in the dosage and regimen used. In the present data no dose–response relation has been found. Further studies with other dose regimens are currently being undertaken. Its true value has to be proven in randomized trials.

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