250 POSTER

EVALUATION OF INCIDENCE OF CISPLATIN (CDDP)—ANEMIA DEVELOPED IN THREE SUBSETS OF NEOPLASTIC PATIENTS (PTS)

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Studies regarding rHuEPO therapy of CDDP-anemia have been recently reported. We reviewed the incidence of this side-effect in pts receiving at least 3 cycles of CDDP-containing chemotherapy over the last 5 yrs. We identified 119 epithelial ovarian cancer pts (CDDP 90 mg/sqm + CTX 900 mg/sqm); 45 testicular cancer pts (CDDP 20 mg/sqm day 1–5, PEB or PVB regimens); 32 non small lung cancer pts (CDDP 120 mg/sqm + VP16 or IFO or MMC). All of pts had normal renal function and hemocytometric controls every 1 or 2 weeks. RBC transfusion were given at a mean Hb level of 7.5 g/dl (range 6.5–8.1). The results are given in the table below:

	Ovarian	Testicular	Lung
No. of pts	119	45	32
Average Hb baseline values	11.07	13.3	13.4
Average Hb nadir	9.07	11.02	9.08
% of pts with Hb < 9 gr/dl during CT	26%	4.40%	34.30%
Total % of transfused pts	4.20%	4.40%	9.3%
% of pts with Hb < 9 gr/dl who required RBC transfusion	16%	100%	17%
Average n. of RBC units transfused/pt	2	2	3

So, considering the current cost of rHuEPO, clinical studies are required to evaluate its cost-effectiveness and to select pts who can most benefit from rHuEPO in relation to the type of neoplasm, life expectancy and response to rHuEPO, with the final aim of optimizing the use of this hormone.

251 PUBLICATION

EXPRESSION OF INSULIN LIKE GROWTH FACTOR-I RECEPTOR AND TRANSFORMING GROWTH FACTOR-ALPHA IN MALIGNANT EFFUSION SMEARS

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The aim of this study was to investigate the expression of Insulin like Growth Factor-I receptor (IGF-Ir) and Transforming Growth Factor-alpha (TGF-α) in 42 effusion smears, using an immunocytochemical technique.

We have studied 18 peritoneal and 24 pleural effusion smears from patients with endometrial (5), ovarian (7), colorectal (3), liver (3), breast (14) and lung (10) carcinomas. Fifteen effusion smears from patients with benign diseases were used as control group.

IGF-Ir immunoreactivity was detected in 15/24 (62.5%) of peritoneal and 14/24 (58.3%) of pleural effusion smears. TGF-α immunoreactivity was observed in 12/18 (66.7%) of peritoneal and 10/18 of pleural effusion smears. Benign effusion smears were found to be negative for IGF-Ir and TGF-α immunoreactivity.

These results suggest that the expression of IGF-Ir and TGF-α in malignant effusion smears plays an important role for the prediction of biologically high malignant potential.

252 PUBLICATION

IDARUBICIN, CYCLOPHOSPHAMIDE, VINCRISTINE AND METHYLPREDNISOLONE FOLLOWED BY G-CSF IN THE TREATMENT OF ADVANCED MULTIPLE MYELOMA

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Seventeen multiple myeloma (2, S.IIA, 1, S.IIB; and 14, S.IIIA) and 1 loco-regional advanced extramedullary myeloma patients were treated with ICOMP chemotherapy (Idarubicin, I 10 mg/m^2 day 1; Cyclophosphamide, CTX 1.2 g/m^2 days 1 and 3; Vincristine, O 1.2 mg/m^2 day 1 and methylprednisolone, MP 250 mg days 1 and 3, 125 mg days 2 and 4). All drugs were given IV. G-CSF (5 μg/kg) was administered SC from day 5 to recovery from neutropenia. All patients, but one, had received prior chemotherapy (median 3 types combinations, range 1–7). Nine had relapsing and 9 resistant disease to previous treatment. Five patients discontinued therapy, 1 after the 1st cycle because of herpes zoster, 3 because of disease progression (1 after the 2nd, 1 after the 3rd and 1 after the 5th cycle). The last developed a non-therapy related myocardial infarction 5 days after the 3rd cycle. Nine PR, 4 SD and 1 PD were observed in the 13 patients who completed at least 6 cycles. In the first 6 cycles, 18/18, 16/17, 14/16, 12/14, 12/14 and 11/13 patients respectively received between 75% and 100% of the planned I dose and 18/18, 16/17, 14/16, 14/14, 13/14 and 12/13 patients 75%–100% of the projected CTX dose. A WBC <1000/cmm was documented in 10/18 (median 3.5 days, range 2–11), 9/17 (4, 2–15), 8/16 (3, 2–6), 7/14 (3, 1–5), 7/14 (3, 1–5) and 5/13 (3, 2–6) from the 1st to the 6th cycle and a platelet count <100,000/cmm in 7/18 (9, 5–28), 9/17 (8, 1–31), 7/16 (10, 3–28), 7/14 (6, 2–28), 8/14 (7, 2–34), 5/13 (2, 1–20). Our results indicate that the therapeutic regimen adopted is reasonably well tolerated as well as active against advanced MM.

253 PUBLICATION

TOLERABILITY OF HIGH-DOSE CYCLOPHOSPHAMIDE AND CARBOPLATINUM FOLLOWED BY GM-CSF INFUSION

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Eighteen patients (5 MM, 4 HD, 9 NHL) in first or later partial or complete remission after receiving one (13) or more (5) conventional chemotherapies were treated sequentially with high-dose cyclophosphamide (CTX, 7 g/m^2) and carboplatinum (CBDCA, 800 mg/m^2) followed by GM-CSF (5 μg/kg). Two patients discontinued GM-CSF after CBDCA. The first, who interrupted after 2 days because of suspected, but unconfirmed, allergy to GM-CSF, did not receive any other cytokine to accelerate haematological recovery. The second was shifted to G-CSF after withdrawal of GM-CSF on the 5th day due to hypotension and dyspnea. Despite this the symptoms reappeared three times while the patient was off treatment. All 18 patients developed leukopaenia (WBC < 1000/cmm) after CTX, WBC were < 500/cmm in 17 patients. Median duration was 9 and 7 days respectively (range 3–19 and 3–16 days). The platelet count was <50 × 10^3/cmm in 11/18, at times as low as <25 × 10^3/cmm in 6 patients. The median duration of piastrinopaenia was 8.5 days (range 1–40). Eight patients received platelet support. Following high-dose CBDCA, leukopaenia was documented in 6 patients whose WBC further decreased to a count <500/cmm. A platelet count <25 × 10^3/cmm (median 10 days, range 2–27 days) was recorded in 16/18 patients. All, but one of these patients required platelet support. Fever, infections, nausea and vomiting were more frequent after CTX than CBDCA. No major side effects were documented during GM-CSF administration. As CTX and CBDCA provoke different types of toxicity, they are ideally suited for sequential use in association with GM-CSF.

254 PUBLICATION

INTERLEUKIN 3 (IL3) IN THE TREATMENT OF THROMBOCYTOPENIA AFTER STANDARD DOSE OF CHEMOTHERAPY

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Neutropenia and/or Thrombocytopenia are the most important toxicities in several chemotherapy regimens, which result in dose- or interval modifications, which may cause a dose intensity reduction. IL3 is a glycoprotein with an *in vitro* and *in vivo* broad spectrum of activity on hematopoiesis with either prompt neutrophil and platelet counts recovery and prevention of significant periods of neutropenia and prevention of thrombocytopenia. This action is based on ability of IL3 to stimulate the differentiation and proliferation of pluripotent precursor cells in bone marrow. With this background, we treated 14 patients (8 females and 6 males, who all gave their informed consent for this pilot study) with thrombocytopenia after standard dose of chemotherapy. Eleven pts were evaluated for response (2 pts too early, 1 pt dropout of the study after only one administration). The sites of diseases were: breast 5 pts, stomach 3 pts, lung 1 pt, LNH 1 pt, mesothelioma 1 pt, neuroblastoma

1 pt, leiomyosarcoma 1 pt, unknown primary site 1 pt. IL3 was given at a dose of 10 mcg/kg/die s.c. from the onset of G1–G4 thrombocytopenia and continued until recovery. IL3 was given for a mean of 5.7 days (range 2–10) and a median of 5 days. So far 17 out 21 cycles of chemotherapy with thrombocytopenia are evaluable. At present our results are as follows:

- thrombocytopenia G1 (4 cycles): mean increase of platelet counts = 32% within a period of 4.75 days (range 2–10);
- thrombocytopenia G2 (8 cycles): mean increase of platelet counts = 31% within a period of 5.75 days (range 2–10);
- thrombocytopenia G3–4 (5 cycles): mean increase of platelet counts = 157% within a period of 7 days (range 4–10).

The main toxicities were: fever G1–2 8 pts; tremor 3 pts; erythema 1 pts; flu-like symptoms 4 pts; nausea/vomiting G2 1 pts; myalgia G2 6 pts; mental derangement 1 pt.

1 pt, after first administration, has developed acute hypersensitivity with lipothymia.

These data seem to show that IL3 is an active drug in the treatment of thrombocytopenia following a standard dose of chemotherapy. The study is still ongoing and definitive results will be discussed.

255 PUBLICATION

COMPARISON BETWEEN RHGM-CSF AND RHG-CSF ADMINISTERED DURING RADIOTHERAPY AND AFTER PROLONGED CARBOPLATIN INFUSION IN PREVENTING LEUKOPENIA AND MUCOSYTES PRODUCED BY CHEMORADIOTHERAPY IN ADVANCED HEAD AND NECK CANCER

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Concomitant radio-chemotherapy is considered the therapy able to increase the percentage of positive responses in advanced head and neck cancer patients. Nevertheless the related toxicity can become important from the clinical point of view, specially the haematological and mucosa one. In order to reduce the severity of the foreseen haematological and mucosa toxicity, a pilot study with haematological growth factors (G-CSF and GM-CSF) has been performed. Both growth factors were given at the end of the chemotherapy schedule and throughout the radiotherapy programme prosecution. Patients were exposed to infusional chemotherapy for 14 days on end with Carboplatin 30 mg/m^2 and concomitant radiotherapy at the dose of 180 cGy/5 d/w on T and N (*Proc ASCO* 1993, **12:902,**). G and GM were given at the dose of 3 μg/kg starting 24 h since the end of the CBD CA infusion for 14 days. Five patients received G-CSF and 6 patients GM-CSF. All patients gave their informed consent to take part in this pilot study. Results were considered according to the incidence of leukopenia, thrombocytopenia and mucosytes severity, in comparison with a previous group of 28 patients treated with radio-chemotherapy (5th International Congress on Anticancer Chemotherapy, Paris, 0–536, 1995).

		GM	G	Control
Mean peak value	WBC	11.630 (9.390–14.400)	22.146 (6.150–31.400)	
Mean nadir value	WBC	2.473	3.012	2.010 (median 1.921)
	Neutropils	1.379	2.254	1.051 (median 943)
	Platelets	76.900	91.460	80.400 (median 74.000)
Mean day to nadir				
	WBC/Neutr.	45	37	40
	Platelets	35	27	32
Mucosytes grade	1	4/6 (67%)	1/5 (20%)	35.7%
	2	2/6 (33%)	2/5 (40%)	50%
	3	0	2/5 (40%)	14.3%

In conclusion these preliminary data show that both GM and G slightly reduce the severity of Leukopenia but GM-CSF delays the nadir mean day. Moreover GM-CSF, given during radiotherapy remarkably reduces the severity of mucosytes in comparison both with the G-CSF and the historical group. These data are very encouraging and support the elaboration of a further and larger clinical trial in order to confirm the important clinical role of GM-CSF in preventing patients, subjected to a radiochemotherapy programme, from the arising of mucosytes problems.

Nervous system tumours in adults and children

256 ORAL

CHEMOTHERAPY WITHOUT IRRADIATION (RT) IN MEDULLOBLASTOMA PATIENTS YOUNGER THAN THREE. A PROSPECTIVE STUDY BY THE FRENCH SOCIETY OF PEDIATRIC ONCOLOGY (SFOP)

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The prognosis of medulloblastoma/PNET of the posterior fossa (PF) in very young children is poor. Survival rate is usually lower than in older children and the quality of life is of particular concern because of the damaging effects of RT on the developing brain. Since 1990, we have been using a post-operative chemotherapy (CT) protocol without RT. The CT regimen included 7 cycles of carboplatin, procarbazine, etoposide, cisplatin, vincristin, cyclophosphamide for 16 to 18 months. In case of progressive disease or relapse under or after conventional CT, salvage treatment including busulfan and thiotepa with bone marrow rescue followed by 50 gy on PF alone was recommended. Thirty-five children <3 yr (median, 16 m) entered this study. Twelve of 35 patients (pts) with no measurable disease after surgery were considered as low risk pts (LR), and 23 with local residue or metastasis as high risk pts (HR). Among the 12 LR pts, 8 are in CR1 with a median follow-up of 30 m (11 to 54 m). Four out of twelve experienced local relapse. Three of them are in CR2 after salvage treatment along with surgery (2 pts), 10 m$^+$, 18 m$^+$ and 30 m$^+$ after relapse. The last pt died without further therapy. Among the 23 HR pts, only 2 achieved CR with conventional CT (17 and 34 m$^+$), 10 relapsed 1 to 19 m after surgery, 11 had progressive disease 1 to 17 m under CT. The 3-yr DFS for LR and HR pts was 67% and 6.5%, respectively (overall DFS, 27%). The 3-yr overall survival for LR and HR pts was 92% and 28% respectively. This protocol appears efficient in LR pts. Another strategy needs to be designed for HR pts. **Supported by ARC, FRANCE.**

257 ORAL

RADIATION THERAPY (RT) IN THE MANAGEMENT OF CRANIOPHARYNGIOMA

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This is a review of 37 children and adolescents treated by RT at IGR between January 1969 and December 1992. Maximum follow-up is 22 years. Mean age is 6.4 years (range 1–15) and the M/F sex ratio is 0.76. RT was applied in the initial management, alone or following a surgical procedure, in 18 cases (49%). In the remaining 19 patients, surgery was used as initial single modality and repeated in 13 of them. In these cases, external RT was considered at the time of a further relapse only. In 2 patients, an intra cystic radiocolloid administration (Re 106) was also employed. External RT delivered 45 to 55 Gy using Megavoltage equipment (Co 60: 15, 5–25 MV, X-rays: 22) in 3 to 5 daily sessions of 1.8 to 3.3 Gy. At the time of analysis, 8 children (22%) presented with a local failure. All were observed in children in which RT had been initiated at the time of relapse, and none if RT had been applied in the initial course ($P < 0.01$). All failures were located in the target volume. Nine patients died: 7/9 died from tumor progression, 1/9 from second malignancy and 1/9 from brain injury. Five and 10 years survival are 89 and 67%. Two