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