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THE EFFECT OF PAMIDRONATE (APD) ON THE MECHANICAL PROPERTIES OF CANINE BONE.

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APD is used in the treatment of hypercalcemia of malignancy, Paget's disease of bone and osteoporosis to prevent bone resorption. In a 3 months study with intermittent injections of APD in dogs, we found that this treatment did not change the mechanical properties of cortical bone either in torsion or in bending. In contrast, APD treatment increased the compressive stiffness and torsional strength of trabecular specimen taken from the vertebrae of the same dogs. In one year study of oral administration of various doses of APD we found a linear increase in the elastic modulus of trabecular bone with the square root of the dose administered. Finally, in a 2 year study (1 year with APD administration and 1 year recovery) we found no difference in the mechanical properties of cortical bone among various doses.

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ANTI-EMETIC EFFICACY & TOLERABILITY OF TROPISETRON IN PATIENTS (PTS) CONDITIONED WITH HIGH DOSE CHEMORADIOTHERAPY (HDC) PRE-BONE MARROW TRANSPLANTATION (BMT).

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Nausea and vomiting (N&V) are very distressing side effects of HDC. BMT conditioning consists of highly emetogenic HDC with or without total body irradiation (TBI). Marked improvement in N&V control was noted since introduction of a new class of antiemetic drugs - 5 HT3 receptor antagonists. Tropisetron (ICS 205-930) is highly potent and selective, and a single 5 mg IV dose has been shown to control N&V in cancer patients (pts). We evaluated efficacy and safety of a single dose in controlling N&V in pts receiving HDC pre-BMT. Its antiemetic efficacy was investigated in a non-homogenous cohort in an open and uncontrolled study. Of 11 pts, 9 (81%) showed complete or major control, with 1 (9%) minor control and 1 (9%) failure. Most common adverse events included diarrhea (46%) and headache (18%). No pts were withdrawn due to adverse effects. We conclude that one 5 mg IV dose of tropisetron is highly effective against HDC with and without TBI-induced N&V in BMT pts. A larger randomized study is warranted to confirm our preliminary results.

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"IMPLANTABLE PORT-CATHETER SYSTEM FOR CHEMOTHERAPY CANCER TREATMENT"

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Between July 1989 and July 1992 100 chest placed in subcutaneous subclavian region ports system, with a 16 french central venous catheters were implanted in adult patients with cancer diagnosis, for chemotherapy/inmunotherapy infusion. The external jugular was the most used vascular acces. The chosen device was the cordis miniport*. With a median duration of implantation, to date, of 20 months, more than 900 polychemotherapy cycles were administered, including vesicant and nonvesicant drugs, and inmunotherapy as « interferon and interleukin-2. All them in differents schedules from weekly to 5 days continuos infusion. The patients acceptance was uniformly excelent, and very few ports/catheters related complications episodes were detected; only slight bleeding at the venipuncture site, ecchymoses, five bacterial port infeccion without sepsis or need of explantation of the system. No thrombosis, important funotional troubles, ball-valve effect were seen. Only the members of the team used the devices (surgeons, oncologyst, nurses) and once after each treatment or monthly (control pts.), the system was washed with saline heparinizated solution. In spite of variables reasons to access, chemo or inmunotherapy, antibiotics, parenteral nutrition, transfusions, routine blood collections, or contrast substances for C.T. scans, the results shows the advantage of using this type of ports, because of cosmetics, clinical and cost/effects reazons in cancer patients.

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PIPERACILLIN-TAZOBACTAM AND AMIKACIN (PT-A) AS EMPIRICAL THERAPY FOR FEVER IN GRANULOCYTOPENIC CANCER PATIENTS (PTS)

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Tazobactam, a new beta-lactamase inhibitor, extends the broad spectrum of Piperacillin to include many beta-lactamase producing bacteria. Hospitalised pts with neutropenia (WBC <1000/mm3) and fever were given PT 4g/0.5g tid and A 15 mg/kg/day, and were evaluable if treated for at least 7 days (except for failure which could be established after 3 days). From 6/91 to 11/92, 40 of 56 treated febrile episodes proved evaluable (corresponding to 35 pts, median age 44); underlying condition was acute leukemia in 90%, median WBC count at study entry was 300/mm^3. There were 21 microbiologically documented infections, 13 of which with bacteremia (5 gram-negative). Sucess rate without modification was 30%(12/40). Response was significantly different according to length of leukopenia (87.5 vs 15.6% for pts with WBC<1000 for less and more than a week respectively) and degree of leukopenia (57% if WBC 500 to 1000 at entry vs 15.3% if <500) (both $p<0.05$). All 28 cases classified as failures had modifications of protocol treatment, most (23) consisting of the addition of Vancomycin. Overall mortality was 20%; no death occured in the first 3 days of true empirical therapy, and all but one occured off-protocol treatment. In 55 episodes evaluable for toxicity, side effects (skin 2,vomiting 5,diarrhea 4,hepatic 6) were grade 1/2, except for 2 cases of grade 3 vomiting. This regimen proved to be well tolerated and deserves further study in febrile neutropenic pts.

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EFFICACY AND TOLERABILITY OF A NEW $5HT_3$-ANTAGONIST, DAU 6215 CL, ON EMESIS OCCURRING IN THE FIRST 24 HRS AFTER CISPLATIN ADMINISTRATION.

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Emesis, a clinically relevant side effect of anticancer therapy, can be effectively prevented by $5HT_3$ receptors antagonists both in animals and in men. In this dose range finding, open label study DAU 6215 CL, a new $5HT_3$-antagonist, was given as a single 15 mins i.v. infusion to cancer patients (pts) at their first course with high dose cisplatin (≥ 50 mg/m²) in order to test its efficacy in the prophylaxis of emesis occurring in the first 24 hours after chemotherapy. Median cisplatin dose was 100 mg/m² b.s. (range 50-120). Ascending doses of 17, 35, 140 and 280 μg/kg body weight DAU 6215 CL were given to 5 subsequent groups of pts, respectively. Response to antiemetic regimen was graded as: *complete* = 0 emetic episodes (eps); *major* = 1-2 eps; *minor* = 3-5 eps; *failure* = > 5 eps or rescue therapy. Complete response was obtained in 0/7 pts treated with 17 μg/kg, 3/8 pts with 35 μg/kg, 2/8 pts with 70 μg/kg, 6/8 pts with 140 μg/kg and 2/7 pts with 280 μg/kg. DAU 6215 CL was well tolerated and no dose related adverse event occurred. A single dose of 140 μg/kg DAU 6215 CL should be tested in further clinical trials.

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PERSISTENCE OF EFFICACY OF ONDANSETRON (OND) PLUS DEXAMETHASONE (DEX) VS METOCLOPRAMIDE (MTC) PLUS DEX AND DIPHENHYDRAMINE (DIP) IN ACUTE EMESIS DURING THREE CONSECUTIVE CYCLES OF CISPLATIN (CDDP) CHEMOTHERAPY (CT).

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The efficacy and tolerability of two antiemetic regimens were analyzed by a prospective randomized double-blind multicenter study in cancer patients (pts) submitted to repeated cycles of CDDP CT. 287 pts receiving CDDP for the first time (≥ 50 mg/m2) were randomly assigned to receive for three consecutive cycles the same antiemetic treatment consisting of: OND 0.15 mg/kg ½ hr before and 1½ and 3½ hrs after CDDP plus DEX 20 mg 45 mins before CDDP or MTC 3 mg/kg ½ hr before and 1½ hrs after CDDP + DEX as above + DIP 50 mg 47 mins before CDDP. With respect to pts treated with MTC+DEX+DIP, those receiving OND+DEX achieved significantly greater complete protection in all three cycles of CT from vomiting (V) (78.7% vs 59.6%, p<0.002 at first cycle; 73.4% vs 51.0%, p <0.002 at second cycle; 73.7% vs 47.5%, p<0.001 at third cycle) but not from nausea (N). Capability of OND+DEX to protect pts from V at first cycle of CT did not change in subsequent cycles, whereas there was a significant reduction of complete protection from N and from both N and V. With MTC+DEX+DIP a significant and greater reduction of complete protection from V, N and both N and V was shown. Protection obtained in previous cycles of CT was shown as the most important prognostic factor for the probability of V, N and both N and V in the three cycles of CT. Adverse events were significantly less frequent with OND+DEX during the three cycles of CT, but no cumulative toxic effects were found with either treatment. In conclusion OND+DEX was significantly more efficacious and better tolerated than MTC+DEX+DIP during three cycles of CT. Furthermore, its efficacy is maintained in susbsequent cycles, at least for V, in contrast to the MTC+DEX+DIP regimen.