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THE USE OF BISPHOSPHONATE (PAMIDRONATE) TREATMENT TO MODULATE FRACTURE REPAIR.

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Functional adaptation of the skeleton enables the mass and architecture of the bones to be optimised in response to changes in functional demand. Bone metastases are a serious problem of tumour disease, mechanical integrity of the skeleton is compromised and fractures often occur. Recent attempts to retard osteolysis in this situation include the use of bisphosphonates. The effects of these compounds on fracture repair are not well documented. This study tests the hypothesis that bisphosphonates will modify the remodelling phase of fracture repair and alter the mechanical strength of the healing bone. The effect of bisphosphonate (Pamidronate, Ciba-Geigy) on the healing of an osteotomy in the mid-diaphysis of the ovine tibia was evaluated, using an established model of fracture repair under rigid unilateral external fixation. The bisphosphonate, pamidronate, modulated indirect fracture repair producing an increase in the amount of callus and ultimate torsional strength, however, no effect was observed on the in vivo or post-mortem stiffness assessments. Histological examination revealed a reduction in the remodelling of callus and cortical fragments. The mechanical effects may result from an increased mass of callus rather than a difference in material characteristics.

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DEXAMETHASONE (DEX) IMPROVES THE EFFICACY OF GRANISETRON (GRAN) IN THE FIRST 24 HOURS FOLLOWING HIGH DOSE CISPLATIN (HDCP) CHEMOTHERAPY. J.Latreille, D.Stewart, F.Laberge, P.Hoskins, J.Rusthoven, E.McMurtrie, D.Warr, L.Yelle, D.Walde, F.Shepherd, H.Dhaliwal, B.Findlay, D.Mee*, J.Pater B. Zee, D. Johnston. National Cancer Institute of Canada, Clinical Trials Group, Kingston, Ontario, Canada and *SmithKline Beecham Pharma, Oakville, Ontario, Canada.

GRAN is a $5HT_3$ receptor antagonist that, when given alone as a single dose (80 μg/kg), was as effective as combination high dose metoclopramide, diphenhydramine and DEX in controlling nausea and vomiting (NV) associated with HDCP[1]. This randomized, double-blind, multicentre study was designed to evaluate whether DEX improves the efficacy of GRAN in controlling NV during the first 24 hours in cancer patients (pts) receiving HDCP ($\geq$ 50 mg/m^2). All 300 pts received GRAN 3 mg IV in a 15 minute infusion completed 5 minutes prior to HDCP and 1 mg PO at +6 and +12 hours. One hundred pts (group 1) received no additional antiemetic while 200 pts (group 2) received DEX 10 mg IV prechemotherapy. Pts completed a self-report diary every six hours with a question pertaining to number of vomiting episodes and a linear analogue scale to measure nausea severity and duration, anxiety and drowsiness. Both groups were balanced as to age, sex, performance status, disease site and alcohol intake. Eleven pts were not assessed due to protocol violations, 4 had missing diaries, 3 were withdrawn prior to treatment and data is due on 17. Of the 265 evaluable pts, complete protection (0 V episodes) was significantly higher in group 2 (65%) than in group 1 (39%)(p=0.0001), while partial protection (0-2 V episodes) was achieved in 85% of pts in the plus DEX group vs 65% in group 1 (p=0.0005). The average nausea severity during the first 24 hours for group 2 vs group 1 are 9mm and 19mm respectively (p=0.0001). Drowsiness was significantly greater in group 1 (31mm vs 15mm, p=0.0001). In conclusion, dexamethasone markedly enhances the antiemetic efficacy of granisetron for acute onset emesis in HDCP.

1. P. Venner. Proc ASCO. Vol 9:1238, 1990.

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Bronchoalveolar Lavage in the Diagnosis of Pneumocystis Carinii Pneumonia in Patients with Hematologic Malignancies

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We examined 71 patients with hematological malignancies because of temperatures,cough,asthma,and/or pathological physical finding in the lungs,and/or pathological x-ray finding. In these patients bronchoalveolar lavage /BAL/ by altogether 200 ml of saline was performed and the bronchoalveolar fluid submitted to a complex examination. In 9 patients Pneumocystis carinii infection was proved. The PC infection was never single,it was always combined with other pathogens. All the patients were treated with trimethoprim and sulphametoxazol or together with amphotericin B,antibiotics and virostatics if need be. In 7 patients pneumonia was cured,2 patients suffering from a not easily manageable basic disease died.PC infection cannot be prognosticated on the basis of any clinical or laboratory data.BAL seems to us to be the only reliable method of proving PC infection.

Keywords: Pneumocystis Carinii,Bronchoalveolar Lavage

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HYPERSENSITIVITY REACTIONS TO CARBOPLATIN

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In appr. 30 pts carboplatin (carbo) hypersensitivity has been reported - we observed two pts (age 57 and 64) with prior uncomplicated carbo treatment, who developed life-threatening reactions with pruritus, nausea, vomiting, rash, facial and oral edema, angina pectoris, tachycardia, hypotension, dyspnea, abdominal pain (1), diarrhea (1), and anxiety. Both pts recovered after treatment with high-dose corticoids, atropin, volume substitution, and antihistamines. Intracutaneous tests gave positive results in both pts and negative results in 5 controls receiving carbo. No delayed reactions were observed. IgE levels were normal. One pt was rechallenged with premedication but symptoms recurred. Both pts tolerated cisplatin well.

Conclusions: 1. Hypersensitivity reactions to carbo can be severe. 2. Diagnosis of relevant events is difficult as symptoms resemble side-effects of chemotherapy. 3. Intracutaneous testing might help to establish the diagnosis - sensitivity and specificity will have to be determined. 4. In most cases, crossover to cisplatin containing regimens is feasible.

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A PLACEBO CONTROLLED DOUBLE-BLIND RANDOMISED CROSSOVER STUDY COMPARING GRANISETRON WITH GRANISETRON PLUS DEXAMETHASONE.

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We have investigated whether dexamethasone (dex) increased the antiemetic activity of granisetron (G), a highly selective $5HT_3$ receptor antagonist. G, 3 mg i.v. plus placebo was compared with G plus dex 20 mg i.v. in patients who received emetogenic chemotherapy including i.v. cisplatin, carboplatin, dacarbazine, cyclophosphamide, doxorubicin or epirubicin.

To date (31-JAN-93), 98 patients (56 male, 42 female; median age=56 [range 18-86] years) have been enrolled, with 16 patients ongoing. Randomisation codes will be broken after completion of the study. The cumulative antiemetic complete response rates (no vomiting +/- mild nausea) for the first day of chemotherapy was 79 % for patients on their first session and 82 % for 67 patients on their second session. Thirty-one patients were withdrawn, 7 due to lack of efficacy, 7 due to change of chemotherapy and 17 due to other reasons. 17 patients had expressed a preference for their first chemotherapy session, 23 their second and 27 expressed no preference. Patient preference appeared to be correlated (r=0.49, p< 0.001) to first day complete response rate. Our data show that a very high overall antiemetic complete response rate has been achieved and only 7 patients (7 %) were withdrawn due to lack of antiemetic efficacy.This study was supported by SmithKline Beecham and E. Merck (Darmstadt)

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AN OBSERVATION OF THE USE OF KYTRIL (GRANISETRON) IN CLINICAL PRACTICE IN SWITZERLAND.

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Forty-nine Swiss oncologists at 40 centres were surveyed on their use of Kytril (Granisetron), a highly selective $5HT_3$ receptor antagonist for the prevention and treatment of chemotherapy induced emesis. Oncologists were instructed to follow the official patient prescribing instructions on use and administration of Kytril, presented as commercially available ampoules each containing 3mg granisetron. Data was collected regarding patient age, gender, number of doses of Kytril given, number of days of chemotherapy treatment and adverse experiences irrespective of causality. 278 patients (102 male, 176 female) were treated. Results on Kytril use are given below.

	mean±SD	min.	max.	mode	median
Patients age (years)	56 ±14	16	92	63	56
Duration of chemotherapy treatment (days)	2.9 ±2.9	1	25	1	2
Total number of Kytril doses per patient	3.77±4.2	1	37	1	3
Number of daily doses of Kytril per patient	1.3 ±0.64	0.7	5.0	1	1

Adverse experiences (AEs) were reported by 33 patients. There were 11 reports of headache (3.9%), 17 reports of nausea/vomiting (7%), 3 reports of constipation (1%) and two reports each of fever, flushing and migraine respectively (1%). No severe AEs or deaths were reported.

In 72.5% of patients a single ampoule of Kytril was used per day. Despite some physicians following alternative dosing schedules to those recommended, the adverse event profile reported in this survey was low.