tree based on our results with the first one (5th Int Congress Anti Cancer Chemot, Paris, 1995, abstr 445) and on the last literature data was used from 02–1994 to 01–1995. All patients treated by chemotherapy (CT) were concerned. We report the results from 9 months of applying. The study concerned clinical efficacy, respect of the decision tree and cost of the antiemetics. **Treatment** (tmt). There were 4 groups corresponding to various emetic situations, with a progression in the use of 9 different schemes for cycle tmt (0,F,G,H,I1,I2,J,K,L), and 3 schemes for postcycle tmt (X,Y,Z). Failure of a scheme was defined by a number of emetic events $\geqslant$ 2/day. In this case the scheme was changed at the next cycle for the following one. **Group 1:** no emetic CT (ex: vinorelbine): **0:** no tmt; **F:** alizapride (alz) 100 mg IV; no pre and post tmt. **Group 2:** moderately emetic CT (ex: FEC-FAC): **G:** alz 100 mg IV hour (H) 0 and H4, methylprednisolone (MP) 120 mg IV H0; **H:** ondansetron (ond) 8 mg IV H0, MP 120 mg H0; pre and post tmt. **Group 3:** CT on several days (ex:BEP): **I1:** D1 granisetron (gra) 3 mg IV H0, MP 120 mg IV H0– D2 to D5 alz 100 mg IV H0 and H4, MP 120 mg IV H0; **I2:** I1 plus chlorazepate 20 mg IV; **J:** ond 8 mg IV H0 D1 to D5, MP 120 mg IV H0 D1 to D5; **L:** chlorpromazine IV 5 mg/sqm/3x/D; pre and post tmt. **Group 4:** highly emetic CT (ex: cisplatine >70 mg/m2): **K:** gra 3 mg IV H0, MP 120 mg IV H0; **L;** pre and post tmt. **Precycle tmt:** alprazolam (alp) 0.25 mg PO 3x/D D-3 to D-1. **Post cycle tmt** for 3 days with 3 schemes. **X:** metoclopramide 20 mg PO 3x/D, MP 16 mg PO 3x/D. **Y:** X plus alp 0.25 mg PO 3x/D. **Z:** ond 8 mg PO x3/D. *Results.* **Group 1:** for 1836 cycles of CT; 0: 92.27%, F:7.3%, G to K: 0.43%; X + Y: 6%. **Group 2:** for 893 cycles of CT; G: 66.41%, H: 28.22%, I1 to L: 5.37%; X: 82.75%, Y + Z: 8.7%. **Group 3:** for 166 cycles of CT; I1: 78.92%, I2: 5.42%, J: 3.01%, K: 7.83%, others: 4.62%; X: 82.5%, Y + Z: 6%. **Group 4:** for 163 cycles of CT; K: 96.93%, others: 3.07%; X: 81.1%, Y + Z: 2.4%. There were 2.6% of mistakes. The decision tree is suitable, with clinical results considered as satisfactory. The cost of treatments has been reduced by a half since the utilization of the decision trees, in spite of an increase in the number of patients.

1233 PUBLICATION

TROPISETRON MONOTHERAPY VS TWO TROPISETRON COMBINATIONS IN CHEMOTHERAPY-INDUCED EMESIS

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To assess the optimal treatment with tropisetron (TRO) single or in combinations for acute and delayed emesis, we performed a study comparing 3 different TRO containing prophylactic treatment regimens: 193 patients with highly emetogenic chemotherapy (CHE; cisplatin, carboplatin, cyclophosphamide, ifosfamide) were randomised to: **A. TRO mono:** 5 mg i.v. once daily during CHE, 10 mg p.o. once daily after end of CHE. **B. TRO + dexamethasone** (DEX, 20 mg i.v. on day 1–2, from day 3: 4 mg i.v./p.o.). **C. TRO + metoclopramide** (MCP, 20 mg i.v. + 20 mg p.o. during CHE, 10 mg per os t.i.d. after end of CHE). TRO/DEX was significantly more effective in prevention of acute/delayed emesis than TRO and TRO/MCP. 49% of patients in group **B** stayed free from vomiting and nausea during the whole study course vs. 26% (group **A**) and 28% (group **C**).

Conclusion: TRO + DEX is the optimal prophylactic treatment to prevent acute as well as delayed emesis. Addition of low dose MCP does not improve the efficacy of TRO substantially.

1234 PUBLICATION

CAN ZINC PICOLINATE IN PATIENTS RECEIVING CHEMOTHERAPY FOR METASTATIC COLORECTAL CARCINOMA PREVENT STOMATITIS?

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30 patients with metastatic colorectal carcinoma receiving chemotherapy were randomized: 20 of these patients received their chemotherapy for the first time and the other 10 pts received previous chemotherapy courses before entering the study. According to the randomization 13 pts received Zinc Picolinate (zinc +) and 17 pts did not (zinc−). 71% of the zinc negative pts developed stomatitis grade I–III, of which 83% was moderate to severe (grade II–III) and persisted throughout all the chemotherapy courses. Only 54% of the zinc positive pts had suffered from stomatitis grade I which disappeared after receiving zinc for four weeks. In conclusion—administration of Zinc Picolinate seems to minimize the incidence and helps the healing of stomatitis, enabling the pts to continue receiving chemotherapy as scheduled.

1235 PUBLICATION

A RANDOMISED STUDY COMPARING ONDANSETRON (OND) WITH ONDANSETRON PLUS DEXAMETHASONE (DEX) IN PATIENTS (PTS) WITH METASTATIC BREAST CANCER (MBC) RECEIVING HIGH DOSE EPIRUBICIN (HDE)—PRELIMINARY REPORT

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We assessed the effect of OND vs OND + DEX in acute and delayed emesis during chemotherapy (CT) with HDE (110 mg/m^2). A total of 61 pts, median age 55 were randomised to receive either (a): OND (n = 26) 24 mg i.v. 30′ prior to CT followed by 8 mg p.o b.i.d days 2–5,or (b): OND 24 mg i.v plus DEX 8 mg i.v (n = 35) 30′ prior to CT followed by 8 mg p.o b.i.d days 2–5. The pts recorded the incidence of vomiting, nausea and other side effects in diaries.

Results: In the acute phase day 1: OND provided complete vomiting control (no vomits or retches) in 42% vs 63% treated with OND + DEX. No nausea or mild nausea occurred in 54% vs 57%. In regard to delayed emesis days 2–5 OND provided complete vomiting control in 59% vs 69% treated with OND + DEX. No nausea or mild nausea occurred in 65% vs 64%. There were no severe side effects in both groups of pts.

Conclusion: First results of an open randomised study comparing OND and OND + DEX in prophylaxis of HDE induced acute and delayed vomiting show that the combination OND + low dose DEX seems to be more effective and superior to the OND alone. No difference between the regimens was found in regard to nausea.

1236 PUBLICATION

MIGRATION OF CATHETER IN CANCER PATIENTS WITH IMPLANTABLE ACCESS PORT SYSTEM, TREATMENT BY PERCUTANEOUS EXTRACTION

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Complications due to subcutaneous devices are rare, mainly venous thrombosis, sepsis and uncommonly pneumothorax, but migration of the catheter has not been yet reported.

In our institution about 820 subcutaneous central venous access devices for chemotherapy have been placed since 1985, mainly by a subclavicular access. We report here 2 cases of migrated catheters, (2.5/1000) one in both pulmonary arteries, the second in right ventricle and pulmonary artery, extracted by a non-invasive technique as out patients.

Extraction of accidentally migrated catheters by lasso's technique is now well-known in vasculary radiology, and must be realized in a ward with continuous cardiologic survey and reanimation means. Catheter's crossing through the right ventricle composes the risk of this technique. Winding a "pig-tail" catheter round the migrated catheter allows its mobilization and removing to the right auricle. In a second step, a strong gripping of the catheter by the lasso permits the final extraction without any cardiac risk.

1237 PUBLICATION

ELECTROCARDIOGRAPHIC EFFECTS OF THE 5-HT$_3$-R-ANTAGONISTS

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5-HT$_3$-r-antagonists are widely used to control the cytotoxic-caused emesis. Since **Ondansetron** has a detectable binding at non 5-HT$_3$ sites (5-HT$_{1b-1c}$) and **Tropisetron** at 5-HT$_4$ and 5-HT$_{2c}$-uptake sites and 5-HT receptors are found in the human **cardiac atria,** an arrhythmogenic potential of these drugs as a dose-dependent prolongation of the QTc interval cannot be excluded. *Aim of our study* was to evaluate the QT interval on the surface ECG expressed as the rate corrected maximum interval according to Bazett (QTc = QT/$\sqrt{}$R–R) before (T_0) and

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

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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

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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

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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

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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)

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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

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