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## Serum immunoreactive thrombopoietin levels in patients and response to ICE-chemotherapy-induced thrombocytopenia

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**Purpose:** The glycoprotein hormone thrombopoietin (TPO) is the primary and specific regulator of platelet production. The aim of our studie was to determine serum TPO concentration in normal subjects and during chemotherapy-induced thrombocytopenia. Additionally, we studied the serum concentration of two other megakaryocyte stimulatory cytokines, IL-6 and IL-11 during this period.

**Methods:** A quantitative sandwich ELISA-technique was employed for measurement of TPO in sera from 37 healthy subjects, 29 untreated tumor patients, and in sera from 6 patients up to 17 days after ICE administration. For L-6 and IL-II commercial ELISA were used.

**Results:** Normal subjectes: platelets 248/nl, TPO 287 pg/ml, Tumor patients: significantly increased to 436 pg/ml, platelets to 310/nl. After ICE platelets decreased to 67/nl during nadir on day 13 and recovered to 112/nl until day 17 This was inversely correlated to the raised serum TPO concentrations of 1050 pg/ml on day 13 and 832 pg/ml on day 17. No correlations between IL-6 and IL-11 and changes of TPO concentrations or platelets were observed.

**Conclusion:** We have elaborated a TPO-specific ELISA to determine the serum TPO concentration. Untreated tumor patients exhibited eleveted serum TPO and increased platelets counts. The serum TPO was inversely correlated to platelet counts, maximum TPO on day 13 after onset of chemotherapy, coincided with platelets nadir. Based on the time course of the changes in platelet counts and the concentration of TPO after chemotherapy, we wish to propose that treatment with recombinant human TPO approximately 4 days before expected platelet nadir could prevent life-threating bleedings and the need for platelet transfusion.

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## Control of acute cisplatin-induced nausea and emesis using a once daily oral treatment regimen of ondansetron plus dexamethasone

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For patients receiving highly emetogenic chemotherapy intravenous (iv) ondansetron (OND) and iv dexamethasone (DEX) is currently recommended for the acute emesis period (0–24 hr). However, tablets may be a useful alternative particularly in an outpatient setting. The purpose of this multicentre, randomised, double-blind, double-dummy, parallel group study was to determine whether oral (po) OND 24 mg given as a single dose (od) plus po DEX 12 mg od is as effective and well tolerated as iv OND 8 mg plus iv DEX 20 mg in acute cisplatin-induced nausea and emesis.

A total of 528 (intent-to-treat population) patients were recruited into the study, 262 in the po group and 266 in the iv group. In the po group, 90% of patients had complete or major control of emesis (0–2 emetic episodes) compared to 89% in the iv group The percentage of patients experiencing none or mild nausea was 85% in both treatment groups of the study and both treatments were well tolerated. In conclusion, there was no significant difference between either once daily oral dosing with OND 24 mg plus DEX 12 mg or iv OND 8 mg plus DEX 20 mg in the control of acute cisplatin induced nausea and emesis.

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## Recombinant human granulocyte colony-stimulating factor (G-SCF) in patients receiving chemotherapy for gynecologic cancer

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**Purpose:** To investigate the value of filgrastim (Granulokine, Roche) on duration of neutropenia, use and duration of antibiotics, duration of hospitalization, incidence and duration of neutropenic fever, incidence of demonstrated infection and mucositis, we evaluated 287 patients with gynecologic cancer.

**Methods:** Patients received filgrastin, 5 mg/Kgr s.c. daily (n = 197) or placebo (n = 90) on days 4–17 of the 21-day treatment cycle. Filgrastim was withdrawn if the post-nadic neutrophil count was $>10 \times 10^9$/lt (12th day). Patients' ages ranged from 33 to 70 years, with median age 56 years.

**Results:** At least one episode of neutropenic fever occurred in 43 out of 90 (47.77%) placebo treated patients compared with only 36 out of 197 (18.27%) filgrastim treated patients ($x^2 = 18.9$, $p < 0.0001$). Median duration of neutropenia (absolute neutrophil count $< 1.0X10^9$/lt in filgrastim treated patients was $2.96 \pm 2.33$ days, compared with $7.76 \pm 4.4$ in the placebo group ($t = 6.56$, $p < 0.0001$), and median duration of fever was shorter in filgrastim group ($4.27 \pm 3.92$ vs $10.35 \pm 8.42$ $t = 6.4$, $p < 0.001$). At least one course of intravenous antibiotics in cases of neutropenic fever was administered to 46.66% and 18.27% of placebo and filgrastim treated patients respectively ($x^2 = 15.36$, $p < 0.0001$). Moreover the duration of antibiotics administration was shorter in filgrastim group ($6.08 \pm 9.41$ vs $13.26 \pm 9.59$, $t = 6.05$, $p < 0.001$). The duration of hospitalization was significantly less in filgrastim group ($7.00 \pm 5.40$ vs $14.19 \pm 9.52$, $t = 6.05$, $p < 0.001$) and there were also fewer confirmed infection in this group (3.55% vs 20%, $x^2 = 19.04$, $p < 0.0001$). Over all cycles the percentage of patients who developed mucositis was reduced from 36.66% in the placebo group to 4.56% in the filgrastim arm ($x^2 = 35.62$, $p < 0.00001$). Adverse effects were similar between groups, except for the incidence of musculoskeletal pain, which was greater in the filgrastim treated group (15.22%).

**Conclusions:** These results indicate that filgrastim is well tolerated and effective in reducing the morbidity associated with chemotherapy-induced neutropenia in women with gynecologic cancer.

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## Drug utilization for prevention of chemotherapy (CT)-induced emesis

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**Purpose:** The combination of a 5-$HT_3$ antagonist with a corticosteroid is the most efficacious treatment for acute emesis induced by both highly and moderately emetogenic CT. However no data exist on antiemetic utilization in daily practice by oncologists. A prospective drug utilization study at 33 Italian oncological centers was carried out.

**Methods:** In June 1996, for two consecutive weeks, all adult patients (pts) starting any CT were blindly monitored for antiemetic prescription. Excluded from the study were pts with acute leukemia and pts receiving high-dose CT or radiotherapy.

**Results:** 1220 pts were evaluated. Of these, 140 received cisplatin (CDDP), 742 moderately emetogenic CT (MEC) (carboplatin, epirubicin, doxorubicin, cyclophosphamide and mitoxantrone) and 338 low emetogenic CT (LEC) (i.e., vincristine, vinblastine, etoposide, etc.). Rates of utilization of different antiemetic drugs were:

| Treatment regimen | CDDP (%) | MEC (%) | LEC (%) |
|---|---|---|---|
| 5-$HT_3$ antagonists alone | 22.8 | 46.0 | 37.0 |
| 5-$HT_3$ antagonists + steroids | 76.4 | 42.3 | 10.6 |
| Steroids alone | 0 | 2.8 | 8.9 |
| Antidopaminergics alone | 0 | 4.3 | 28.1 |
| Other | 0.8 | 3.1 | 4.5 |
| No antiemetic treatment | 0 | 1.5 | 10.9 |

Prophylaxis for delayed emesis was prescribed overall in 30.9% of pts (52.9% receiving CDDP, 33.6% MEC and 15.7% LEC).

**Conclusion:** The study showed that both undertreatment and overtreatment occurred in many pts with respect to the evidence provided by clinical trials

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## Amelioration doxorubicin efficacy through reduction of anthracycline toxicity by calcium gluconate

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The study was undertaken to investigate the influence of modulator of calcium dependent ion pump by calcium gluconate (CaG) on the biological effects of doxorubicin (DOX). In acute toxicological experiments we have