after at least 3 cycles of therapy (T_1–T_2–T_3). In **121 cancer pts** (97 females; PS 0–1; from 31 to 72 years), treated with >60 mg/m^2 cisplatin-including (45 pts) or not chemotherapies plus **Ondansetron** (16 mg i.v. day 1 + 16 mg p.o. on day 2–5; 46 pts) of **Granisetron** (3 mg i.v. day 1; 41 pts) or **Tropisetron** (5 mg i.v. day 1 + 5 mg p.o. on day 2–5; 34 pts). *Results* are:

	T_0	T_1	T_2	T_3
ONDA	0.394	0.389	0.397	0.380
	(*P* 0.980	(*P* 0.816)	(*P* 0.597)	(*P* 0.643)
GRANI	0.398	0.407	0.407	0.402
	(*P* 0.836)	(*P* 0.622)	(*P* 0.650)	(*P* 0.464)
TROPI	0.391	0.385	0.394	0.398

Values of QTc little higher than the max normal range (never pathologic) were found at T_0 in 6 pts (2 ONDA, 2 GRANI, 2 TROPI) and in 12 pts during the cycles (6 ONDA, 3 GRANI, 3 TROPI). **In conclusion** the three 5-HT_3 drugs at ordinary doses are not surely responsible for arrhythmic effects; on the other hand the slight increase of the QTc that we found may be correlated with the antiblastic agents itself (as doxorubicin) and/or concomitant medications (as hyperydration in cisplatin therapy).

1238 PUBLICATION

A PHASE III RANDOMIZED COMPARISON OF MDL(METOCLOPRAMIDE, DEXAMETHASONE, AND LORAZEPAM) PLUS GRANISETRON WITH MDL ALONE IN THE PREVENTION OF NAUSEA AND VOMITING ASSOCIATED WITH MULTI-DAY CISPLATIN-CONTAINING CHEMOTHERAPY

Y.-K. Kang, Y.-K. Cheon, Y.-H. Im, C.-M. Kim, J.-O. Lee, T.-W. Kang
Department of Internal Medicine, Korea Cancer Center Hospital, Seoul, Korea

This study is designed to determine if the addition of granisetron, a potent serotonin-receptor antagonist, to the combination of metoclopramide, dexamethasone, and lorazepam (MDL) could improve the prevention of nausea and vomiting in patients receiving multi-day cisplatin-containing chemotherapy.

One hundred and seventy one cancer patients receiving their initial combination chemotherapy including 20 mg/M of cisplatin daily for 5 days were randomized to receive metoclopramide (2 mg/kg × 2 i.v., D1–5), dexamethasone (8 mg × 1, 4 mg × 2 i.v., D1–2; 4 mg × 1, 2 mg × 2 i.v., D3–5), and lorazepam (1 mg × 1 p.o., D1–5) (MDL) or the identical MDL plus granisetron (3 mg × 1 i.v., D1–5) (MDL + G). Sixty six of 88 patients (75%) on MDL + G had fewer than three emetic episodes throughout the 5 days of study period, compared with 44 of 83 (53%) on MDL ($P = 0.0027$), and 52% of patients on MDL + G had no emetic episodes, compared with 35% on MDL ($P = 0.022$). The treatment failure rates were 16% in MDL + G arm and 27% in MDL arm ($P = 0.12$). Hiccup (27%), insomnia (11%), extrapyramidal symptoms (total 10%, dystonia 0.6%), facial flushing (9%), constipation (7%), and headache (6%) were the most common side effects. However, these were well tolerated and there was no significant difference in these side effects between the two arms. These results suggest that the addition of granisetron to standard MDL could safely improve the prevention of nausea and vomiting associated with multi-day cisplatin-containing chemotherapy.

1239 PUBLICATION

ACCEPTANCE OF TROPISETRON AND METOCLOPRAMIDE IN AMBULANT PATIENTS RECEIVING 5-FU CHEMOTHERAPY

H.J. Koenig[1], L. Faerber[2], S. Drechsler[2]
[1] *University Hospital Erlangen*
[2] *Sandoz AG Nuremberg, Germany*

In highly emetogenic chemotherapy (CHE) tropisetron (TRO) is more effective and better tolerated than conventional antiemetics. Due to good tolerability and long duration of action TRO could be advantageous also in ambulant settings with less emetogenic treatments. This study examines the acceptance of TRO vs. metoclopramide (MCP) in outpatients receiving 5-FU-treatment. 40 patients were randomised in a cross-over trial to receive TRO 5 mg or MCP 50 mg once daily (day 1–3) each during one study course. Both treatments were rated equally regarding efficacy. Tolerability was judged significantly better for TRO ($P < 0.05$). With MCP, patients suffered significantly more from tiredness and restlessness. With respect to overall acceptance of therapy by patients, TRO superseded MCP ($P < 0.01$).

Conclusion: The favourable side effect profile of TRO makes it clearly more useful than MCP for antiemetic prophylaxis in outpatients undergoing moderately emetogenic CHE.

1240 PUBLICATION

INTRAVENOUS CLODRONATE FOR METASTATIC BONE PAIN

I. Kovalchuk, J. Shparik, B. Bilynsky, R. Petriv
Department Oncology, P.O.Box 2468, Lviv, 290029, Ukraine

To evaluate pain-relieving effect of bisphosphonates in metastatic cancer a preliminary study was initiated in patients (pts) without associated hypercalcemia. From April 1994 through February 1995, 56 pts (primaries include breast 32, lung 15, prostate 3, myeloma 4, colon 1, unknown 1) were given 1.5 g Clodronate iv in 500 ml normal saline over 5 h or 300 mg iv daily for 5 consecutive days. Total 94 infusions. *Results:* 39/56 (70%) noticed significant pain relief, decreased narcotic requirements and improved quality of life; 17/56 (30%) were not able to tell any significant difference, while none noticed an increase in pain or narcotic requirements. Side effects included low-grade fever, asymptomatic hypocalcemia, and hypomagnesemia. It deserves further investigation as an adjuvant therapy and in patients with nonosseous recurrence who are at high risk for bone metastases. Intravenous Clodronate appears to be efficacious in refractory pain from metastatic bone disease; however, further study is warranted.

1241 PUBLICATION

IMPACT OF IMPROVED SUPPORTIVE CARE ON TREATMENT OUTCOME IN ACUTE LYMPHOBLASTIC LEUKEMIA—AN INDIAN EXPERIENCE

P. Kurkure, S. Pai, S. Vaidya, G. Kapoor, C. Nair, R. Gopal, T. Saikia, P. Parikh, V. Pai, I. Magrath, S. Advani
Department of Medical Oncology, Tata Memorial Hospital, Bombay, India

Five hundred and fifty-two patients of Acute Lymphoblastic Leukemia (ALL) were accrued on the MCP-841 protocol from August 1986 to December 1992. 97% of the patients belonged to the high risk category. The only prognostic factor affecting the event free survival (EFS) was the year of accrual ($P < 0.001$). The treatment protocol being uniform for all the patients, the only factor which has changed over the years is the supportive care. Infection was a major cause of death in the early years. The rate of infection mortality has now decreased from >20% (1986–87) to <5% (1992). Prompt empirical treatment of febrile neutropenic episodes, management of these patients in organised outdoor setup and anticipation and prevention of other drug related problems has enabled us to decrease treatment related mortality and thereby improve EFS from <40% (1986–87) to >60% (1992).

1242 PUBLICATION

GRANISETRON (G)-DEXAMETHASONE (D) COMBINATION FOR MULTIPLE DAY CISPLATIN (C)

P.L. Losardo, M. Landucci, A. Vigani, F. Vaira, E. Cantinotti, P. Pronzato
Department of Clinical Oncology, Ospedale S Andrea, LA Spezia, Italy

34 patients (pts) being given polychemotherapy schedules including C at the dose of 20 mg/m^2 for 5 days entered an antiemetic protocol with G and D at the doses of 3 mg and 8 mg respectively, both administered i.v. before cisplatin. Pts received 108 cycles (range 1–6). A complete antiemetic response has been observed in 14/34 (41.1%) pts and 80/108 (70.4%) cycles; a major response has been observed in 12/34 (35.3%) pts and 16/108 (14.8%) cycles; a minor response in 2/34 (5.8%) pts and 5/108 (4.6%) cycles; a failure in 6/34 (17.6%) pts and 7/108 (6.4%) cycles. Nausea was absent in 424/540 days of therapy, rare in 72/540 and frequent in 44/540 days. Cefalea was in 16/34 pts and stipsis in 8/34 pts. G-D is able to determinate a high rate of antiemetic control in the special set of multiple day C treated pts.

1243 PUBLICATION

THROMBOLYTIC THERAPY IN CANCER PATIENTS WITH MAJOR PULMONARY EMBOLISM

T.S. Bishiniotis, D.K. Mouratidou, A.V. Tsiberidou, G.P. Katseas, A.A. Michalelia, A.G. Litos, P.J. Hatseras
"Theagenion" Cancer Hospital, Thessaloniki, Macedonia, Greece

Introduction: Neoplastic diseases consist the most common cause of secondary hypercoagulability. Thromboembolic disease in cancer patients

ranges from 1–11%. The aim of this study was to evaluate the effectiveness of thrombolytic therapy in the management of oncologic patients with major pulmonary embolism (PE).

Methods: Nineteen cancer patients (mean age 53.5 ± 9, M/F: 9/10) were reviewed. The initial diagnosis was gynecologic cancer (n = 7), lung cancer (n = 4), breast cancer (n = 2), lymphoma (n = 2), prostate cancer (n = 1), histiocytoma (n = 1), osteosarcoma (n = 1) and hepatoma (n = 1). The clinical suspicion of PE was set by the physical examination, the ECG, the chest X-ray, the echocardiogram and the right heart catheterization findings and confirmed by lung perfusion scan. The fibrinogen during the acute phase of PE was markedly elevated (mean value 794 ± 400 mg/dl). The therapy was initiated with IV streptokinase 250,000 IU per hour for 24–72 hours and was continued with IV heparin administration for 5–7 days. *Results:* Fourteen out of nineteen patients survived and there was improvement of the clinical and scintigraphic status. The thrombolytic therapy in one patient was stopped because of major gastrointestinal bleeding. Four patients died of respiratory failure.

Conclusion: The thrombolytic treatment in oncologic patients with major pulmonary embolism seems to be effective with relatively few hemorrhagic complications.

1244 PUBLICATION

CENTRAL VENOUS CATHETER WITH RESERVOIR IN ONCOLOGICAL PATIENTS. TWO YEARS' EXPERIENCE

A. Delgado, J. Montesdeoca, M. Marrero, A. Murias, J. Almenares, F. Molano

Medical Oncology Unit, Hospital Insular de Gran Canaria, Las Palmas, Canary Island, Spain

From Feb/93, a prospective study was initiated with oncological patients who had had a central venous catheter with reservoir (CVCR) implantation, in order to evaluate tolerance and incidence of complications. A total of 218 patients were included, of which 97 were male (44.3%) and 122 female (55.7%). The median age was 52.5 years (age range 9–76 years); 80% of whom had a Karnofsky >70. The most frequent diagnoses were breast cancer (37%), head and neck cancer (14.2%) and lymphomas (13.7%). In 85.3% of the patients the reservoir was implanted in the right hemithorax (HT) and in 14% the left HT. The vein most frequently used for implantation was the jugular vein (97.7%). The median duration of catheter implantation was 8 months (1–24). In the main, the drugs used were ADM (18%), 5-FU (17.4%), CTX (14.4%). 32.2% of the cases received 24-hours continuous infusion. The median usage of the catheter was 18.8 times (1–62). The percentage of complications was 14.4% and in order of frequence: no blood return (5%), infections (3.2%), thrombosis (2.75%), pain (1.9%), rejection (1.83%) migration (1.8%), rotation of reservoir (0.4%).

Conclusion: There have been few complications and 94% of the patients have indicated that they are content with the catheter.

1245 PUBLICATION

ERYTHROPOIETIN AND CHEMOTHERAPY: EFFECTS ON HEMOSTASIS AND FIBRINOLYSIS

C. Oberhoff, B. Krummeich, U.H. Winkler, A.E. Schindler

Department of Gynecology, University Hospital, D-45122 Essen, Germany

Data from hemodialysis patients who received erythropoietin (EPO) for anaemia report an increased incidence of thrombosis.

We studied hemostasis in 13 patients with gynecological cancer receiving 5000 I.E. EPO (Boehringer Mannheim) s.c. daily, for 12 weeks because of chemotherapy-induced anaemia (Hb < 11/g/dl). Blood sampling was done before and monthly on therapy. Pretreatment procoagulant activity, anticoagulation, fibrinolysis and antifibrinolysis were found within the normal range. D-dimer fibrin-split product (1122 ng/ml) were elevated. No change in the dynamic parameters of coagulation and fibrinolysis was seen on therapy except a significant decrease of protein C (50%).

Protein C deficiency is a common complication of anticancer chemotherapy in gynecology. In absence of any increased intravascular coagulation, we suggest that EPO therapy induces no additional risk for thrombosis, but further analysis might be necessary to evaluate if EPO enhances iatrogenic protein C deficiency.

1246 PUBLICATION

BACTEREMIAS IN PATIENTS (PTS) WITH HEMATOLOGIC MALIGNANCIES

K. Palla, M. Hatziyianni, M. Gilianos, G. Christakis[1], A. Katrachoura[1], A.E. Athanassiou, V. Seitanides

Hematology Dept.

[1] Microbiology Department, Metaxa Cancer Hospital, Pireas 185 37, Greece

All positive blood culture isolates from a hematology unit, between 1991 and 1992, were evaluated retrospectively. A total of 88 bacteremic episodes (105 pathogens) were recorded. Patient population consisted of 31 males and 17 females and their age ranged from 17 to 78 years (median 57). 24/48 (50%) pts had 1 bacteremic episode, 12 (25%) pts had 2 episodes, 8 (17%) pts had 3 episodes and 4 (8%) pts had 4 episodes. Nearly all pts suffered from hematologic malignancies. Fever <38°C was present in 78/88 (88.6%) cases. Severe Neutropenia was present in 64/88 (72%) cases. Gram-positive bacteria were isolated in 64 (61%) cases, Gram-negative in 37 (35.2%), and others in 4 (3.8%) [1 Bacillus, 1 Listeria, 1 Bacteroides, 1 Candida]. A total of 10 pts had died within 3 weeks of first positive blood culture. Of these fatal cases, Gram-negative bacteria were isolated in 8 episodes, Gram-positive in 5, and Candida in 1 (3 polymicrobial isolates). Among them, Pseudomonas aerug. (3 cases) and E. coli (3 cases) were the most prevalent. In conclusion, although Gram-positive bacteremias are increasing steadily (61% versus 40% during 1988–89 in the same unit), Gram-negative infections proved acting as main contributing factor for fatal bacteremias.

1247 PUBLICATION

SUPPORTIVE ERYTHROPOIETIN TREATMENT IN PATIENTS WITH OVARIAN CARCINOMA UNDER CHEMOTHERAPY WITH CIS-PLATINUM

P.S. Paraskevopoulos, P. Kourtidu, P. Eliopoulos, L. Zepirides, A. Papadopoulou-Boutis[1], L. Boutis

1st Department of Clinical Oncology

[1] Biological-Chemistry Laboratory of Anticancer Institute of Thessaloniki "THEAGENIO", Greece

In a randomized prospective study we evaluated the efficacy of erythropoietin to maintain the hematocrite levels above 30% in patients with stage III ovarian carcinoma under cis-platinum containing chemotherapy. In this study 20 patients were entered divided into two groups. Group A was the under investigation group with ten patients (mean age 60.4 y) and was treated with Cis-platinum 80 mg/m^2 + Epirubicin 60 mg/m^2 + Cyclophosphamide 600 mg/m^2 (PECX6) every four weeks, and simultaneously received erythropoietin (Epo) 2000 U subcutaneously three times a week. Group B or control group (ten patients with mean age 61.5 y) received the same chemotherapy regimen (PECX6) without Epo supportive treatment. The oscillation of hematocrite, hemoglobin and reticuloerythrocytes were measured during the 6 cycles of PEC chemotherapy, in all 20 patients, as well as the red blood cell units transfused in each patient in order to be able to continue their chemotherapy. The analysis of the results showed an increase of hematocrite in 5 patients of group A (Epo) and stable levels of hematocrit in the other 5 patients of the same group, and only 2 patients needed transfusion with 3 red blood cell units. In the control group B hematocrit decreased in all ten patients and 7 patients needed transfusion with 15 red blood cell units. From the above results we conclude that Epo supports the hematocrit levels satisfactorily. Also requiring considerably fewer red blood cell units for transfusion with all the benefits from the avoidance of adverse effects from the blood transfusion.

1248 PUBLICATION

USE OF METHYLENE BLUE AND BICARBONATE IN IFOSFAMIDE-RELATED CNS TOXICITY. CASE REPORT

H. Serve, E. Hilgenfeld, J. Maurer, E. Thiel, W.E. Berdel

Department of Hematology and Oncology, Benjamin Franklin Hospital, Freie Universität, Berlin, Germany

Severe, sometimes fatal CNS toxicity is a rare, dose-related side effect of ifosfamide (IFO). It has been suggested to be due to toxic effects of IFO metabolites on electron transport. Methylene blue (MB) has been tested in a few patients as an antidote. We have treated 2 adults with MB, who presented with severe IFO-related CNS toxicity. The 1st patient received combination chemotherapy for Wilms-Tumor containing 3.5 g IFO i.v for 3 days. On day 1 of IFO infusion, he developed paranoid hallucinations, agitation and coma (CTC grade 4) for 3 days. With 5 further cycles of an equal chemotherapy he received 50 mg MB 4×/d