1209 ORAL

STUDIES ON VITALITY OF ORAL EPITHELIAL CELLS DURING AND AFTER HIGH-DOSE CHEMOTHERAPY; A NEW ASSAY FOR QUANTITATION OF CHEMOTHERAPY-INDUCED MUCOSITIS

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Introduction: Patients receiving high-dose chemotherapy followed by stem cell transplantation are at risk of devastating mucositis. Most previous prevention strategies are evaluated by clinical judgment, such as the WHO scale. Our aim was to develop a quantitative *in vitro* assay for mucositis, that can be used for quantitation of such interventions. *Patients and Methods:* Nine patients with locally advanced breast carcinoma received after induction chemotherapy, high-dose chemotherapy with CTC (carboplatin 1600 mg/m^2, thiotepa 480 mg/m^2, cyclophosphamide 6 g/m^2 divided over four days) followed by peripheral stem cell transplantation. Prior to and twice weekly during CTC, oral washings with 10 mL sterile saline were obtained. Vitality of mucosal cells was determined by trypan blue dye exclusion. Leucocytes were counted by fluorescence microscopy after incubation with acridine orange. At the same days morphology of cells was assessed by buccal mucosa smears stained according to Papanicolaou. *Results:* The mean vitality of buccal cells increased after CTC with a significant difference on day 7 compared to pretreatment. During therapy there was a tendency from mature to immature cells in buccal mucosa smears. Oral leucocyte levels were closely correlated with the blood leucocyte counts. *Conclusions:* Vitality of buccal cells obtained by oral washings increases during high-dose chemotherapy. This is possibly due to desquamation of the upper oral mucosa layer, with a shift from mature to more immature cells. These data can be quantitated and this assay may therefore be useful in studies aimed at prevention of mucositis.

1210 ORAL

COMPLICATIONS OF VENOUS ACCESS PORT (VAP) IN PATIENTS WITH NON-SEMINOMATOUS TESTICULAR GERM CELL TUMOURS

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Introduction The complications related to the use of VAP's for the administration of CDDP based chemotherapy in patients with non-seminomatous testicular germ cell tumours (NSTGenCT) was retrospectively analyzed.

Patients & Methods During 1983–1993 128 VAP's (Infuse a Port, Infusaid) were implanted in 125 consecutive NSTGCT patients, median age 28 (range 16–55) yrs. Median VAP in situ time was 396 (range 7–1400) days.

Results 128 VAP's were together 50598 days in situ. In 23 pts 28 complications (21.9%) occurred. Complications were analyzed per 1000 VAP days (Ratio 0.55). Multivariant analysis showed increased risk of complications when VAP's were implanted during chemotherapy vs pre-chemotherapy ($P < .0005$), and local vs general anesthesia ($P < .05$).

Complication	Number	Ratio
Thrombosis	9 (7%)	0.18
Obstruction	7 (5.5%)	0.14
Catheter fracture	5 (3.9%)	0.10
Infection	4 (3.1%)	0.08
Skin necrosis	2 (1.6%)	0.04
Extravasation	1 (0.8%)	0.02

Conclusion VAP's are useful for the administration of chemotherapy in NSTGCT pts and should be implanted before chemotherapy is initiated to reduce the complication rate, especially thrombosis and obstruction.

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RANDOMISED DOUBLE-BLIND COMPARISON OF PAMIDRONATE OR CLODRONATE FOR HYPERCALCAEMIA OF MALIGNANCY: EFFECTS ON BONE METABOLISM MARKERS

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New and potentially more specific markers of bone resorption were recently identified: deoxypyridinoline (Dpd), pyridinoline (Pyd) (which are total cross-links) and the C-telopeptide of type I collagen (peptide-bound cross-links). We evaluated 32 hypercalcaemic pts. after 48 hr of intravenous rehydration who received either 90 mg pamidronate or 1500 mg clodronate as a 4 hr infusion. Serum and urine samples were collected at baseline, 2, 4, 7, 14, 21 and 28 days. We measured serum Ca, PO4 and PTH; and in a 2nd voided morning urine sample: urinary calcium (uCa), Dpd, Pyd (both by HPLC) and the C-telopeptide (Cross-laps) by an ELISA assay. Both bisphosphonates were effective treatments for hypercalcaemia, but the duration of normocalcaemia was longer after pamidronate (28 vs 14 days, $P = 0.01$). UCa (considered as the standard resorption marker) fell significantly in both arms partially reflecting inhibition of bone resorption, but also an increase in PTH. Dpd, Pyd and C-telopeptide had a significant larger and longer lasting decrease after pamidronate ($P < 0.01$). The C-telopeptide fall was significantly larger than Dpd or Pyd fall in both arms ($P < 0.01$). C-telopeptide is easier and faster to perform than Dpd and Pyd. The prolonged effect of pamidronate on hypercalcaemia is explained by the longer suppression of bone resorption than clodronate.

1212 POSTER

PROTECTION OF IRRADIATED HUMAN SKIN BY SELF-ADHESIVE, SILICONE-COATED POLYAMIDE NET DRESSING

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There is no established biological or pharmacological procedure to prevent acute skin reactions during irradiation. Mechanical protection of irradiated skin during treatment is therefore essential. Some silicone-coated materials developed for skin transplants may be beneficial to irradiated patients in this respect. In a prospective study, the tolerance of silicone-coated polyamide net was tested in 21 patients receiving radiotherapy due to malignant disease. In 7 patients the portal skin was intact and in 14 patients the portal included an epitheliolysis and a skin ulcer. The ability of silicone-coated net strips to adhere to irradiated skin and the local skin irritation under the adherent net was evaluated. Patient tolerance of dressing strips was good. There were no reactions to the adherent dressing net by non-irradiated skin. No additional skin irritation due to the tested material was observed in the irradiated region. The ulcers covered by silicone-coated dressings re-epithelialized quickly during radiotherapy. There was no injury to new epithelium during changes of dressing. Our results demonstrate that silicone-coated polyamide net dressings could be used for skin protection during irradiation. We expect that this material will facilitate the intensification of percutaneous radiotherapy.

1213 POSTER

DOUBLE-BLIND, COMPARATIVE TRIAL OF THE ANTIEMETIC EFFICACY OF TWO IV DOSES OF DOLASETRON MESILATE (DM) AND GRANISETRON (G) AFTER INFUSION OF HIGH-DOSE CISPLATIN CHEMOTHERAPY (CT)

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This 24-hour trial randomized 476 cancer patients at 29 centers to 1.8 or 2.4 mg/kg IV DM or G (3 mg) 30 minutes prior to $\geqslant$80 mg/m^2 IV cisplatin CT. Patients were stratified using gender and previous CT to four groups: male naive and non-naive and female naive and non-naive. Efficacy was measured using complete response (CR: 0 emetic episodes

[EE] and no rescue medication [RM]); CR + major response (CMR: 1–2 EE and no RM); ratings of nausea and satisfaction by patients on a 100 mm visual analog scale (VAS); and physician assessment of nausea severity and global efficacy on a discrete scale (DS: none, slight, good, excellent). CR rates were 54%, 47%, and 48%, respectively, for DM 1.8 and 2.4 mg/kg and G. CR rates for both DM doses were statistically equivalent to G and pairwise comparisons of CR rates between DM 1.8 mg/kg and G ($P = .0893$) and between the two DM doses ($P = .0602$) were not statistically significant. Equivalence between treatments was further confirmed by CMR, by median time to first EE/RM, by patient VAS assessments, by the rigorous CR + no nausea (<5 mm VAS) analysis, and by physician DS ratings. The efficacy of DM 1.8 and 2.4 mg/kg and G was similar in each of the four patient strata. There were no statistically significant differences in incidence of adverse events between treatments. Headache (≈ 25%) was the most frequently reported adverse event with each treatment. In conclusion, DM at doses of 1.8 and 2.4 mg/kg was equivalent to G in preventing nausea and emesis induced by high-dose cisplatin CT.

1214 POSTER

SUPPORTIVE CARE DURING HEAD AND NECK IRRADIATION: PERCUTANEOUS ENDOSCOPIC GASTROENTEROSTOMIE

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Patients with head and neck tumors undergoing chemo- and irradiation therapy are routinely receiving percutaneous endoscopic gastroenterostomie (PEG). Since PEGs are essential supportive measures we evaluated their availability, side effects including infection as well as comfort to the patient and follow up.

During September 1994 and February 1995 sixteen patients with head and neck cancer (maxillary sinus 1, larynx 2, pharynx 1, floor of mouth 7, tonsils 2, thyroid 1, hypopharynx 1; oesophagus 1 pt) were given a PEG. Side effects observed were (during following four weeks): infection (n = 5 pts, with streptococcus 2, proteus 1, acinetobacter 1, enterococcus, enterobacter 1, E. coli 2, candida 2 pts), subileus (n = 1 pts, no removal necessary), gastritis (n = 1 pts, three weeks treated, removal), nausea and vomiting (n = 5 pts, frequency > three times per day, treatment by metoclopramide during several weeks). Infections were treated with amoxicilline and clavulane acid (n = 2 pts), cefotaxime (n = 5 pts), ciprofloxacine (n = 1 pts), metronidazole (n = 2 pts), and ketoconazole (n = 4 pts).

Thus for, PEGs were used for median time of 12.5+ weeks (range, 1–22 weeks). No irradiation treatment combined with chemotherapy (carboplatin) has been delayed or cancelled due to events related to PEG placement. Contrary, treatments were finalized in most pts. (n = 13 pts, rapid tumor progression n = 3 pts) as planned and earlier weight loss was slowed down. Weight gain was observed in five of sixteen patients with locally extensive disease.

In summary, PEG application has tolerable side effects and seems warranted in pts with head and neck tumor prior to irradiation/chemotherapy.

1215 POSTER

TROPISETRON FOR PREVENTION OF NAUSEA AND VOMITING INDUCED BY IRRADIATION

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Oral tropisetron (trop) 5 mg/day was evaluated for its antiemetic and antidiarrhoeic effects in a pilot study in patients receiving abdominal and/or pelvic irradiation. Of the total 38 patients (36 gynecologic, one prostate, and one lymphoma) 10 received trop prophylactically for 5 weeks of irradiation, 10 received metoclopramide (meto) (3 × 20 mg/day) for the same purpose, and 18 were in the control arm and used no prophylactic antiemetic during irradiation. Treatment arms were comparable in age, body weight, cancer diagnosis, radiotherapy field, total radiation dose. Nausea was recorded as follows: Trop, 7 total and 3 major control; meto, 8 major and 2 no control; control arm, 14 major and 4 no control. Vomiting was recorded as follows: Trop, 10 total control; meto, 8 total and 2 minor control; control arm, 15 total, 1 minor and 2 no control. Diarrhoea was not reported in the two antiemetic arms, but, antidiarrhoeic medication was needed in 3/18 in the control arm. No major side effect was reported in the trop or meto arms. Trop is an effective antiemetic in prophylaxis of radiation induced nausea and vomiting, and seems to be well tolerated in conjunction with radiotherapy when used daily over five weeks.

1216 POSTER

EFFICACY OF ONDANSETRON AND METOCLOPRAMIDE (WITH DEXAMETHASONE): IN THE PREVENTION OF CARBOPLATIN-INDUCED EMESIS

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A double-blind, international, parallel-group study in 189 ovarian cancer patients compared the efficacy of ondansetron 8 mg iv and metoclopramide 60 mg iv both in combination with dexamethasone 20 mg iv in the prevention of carboplatin-induced emesis and nausea over days 1–3 following chemotherapy. The ondansetron regimen was significantly superior to the metoclopramide regimen on day 1 and days 1–3.

	Emesis (≤ 2 emetic episodes)		Nausea ∇ (none or mild)	
Regimen	Day 1	Days 1–3	Day 1	Days 1–3
Ond	97%*	87%*	97%*	80%*
Met	74%	66%	72%	65%

* $P < 0.001$; ∇ based on distribution of grades.

Fewer patients from the ondansetron regimen (13%) reported adverse events compared with the metoclopramide regimen (21%). The combination of ondansetron plus dexamethasone is a highly effective, well tolerated treatment in the prevention of carboplatin-induced emesis and nausea, and is significantly superior to metoclopramide plus dexamethasone.

1217 POSTER

DOUBLE-BLIND, COMPARATIVE TRIAL OF FOUR SINGLE ORAL DOSES OF DOLASETRON MESILATE (DM) AND MULTIPLE DOSES OF ONDANSETRON (OND) FOR EMESIS PREVENTION AFTER MODERATELY EMETOGENIC CHEMOTHERAPY (CT)

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This 24-hour trial randomized 398 cancer patients at 26 centers to 25, 50, 100, 200 mg DM or OND (8 mg × 4; 8 mg × 3 at four centers) prior to IV CT primarily with cyclophosphamide (≥600 mg/m^2), doxorubicin (≥40 mg/m^2), or carboplatin (≥300 mg/m^2). Efficacy was assessed by complete response (CR: 0 emetic episodes [EE] and no rescue medication [RM]); CR + major response (CMR: 1–2 EE and no RM); and patient ratings of nausea and satisfaction on a 100 mm visual analog scale (VAS). A statistically significant linear trend with dose was observed across the 25, 50, 100, 200 mg doses of DM ($P < 0.0001$) both for CR (45.0%, 49.4%, 60.5%, and 76.3%), respectively, and for CMR. The CR rate for OND was 72.3%. CR and CMR rates for DM 200 mg were equivalent to OND. Linear trends across the four DM doses were statistically significant for median time to first EE/RM, for patient VAS nausea-level scores, and for the combined parameter of CR + no nausea (<5 mm VAS), ($P < 0.0001$ for all parameters). For the stringent CR + no nausea test, DM 200 mg (63.8%) was numerically superior to OND (49.4%). DM and OND were equivalent in the safety analysis and there was no statistically significant trends with dose for adverse events with DM. In conclusion, a single oral dose of DM 200 mg was equivalent to multiple doses of OND in preventing nausea and emesis induced by moderately emetogenic CT.