1332 POSTER

## Levomepromazine (nozinan) has efficacy in delayed chemotherapy induced emesis (DCIE) following platinum-based treatment

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**Introduction:** Up to 50% patients may experience DCIE post platinum-based regimes, despite receiving recommended dexamethasone-based combinations post chemotherapy. Levomepromazine can quickly rescue patients from DCIE and prevent it in future cycles. We retrospectively studied our implemented policy of subcutaneous nozinan for rescue (SCR), prophylactic subcutaneous nozinan (PSCN)with chemotherapy, and post-chemotherapy oral nozinan (PON). The latter 2 interventions replaced pre-chemotherapy dexamethasone/ondansetron, and post-chemotherapy dexamethasone/metoclopramide, respectively.

**Methods:** (May 2000-February 2001): the above groups were identified in a population treated with platinum agents. Doses: SCR/PSCN=25mg/24hrs, PON=12.5mg BD for 3 days. Assessable parameters: control of nausea and vomiting within 24 and 48 hours, and side-effects. (NCI CTC grading).

**Results:** 21 patients (12 female, 9 male) had DCIE following either high-dose cisplatin (18) or carboplatin (3)based regimes. 18 patients required admission-16 received SCR, 2 declined and received oral rescue (POR). 6 received PSCN for future cycles, 9 also received PON for future cycles. 3 did not present, despite DCIE, and received PSCN (1), PSCN and PON (1), or PON(1).

20 cycles of chemotherapy in 18 patients required rescue: In 18/20 cycles (90%), complete control (CC)of nausea, and in 19/20 cycles (95%)CC of vomiting, was obtained within 24 hours of rescue. 21 cycles of chemotherapy required PSCN. In 19/21 cycles (90.5%) complete prevention (CP) of nausea and vomiting was obtained in the first 24 hours post-chemotherapy.45 cycles of chemotherapy was followed by PON, with CP of nausea and vomiting in 43/45 cycles (95.5%), within 24 hours post-chemotherapy. At 48 hours post-rescue, only 2/20 cycles (10%) were not CC for nausea, and 1/20 (5%) not CC for vomiting. 48 hours post-chemotherapy,2/21 cycles (9.5%)were not CP for nausea and vomiting in the PSCN group, and in 2/45 cycles (4.4%)for the PON group. The 2 failures in the PON group were amenable to re-rescue with SCR. Nozinan was discontinued in 4 (19%) due to: sedation (1), hypotension (1), headache (1) and focal fit (1).

**Conclusion:** Levomepromazine appears effective in rescuing patients from platinum-DCIE not prevented with standard treatments, and in preventing emesis in vulnerable patients for whom recognised standard antiemetic regimes are ineffective.

1333 POSTER

## Administration of GM-CSF as enemas in the management of radiation proctitis

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**Aim:** To evaluate the effectiveness of the GM-CSF in the treatment of radiation proctitis.

**Patients - Methods:** Four men with a mean age of 63.5 years (average age: 62–71 years) who suffered from radiation proctitis was the material of this preliminary study. All patients had a long-term history of proctitis (average 2–4 years) previously treated with various methods of treatment. In these patients 800 $\mu$g GM - CSF was administrated daily as enemas for 15 days. Rectosigmoidoscopy and biopsies were performed before and after the treatment.

**Results:** Significant improvement, both clinically and endoscopically, was observed in all patients after the treatment. Only one patient had recurrence of symptoms four months after treatment, during the six months follow - up period. This patient presented regression of symptomatology after additional GM - CSF medication.

**Conclusion:** It seems that GM - CSF topical therapy exerts a significant therapeutic effect against radiation proctitis. These data have to be confirmed with larger number of patients.

1334 POSTER

## Protective effect of Amifostine during fractionated radiotherapy in patients with pelvic carcinomas: results of a randomized trial

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**Purpose:** Bowel and bladder toxicity is a significant side effect in patients (pts) irradiated for pelvic malignacies. Preclinical and clinical data have shown that amifostine has a radioprotective effect on normal tissues. The aim of this randomized trial is to evaluate whether pretreatment with amifostine can reduce treatment induced toxicity in pts with rectal, bladder, prostate and gynecological cancer treated with radiotherapy.

**Methods:** Two hundred and six (206) pts with pelvic malignacies (rectal: n = 32, bladder: n = 47, prostate: n = 40, gynecological: n = 87) were randomized to receive radiotherapy (group A: 95 pts) or radiotherapy plus amifostine (group B: 111 pts). Amifostine 340 mg/sqm was administered IV 15 minutes before radiotherapy. Antiemetics were given routinely before the infusion of amifostine. The pts characteristics were comparable for both treatment groups. All patients received conventional radiotherapy (1.8–2.0 Gy daily, 5 days/week), radical (65–70 Gy) of postoperative (50–60 Gy), 45 Gy given to the whole pelvis. Skin, bowel, bladder and hematological toxicities were evaluated according to the RTOG/EORTC scoring system.

**Results:** Acute toxicity grade 2/3 of lower GI tract and bladder was significantly reduced in the amifostine group ($p < 0.05$ in wks 3–7 of treatment). In a median follow up of 9 months few late effects grade 2/3 were observed in both groups (bladder: 1 pt of group A, small intestine: 1 pt of group B). Response of pts with evaluable disease 6 weeks after completion of radiotherapy, showed no statistically significant difference between the two groups. (CR/PR: group A: 85.8%, group B: 90.6%, $p = 0.87$). Local relapse: 10 pts (4 pts of group A, 6 pts of group B). Distant metastasis: 8 pts (4 pts of group A, 4 pts of group B). Amifostine was well tolerated; moderate hypotension occurred in 2 pts and moderate nausea in 1 pt.

**Conclusions:** This randomized trial confirms that amifostine reduces radiation-related toxicity of bladder and lower GI tract in pts with pelvic malignancies without evidence of tumor protection. Longer follow up will show the effect of amifostine on late toxicity.

1335 POSTER

## The patterns of symptom identification and response in a community-based oncology practice

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**Purpose:** The literature suggests that symptoms experienced by cancer patients receiving chemotherapy are often under-identified and under-managed. In a retrospective study the pattern of symptom identification and management was examined.

**Methods:** The charts of 230 breast, colon and lung cancer patients were audited to determine how symptoms were noted in the chart (mentioned or identified as a problem) and what actions were subsequently taken to manage the symptoms. A modified chart-stimulated interview process involving nurses and oncologists at the 2 sites was used to identify 'themes' regarding how symptoms are identified and why actions are taken to manage some of them.

**Results:** 95% of patients had a least one symptom mentioned in the chart, with 55% having 5 or more symptoms mentioned. The most common symptoms mentioned were local site injection reactions (71%), pain (53%), fatigue (51%) and nausea (51%). The pattern of symptom occurrence varied by cancer site. For most symptoms actions to manage the symptom were more likely to be taken when it was identified as a problem versus being mentioned in the chart. The actions taken to manage symptoms (education/monitoring, medications, referral) varied by cancer site as well as by type of symptom. There was significant physician variability in the identification and management of symptoms. Logistic regression analyses revealed that actions were more likely to be taken when the symptom was identified as a problem, and when the symptom was pain, stomatitis or leukopenia. Oncologists infrequently identified and intervened with psychosocial and quality-of-life symptoms. The qualitative analyses revealed that oncologists that have a treatment care orientation (versus a total care orientation) fo-

cused almost exclusively on symptoms that had a dose-limiting effect of chemotherapy.

**Conclusion:** There is significant variability in the pattern of identifying chemotherapy-related symptoms among oncologists, and when symptoms are identified efficacious actions to manage them are not routinely taken. The routine use of clinical information systems with direct patient input regarding symptom presence and severity should help to ensure symptoms are identified in a timely manner and intervened with appropriately, especially if oncologists receive tailored feedback on the symptom status of their patients and the efficacy of the actions they took to manage the symptoms.

1336 POSTER

## Neuroprotective effect of vitamin e supplementation in patients treated with cisplatin-based chemotherapy

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**Aim:** Clinical and neuropathological features observed in cis-platin(DDP)-induced neuropathy are similar to those observed in Vitamin E deficiency neuropathy. The aim of the present study is to evaluate the neuroprotective effect of the antioxidant Vit E supplementation in patients treated with DDP - based chemotherapy (CT).

**Patients and Methods:** Forty-six untreated patients(pts)were enrolled in the study (age ranged from 20 to 65 yrs). Patients candidate to DDP treatment,given alone or in association with other non neurotoxic drugs, were assigned after informed consent to (group A) oral administration of 300 mg/day of Vit E during DDP treatment,or to(group B) DDP-based CT alone. Neurotoxicity was evaluated by an elettrophysiological examination of sensory median and sural nerves and was performed at basal condition, after 3 and after 6 courses of CT. The neurotoxicity was graded following the Chaudry score. A measurement of Vit E plasma levels was also performed for all patients before treatment and at the end of CT. Statistical analysis was carried out with the paired t-Student test.

**Results:** Twenty-one pts were excluded due to disease progression(18pts),or discontinuation of Vit E (2pts). Twenty-five completed 6 corses of CT (group A=11, group B=14) and were evaluable for the study. The mean total dose of DDP administered for each pt was 480 mg/m2. No significant difference in response rate was observed in both groups. Median Vit E plasma value measured before treatment was similar in the two groups. Mean neurotoxicity score in pts of group A(Vit E)was 1.6. Only 4/11 pts complained mild signs of peripheral neurotoxicity (36%). Patients of the group B (control) showed clinical signs of neurotoxicity in 11/14 cases, with a mean toxicity score of 4.6 ($p<0.00$). Only 2 pts did not complain signs of peripheral toxicity, while in 12/14 cases(85%,$p<0.00$) neurotoxicity resulted moderate to severe. Vit E plasma levels assessment after 6 couses of CT is still ongoing and will be shown.

**Conclusion:** Patients undergoing daily assumption of 300 mg of Vit E from the beginning of DDP-based CT to discontinuation of treatment do not complain toxicity,or suffer of mild signs of peripheral neurotoxicity when compared to a control group. These data seem to indicate a neuroprotective effect of Vit E in patients with potential development of neurosensitive damage and encourage to a more extended experiences. Supported by Fondazione per la Ricerca Oncologica (F.O.R.O. ONLUS)

1337 POSTER

## The role of serum cystatin c and TC-99M MAG-3 renal scintigraphy for predicting cisplatin induced nephrotoxicity in cancer patients

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Cisplatin, a nonclassic alkylating agent, is one of the most effective agents available for treating solid tumors. However, its clinical utility is compromised by the onset of severe dose-limiting toxicities, especially nephrotoxicity. In recent years several reports have confirmed that cystatin C demonstrates a better correlation with glomerular filtration rate than serum creatinine. In this study we compared serum cystatin C level with serum creatinine and renal scintigraphy. Serum cys-C, serum creatinine concentrations and 99mTc-MAG-3 scintigraphy were studied in 22 cisplatin-naive cancer patients before and 24 hours after cisplatin-based chemotherapy. Serum cystatin C (0.86±0.34 mg/dl vs 0.96±0.45 mg/dl) and creatinine levels (0.78±0.14 mg/L vs 0.82±0.20 mg/L) increased in cancer patients after chemotherapy, but these differences were not statistically significant ($p>0.05$). Semiquantitative variables of 99mTc-MAG-3 scintigraphy (T **, R 20/max*, Tmax**) significantly elevated after chemotherapy. (T *-min: 10.27±5.00 vs 16.17±9.40, R 20/max: 0.40±0.12 vs 0.67±0.45, Tmax-min: 5.40±4.01 vs 7.59±5.30: *$p<0.001$, **$p<0.01$). Significant correlation was found between pre- and post-therapy values of cystatin C and creatinine ($r=0.61$, $p<0.001$). There was no significant correlation between pre- and post-therapy values of T*, R 20/max and creatinine ($r=0.06$, $r=0.13$, $p>0.05$; respectively). Significant correlation was found between pre- and post-therapy values of T * and cys-C ($r=0.29$, $p<0.05$). No significant correlation was found between pre- and post-therapy values of R20/max and cys-C ($r=0.03$, $p>0.05$). These data suggest that MAG-3 scintigraphy is highly sensitive method to cisplatin-induced nephrotoxicity. The efficacy of cystatin C for early detection of cisplatin-induced nephrotoxicity may be superior compared with creatinine. However, additional long-term, wide scope studies are needed to determine a standard procedure for clinical usefulness of cystatin C.

1338 POSTER

## 99mTc-MIBI myocardial perfusion scintigraphy in the assessment of early cardiac effects of anthracycline cancer therapy

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Detection of early adverse cardiac effects after anthracycline cancer treatment may enable recognition of patients of risk of late cardiotoxicity at retreatment.

We investigated 26 patients/pts (age 32-69, median age 46,6) with breast cancer, before treatment and after 2 courses haemotherapy: Gr.I(n6) with CMF (cyclophosphamide,methotrexate,5 fluorouracil) and Gr.II (n20) with FEC therapy (5 fluorouracil, epirubicine, cyclophosphamide).

Investigation of myocardial perfusion with 99mTc-MIBI and evaluation of systolic function and LVEF (left ventricular ejection fraction) echocardiographicaly were performed. Myocardial perfusion scintigraphy was fulfilled on SPECT gamma camera Siemens,Diacam at rest condition after application of 370 MBq 99mTc-MIBI. Segmental tracer activity was analyzed quantitavely (Siemens Quantitative Heart Application)

Before treatment a total number of patients have normal myocardial perfusion and systolic function.After treat-ment we established 2 groups of patients: Gr.I (CMF)is a control group. A total number of patients (n6) had normal myocardial perfusion after treatment. Gr. II (n20)- FEC therapy: Gr.IIa-12 pts. had normal myocardial perfusion, normal systolic function of LV; Gr.IIb-2 pts. were with myocardial hypoperfusion, decreased LVEF; Gr.IIc- 5 pts.- with myocardial hypoperfusion, normal LVEF; GrIId- 1 pt with normal myocardial perfusion, decreased LVEF. Hypoperfused segments in pts GrIIb were severely hypoperfused- range 37%-43%, mean 40% as well as EF- range 40%-52%, mean 46% also showed decrease. Hypoperfused segments in pts Gr.IIc established mild to moderate hy-poperfusion range 58%-70%, mean 61%. The comparison between the two groups indicated the highest incidence of early cardiac adverse effects after anthracycline therapy.

It is concluded that evaluation of early cardiac effects from anthracycline cancer therapy with 99mTc-MIBI ap-pears to be feasible. In these pts an early identification of myocardial hypoperfusion after low doses anthracyclines may diminish the cardiac risk for cancer retreatment by means of follow up the cardiac status.

1339 POSTER

## The effect of prednisolone following whole brain irrdiation on blood-brain barrier of the mouse – In the view of acute change

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**Purpose:** The radiation induced blood-brain barrier (BBB) breakdown is of interest in the view of pathophysiological mechanism leading to development of acute brain edema. Gluticorticoids are widely used concurrently with radiotherapy for their putative salutary effect on brain edema. But the action mechanism of gluticorticoid on the afflicted brain remains for the most part an enigma. This study was tried to determine the peak time of radiation damage on BBB of mice. We also observed whether prednisolone can