Table 2. Observed toxic effects in 154 cycles for 52 patients

	WHO grade				
	0 (%)	1 (%)	2 (%)	3 (%)	4 (%)
Leucocytes*	67 (44)	28 (18)	29 (19)	24 (16)	6 (4)
Neutrophils*	55 (36)	14 (9)	23 (15)	22 (14)	40 (26)
Platelets*	151 (98)	1 (1)	1 (1)	—	1 (1)
Haemoglobin*	117 (76)	25 (16)	10 (6)	1 (1)	1 (1)
Constipation†	86 (56)	32 (21)	35 (23)	1 (1)	—
Peripheral neuropathy†	134 (87)	11 (7)	7 (5)	1 (1)	1 (1)

*Lower nadir checked between two WBC per cycle made on days 10 and 14; 31 and 35; 52 and 56.
†Evaluated at days 21, 42 and 63.

We have previously reported comparable results with the MVP regimen (introduced by the Memorial Sloan Kettering Cancer Center), in term of both response rate (29 vs. 28%) and MST (9 vs. 8 months). Toxicities, either haematological or other, were also comparable, despite different drugs (5-FU by CI instead of mitomycin C) and different schedules of VDS (weekly bolus vs. three weekly CI). The present VDS schedule allowed us to optimise drug administration on a three weekly basis, and to avoid dose delay or reduction, that are often required with weekly VDS. Actually, in spite of the different VDS doses in the two regimens (3 mg/m^2 weekly in MVP vs. 0.8 mg/m^2 daily for 4 days every 3 weeks in FVP), weekly dose intensity was 1.8 mg/m^2 for MVP vs. 1.1 mg/m^2 for FVP (a 0.6 ratio). With respect to 5-FU by CI, dose intensity was clearly suboptimal, since the drug was administered at a lower dose compared to conventional schedules, namely 800 mg/m^2 daily for 4 days vs. 1000 mg/m^2 daily for 5 days. Accordingly, we started a new trial of the same FVP combination in NSCLC patients, adding folinic acid (leucovorin) with the aim to potentiate 5-FU activity.

In conclusion, the FVP could represent an alternative to MVP in NSCLC, in order to obviate the major risk associated with weekly VDS, namely delayed courses and reduced dose intensity.

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Ineffectiveness of Relaxation on Vomiting Induced by Cancer Chemotherapy

Kaija Holli

EMESIS IS a complex physiological and psychological process with multifactorial aetiology. The aim of the randomised study reported here was to evaluate the effect of a non-pharmacological method (relaxation) on vomiting induced by cancer chemotherapy.

67 adult inpatients (aged 19–84) from Tampere University Hospital area with different forms of cancer, whose performance status was good (Zubrod 0–1) and who were receiving chemotherapy participated.

Patients were randomised into controls (24) and cases (43) aiming at a case–control ratio of two to one. The controls received no active study intervention beyond completion of evaluation required of all participants. The cases were relaxed by a physiotherapist 1 h before chemotherapy infusion and they continued self relaxation during the infusion. Standard progressive deep-muscle relaxation was used [1]. Both groups were given the normal pharmacological antiemetics (mainly lorazepam, methylprednisolone and metoclopramide dihydrocloride) before chemotherapy infusion. 5-HT$_3$ receptor antagonists were not used routinely at the time.

Both self-reported (subjective) and observer-rated (objective) methods were used to report the time of onset, quantity and

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Table 1. Quantity, onset and duration of vomiting and the experience of chemotherapy in controls and cases

Indicator of effect	Controls n	Controls %	Cases n	Cases %
Any vomiting	6	25	16	37
Onset of vomiting ≤ 4 h	3	13	10	21
Duration of vomiting ≥ 3 h	3	13	8	19
Patient rating chemotherapy intolerable	2	8	6	14

duration of vomiting. The tolerability of vomiting and chemotherapy were assessed according to the patient's report.

There were no differences between 43 cases and 24 controls by age, sex, diagnosis, chemotherapy schedule or duration of schedule. One third of the patients had more or less severe vomiting. Cases vomited more frequently but the difference was not statistically significant (Table 1). Most commonly vomiting began within 4 h of the infusion and it lasted more than 3 h (13% in controls and 19% in cases). The correlation to self-reported and observer-rated information was good. Cases found chemotherapy to be intolerable more commonly but there was no significant difference.

Differences in emesis occurred between patients receiving the same type of chemotherapy and between similar treatment courses in the same patient. Many individual factors contribute to the differences in gastrointestinal distress associated with chemotherapy. Earlier experience, susceptibility to nausea in the past, anxiety and the information on side-effects given to the patient may contribute. If the preparation of a patient for chemotherapy is too careful this can induce unnecessary anxiety and may increase emesis. On the other hand patients cannot cope with side-effects if they do not get practical advice about them [2].

In some studies systemic desensitisation and other behavioral interventions, such as relaxation or hypnosis were observed to be useful in the management of chemotherapy-related emesis [3, 4].

The failure in this study to demonstrate any benefit does not prove that non-pharmacological methods have no other beneficial effects on patients.

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Tauromustine (TCNU) Combined with 5-Fluorouracil and Leucovorin in the Treatment of Advanced Colon Cancer

Babs G. Taal, W.W. Ten Bokkel Huinink and S. Rodenhuis

ALTHOUGH 5-FLUOROURACIL (5-FU) was introduced more than 30 years ago, it is still the mainstay of treatment for advanced colorectal carcinoma, achieving response rates of 10–20% [1–3]. Tauromustine (TCNU), a novel nitrosurea derivative, has also shown antitumour activity: a response rate of 14% which including a single complete remission has been observed in 57 patients [4]. We have previously reported that a combination of 5-FU and TCNU yielded only a 10% response rate in 31 patients [5]. At that time, this disappointing outcome was difficult to explain. *In vitro* experiments with the human colon cancer cell line HT 29 by Hartley-Asp and Alenfall [6] have shown that simultaneous exposure to both TCNU and 5-FU produced less-than-additive cytotoxicity. In contrast, enhanced tumour cell kill was achieved when TCNU was added 24 h before the 5-FU. To determine whether this sequence dependence can also be shown to be present in patients, we studied a combination of TCNU with one of the most effective regimens available in colon cancer, 5-FU and leucovorin (LV) [7]. Because of its convenience and its suitability for administration in the out-patient setting, a weekly schedule with an intermediate dose of leucovorin was selected [8] to which tauromustine was added [9].

Patients with symptomatic advanced colorectal adenocarcinoma and no prior history of chemotherapy were treated. All patients had measurable lesions, a WHO performance status ≤ 2, were under 75 years of age, and had adequate bone marrow, renal and hepatic functions. The chemotherapy was administered every week as a 1-h infusion of LV (80 mg/m^2), followed by an intravenous (i.v.) push of 5-FU (400 mg/m^2) during weeks 1–8. TCNU was administered as a weekly oral dose of 40 mg/m^2, 24–28 h before the 5-FU/LV administration during weeks 1–4 [9]. Dose modifications and/or treatment delay depended on haematological and gastrointestinal toxicity. Patients were considered evaluable for both toxicity and efficacy when they had received at least one full treatment cycle of 8 weeks. Toxicity grades and responses were defined according to WHO criteria.

Between January 1989 and August 1991, 18 patients were entered (Table 1). All were evaluable for both toxicity and response. Toxicity consisted mainly of myelosuppression. Four of 31 courses had to be delayed and in three courses dose reductions were applied because of thrombocytopenia. Grade

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