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

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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

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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

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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

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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

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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

i.v. His urine pH was kept above 7.0 with i.v bicarbonate. No CNS toxicity was observed. The 2nd patient was treated with PEI for testicular cancer, containing only Ig IFO for 4 days because of preexisting renal failure. On day 1, he developed paranoia, agitation and disorientation (CTC grade 3). IFO was continued together with MB and bicarbonate as described. All CNS symptoms resolved within 48 h. We conclude, that iv administration of MB might be effective against IFO-related CNS toxicity. A phase II trial is currently being conducted.

1249 PUBLICATION

OPTIMAL COMBINATION THERAPY IN THE PREVENTION OF ACUTE AND DELAYED EMESIS INDUCED BY HIGHLY EMETOGENIC CHEMOTHERAPY (CT)

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In an attempt to improve the control of both acute and delayed nausea and emesis for patients (pts) receiving combination CT, we designed a combination of antiemetic drugs as follows: day (d) 1: granisetron 3 mg IV + methylprednisolone (MPL) 240 mg IV + alprazolam (A) 0.5 mg tid per os (po), then po d2: MPL 48 mg + A 0.5 mg tid + Métoclopramide (M) 20 mg tid, d3: MPL 32 mg + M 20 mg tid, d4: MPL 16 mg + M 20 mg tid, d5: M 20 mg tid. Pts with or without previous CT were eligible if CT included cisplatin (P) >75 mg/m^2 or carboplatin >300 mg/m^2 or cyclophosphamide >1 g/m^2 on d1 and no highly emetogenic drugs on the following days. 318 pts were included: 59% male; mean age 57 y; 59% non naive pts (60% had prior emesis experience: EE). Main primary tumor sites were lung 49%, ovary 19%, head and neck 11%. 81% pts received P at a mean dose of 95 mg/m^2 (75–180). Mild adverse effects occurred in 31%: 12% headache, 9% drowsiness, 6% insomnia, 7% agitation, 5% hiccough. Outcome are summarized below:

Day	D_1	D_2	D_3	D_4	D_5	D_6	D_7
No Nausea % cumulative	82	70	59	53	50	48	47
No vomiting % cumulative	85	78	71	66	65	60	60

For non naïve pts with RC (no EE, no or mild nausea) and not RC at previous course, RC was recorded at day 1 respectively 91% and 56%. *Conclusion:* This combination appears feasible and effective with promising results in overall control of the emesis but delayed emesis remains a significant problem despite specifically designed antiemetic protocol.

1250 PUBLICATION

AN OPEN RANDOMIZED STUDY OF GRANISETRON (G) VERSUS GRANISETRON PLUS DEXAMETHASONE (G + D) IN THE TREATMENT OF CYTOSTATIC-INDUCED EMESIS

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The effectiveness and tolerability of the 5-HT$_3$ antagonist, granisetron (G) has been compared in an open randomized study with G + dexamethasone (G + D) in patients (pts) receiving high dose cisplatin (>100 mg/m^2). G was given as a single dose of 3 mg i.v. over 5 minutes or combined with D (D 8 mg i.v. and 4 mg orally bid on day 2–4). One hundred pts: 22 males, 28 females received G; 29 males, 21 females received G + D. Median age of pts were 60 yrs and 62 yrs in G and G + D arm. Tumor types are lung, cervical, head and neck, ovarian and unknown primary cancer. During the first 24 hrs, of 50 pts treated with G 66% had complete (no nausea, no vomiting (v)) + major response (1 episode of vomiting). Of 50 pts treated with G + D 80% had complete + major response. Response during day 2 to 7 for G vs G + D group were 28 vs 50, 28 vs 60, 58 vs 74, 64 vs 82, 82 vs 90 and 82 vs 100% respectively. Adverse effects consisted of headache, lightheadedness, diarrhoea.

This study in an Asian population treated with high dose cisplatin confirm and extends the observation that steroids enhance the antiemetic activity of 5-HT$_3$ antagonists.

1251 PUBLICATION

CEFTRIAXONE (CRO) PLUS GENTAMYCIN (GEN) AND G-CSF, VERSUS CIPROFLOXACIN (CPR) PLUS GEN AND G-CSF, IN FEBRILE PATIENTS (PTS) WITH CHEMOTHERAPY INDUCED NEUTROPENIA

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In a prospective randomized study, 63 episodes of fever (>38°C) and granulocytopenia (absolute neutrophil count, ANC < 1000/mm^3), occurring in 63 cancer pts, were empirically treated with CRO 2 g/d IV, once daily [arm A = 31 pts], or CPR 400 mg IV, every 12 hours [arm B = 32 pts]. All pts received GEN 5 μg/kg/d IV, in a single dose, during the first 3 d, and G-CSF 5 μg/kg/d SC beginning on the day of neutropenia and until ANC recovery. In the A and B arms respectively, median age (range) was 61 (25–83) and 62 (27–83) years, 16/31 (52%) and 18/32 (56%) were men, 25/31 (80%) and 22/32 (69%) had ANC < 500/mm^3. Bacteremia, clinically documented infection and possible infection were documented in 4, 5 and 13 pts [arm A] and in 3, 6 and 14 pts [arm B]. Neutropenia lasted 4 days on average (range 1 to 10 days) in both arms. At 72 h, response without treatment modification occurred in 25/31 (80%) pts [arm A] and in 25/32 (78%) [arm B]. Days on the study drug (CRO or CPR) were 5 (2–10) for both arms. For bacteremic infections, responses were 2/4 for arm A and 2/3 for B. No adverse events or superinfections occurred. 2 pts in arm A died, because of treatment failure. The survival rate was 100% for arm B. In conclusion, CRO and CPR (both with GEN and G-CSF), were equally effective and safe as initial therapy in these febrile neutropenic pts.

1252 PUBLICATION

ONDANSETRON (ODS) + METOCLOPRAMIDE (MTP) + DEXAMETHASONE (DXM) VS ONDANSETRON + DEXAMETHASONE DURING CDDP BASED CHEMOTHERAPY (CT)

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During high dose (>50 mg/m^2) CDDP based CT, 51 pts randomized to either regimen A (ODS 40 mg IV d 1–2 & 8 mg PO q 8h d 3–5, MTP 20 mg IV q 4h d 1–2 & 20 mg PO q 4h d 3–5 plus DXM 32 mg IV d 1 or regimen B (as above exempting MTP). Pts randomized to A were given B during the 2nd course & vice versa, followed by alternating A&B thereafter. Vomiting & nausea was evaluated for each 24 h & the first 5d. *Results.* 147 courses were given 70 of A & 77 of B. Vomiting: With A, CR (no vomiting) was achieved in 62 (88%), 39 (56%), 48 (69%), 60 (86%) & 64 (91%) of 70 courses each 1, 2, 3, 4 & 5 d, respectively vs 55 (71%, $P < 0.025$), 19 (25%, $P < 0.001$), 22 (29%, $P < 0.001$), 46 (60%, $P < 0.001$) & 61 (79% – p < .05) of 77 courses with B. For all 5 d, CR was achieved in 35/70 (50%) courses with A vs 14/77 (18%) with B ($P < 0.001$) Nausea: With A, nausea was observed in 14 (20%), 24 (34%), 20 (29%), 14 (20%) & 4 (6%) of 70 courses each 1, 2, 3, 4 & 5 d, respectively vs 26 (34%, P = NS), 51 (66%, $P < 0.001$), 46 (60%, $P < 0.001$), 32 (42%, $P < 0.001$) & 15 (19%, $P < 0.025$) of 77 courses with B. For all 5 d, nausea was observed in 32/70 (46%) courses with A vs 58/77 (75%) with B ($P < 0.001$). The intrapatient comparison in 38 pts who received so far both A&B, demonstrated significantly better control of vomiting & nausea with A. Delayed emesis was also less with A. Toxicity was comparable in A&B regimens.

1253 PUBLICATION

EFFICACY OF MEGESTROL ACETATE ON ANOREXIA IN PATIENTS WITH ADVANCED NON HORMONE-RELATED TUMORS: A DOUBLE-BLIND PLACEBO CONTROLLED CLINICAL TRIAL

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Megestrol acetate (MA) was reported to induce weight gain and increase of appetite in cancer patients.

Methods: Out-patients of the "Divisione Terapia del Dolore" of the "Istituto Nazionale per la Cura dei Tumori" (Milano) with advanced non hormone-responsive tumors and loss or absence of appetite, who didn't assume any corticosteroid were randomized for a Phase III trial, that