5-hydroxytryptamine-3 (5-HT3) serotonin receptor antagonist, dexamethasone (DEX), and aprepitant is recommended before chemotherapy of high emetic risk. 5-HT3 serotonin receptor antagonist has been great benefit in the prevention of acute emesis, especially for moderate to high emetogenic chemotherapy. Granisetron (GRN) is one of the worldwide used 5-HT3 serotonin receptor antagonists. 1 mg or 0.01 mg/kg GRN dose is recommended by antiemetic guidelines. In Japan, high dose GRN (3 mg) combined with DEX is routinely used, aprepitant has not been approved yet. We conducted randomized controlled trial to compare the two different doses of GRN (3 mg VS 1 mg) in prevention from acute emesis.
Material and Methods: Patients who receiving moderate or high emetogenic chemotherapy in Japan were randomly assigned to GRN 3 mg (arm A) or 1 mg (arm B) with adequate amount of DEX according to emetic risk category. Patients were stratified according to previous history of chemotherapy, regimen (cisplatin containing or not) and institutions. Primary endpoint was proportion of patients with complete response (defined as no vomiting episodes and no use of rescue medication) in the first 24 hours after chemotherapy. Non-inferiority margin was predefined in this study protocol as a 15% difference between groups in the proportion of patients with complete response. This study is registered with UMIN, number UMIN000000984.
Result: From January 2008 to January 2009, 365 patients from 10 medical centers were recruited. 183 patients were assigned to arm A and 182 to arm B. In the first 24 hours after chemotherapy, complete response was achieved by 90 and 88 percent of patients, respectively. Non-inferiority was proven statistically. In subgroup analysis, no favorable trend was detected. Antiemetic treatment was equally well tolerated, and no significant difference was found in the incidence of adverse events.
Conclusions: GRN 1 mg combined with DEX is not inferior to 3 mg combined with DEX for the prevention of acute emesis induced by moderate or high emetogenic chemotherapy. Our study confirms no differences in both groups. We think this is the first randomized controlled trial, presenting non-inferiority between 3 mg and 1 mg GRN statistically. Consequently, 1 mg dose of GRN combined with DEX should be considered the most appropriate prophylactic regimen for the prevention of acute emesis.

3081 POSTER

Reduced therapy-related fatigue in mice with nab-paclitaxel as compared with Cremophor-based paclitaxel

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Background: The frequent occurrence of fatigue in cancer patients and survivors negatively impacts the quality of life and clinical outcome. *Nab*-paclitaxel (Abraxane®) is an albumin-bound 130-nm particle form of paclitaxel that demonstrated higher efficacy and was well tolerated compared to Cremophor EL-based paclitaxel (Taxol®) in clinical trials for metastatic breast cancer. In this study, we developed a mouse model for quantifying fatigue and objectively compared fatigue induced by Abraxane and Taxol.
Materials and Methods: Female BALBIcJ mice were implanted with a telemetry device that transmitted information on both core temperature and horizontal locomotor activity. Activity, wheel running, temperature, food intake, and body weight were monitored before, during, and after administration of Taxol or Abraxane (10 mg/kg iv, qd × 5; n = 9/group). To determine the potential causes of chemotherapy-induced fatigue, measurements were conducted for the levels of proinflammatory cytokines, anemia, general debilitation, neuromuscular impairment, and sleep disturbance.
Results: Taxol and Abraxane both reduced horizontal locomotor activity and wheel running in mice. With either drug, mice showed essentially normal activity during the first two hours of the dark phase. However, activity fell below normal for both measures in the remainder of the dark phase during the drug administration and the first week after chemotherapy. Mice treated with Abraxane resumed normal amounts of dark-phase activity 2 weeks after treatment, whereas mice treated with Taxol remained depressed until week 4 after treatment. During periods of fatigue, mice did not show anemia, elevated serum concentrations of proinflammatory sleep-modulatory cytokines, or disturbed sleep. However, mild general debilitation (i.e., weight loss, anorexia, and hypothermia) and mild neuromuscular impairment were observed.
Conclusions: This study provides a reliable model for quantatively measuring chemotherapy-induced fatigue. The combined assessment of running wheel activity and horizontal locomotor activity demonstrated that mice treated with taxane chemotherapy developed fatigue. Compared with Taxol, Abraxane treatment resulted in less fatigue and a faster recovery, potentially due to its rapid tissue distribution and the absence of toxic solvents. These observations are consistent with clinical data for Abraxane which shows a more rapid resolution of peripheral neuropathy compared with Taxol.

3082 POSTER

Efficacy of a survaillance dental programm on prevention of osteonecrosis of the jaw in cancer patients with bone metastases: a single institution preliminary experience

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Background: osteonecrosis of the jaw (ONJ) is a dismal event associated with bisphosphonates (BPs) therapy for cancer patients with bone metastases (BM). We designed a preventive dental programme during or prior to BPs therapy to attempt a reduction in the risk of ONJ.
Patients and Methods: Starting from February 2007 through February 2009, 137 consecutive cancer patients with BM scheduled for BPs therapy (zoledronic acid, pamidronate or ibandronate) were prospectively offered an educational training on oral hygiene and an odontoiatric evaluation (dental visit and orthopantomography of the jaw) to detect odontoiatric risk factors and treat them, both at baseline and every six months afterwards. 46 patients (33.6%) had already received a median of 7 monthly BPs (range 1−48) at the time of baseline evaluation, while 91 patients (66.4%) had not yet been treated. Both groups of patients were offered the same preventive programme.
Results: Overall, the total patient population received median of 8 months of BPs (range 1- 48): 12 months (range 1- 48) for the pretreated and 5 (range 1−23) for the not-pretreated population of patients, respectively. Only two cases of ONJ were described, both in the pretreated group. The first one was diagnosed after 3 cycles of zoledronic acid and was related to a recent dental avulsion. Of note, this patient had been treated with risendronate for a long period for osteoporosis just before the development of BM. The other case was observed after 7 cycles of zoledronic acid in a patient with BM from kidney cancer while on concomitant treatment with sunitinib. Because there are some evidences that anti-angiogenic therapies may increased ONJ risk, we cannot exclude an interaction of the therapy with preexisting risk factors.
Conclusions: Our prospective single-institution experience of systematic adoption of a preventive dental programme for patients scheduled to undergo BPs therapy for BM seems to confirm reported literature evidence of the importance of odontoiatric evaluation and treatment before starting BPs therapy in reducing the risk of ONJ.

3083 POSTER

Patients experience with treatments of chemotherapy induced anemia (CIA) and myelodysplastic syndromes (MDS)

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Background: Anemia, a common hematologic complication of cancer and cytotoxic treatments, is often treated with erythropoiesis stimulating agents (ESAs) and red blood cell (RBC) transfusions. While some studies have explored patient treatment experience (e.g., routine disruption, and emotional/social strain), gaps remain in the literature. The objective of this study was to assess anemia treatment experiences from patients' perspectives and to explore potential concepts for inclusion in new anemia treatment experience instruments.
Material and Methods: Focus groups and individual interviews were conducted with adult patients with CIA or MDS receiving ESAs and/or RBC transfusions within 28 days prior to interview. Domains explored in the discussion guide included administration pain/discomfort, temporal effects, treatment outcomes, out of pocket (OOP) expenses, effects on employment, and social support. Transcripts were coded and qualitatively analyzed with Atlas.Ti. Sociodemographic and clinical information was collected through questionnaires and analyzed descriptively.
Results: 6 focus groups and 10 individual interviews were conducted with 28 patients (mean age: 68, SD age: 12, female: 54%, CIA: 50%, MDS: 50%, ESA only: 57%, ESA and transfusion: 43%).
Patients mentioned temporary stinging or burning sensation from ESA and discomfort of keeping their arms in a specific position during transfusion. Timing and location issues were discussed. Many CIA patients received ESAs on the same day and at the same clinical site as chemotherapy. All transfusions received by CIA patients were on different days than chemotherapy. On average, ESAs took less than 1 minute to administer and the entire visits took less than 1 hour. Transfusion patients had blood cross-matched at least 1 day before treatment and transfusions took 6+ hours to complete. As for treatment effects, patients focused on how quickly they

felt improvements in energy levels and emotional well-being. Insurance co-pays and transportation costs were OOP expenses for patients. Patients discussed impacts on their employment such as work absences. Some patients reported safety concerns with treatments. Transportation and household chores were mentioned as two types of tangible assistance utilized.
Conclusions: Overall, patients discussed the timing, location, physical and emotional effects, and social support needs. The key concepts identified in this study should be considered in developing anemia treatment experience instruments.

3084 POSTER

Prior oral treatment with lectin ATL-104 limited intestinal damage caused in rats by 5-fluorouracil and repair of the epithelium

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Background: Anti-cancer treatments disrupt the alimentary tract, leading to epithelial breakdown and ulceration (dose-limiting mucositis). Treatment with ATL-104 reduced the duration/severity of oral mucositis in peripheral blood SCT patients (Hunter *et al*, 2008. Bone Marrow Transplantation 10 Nov 08, 1−7.). The mode of action of ATL-104 in ameliorating intestinal damage caused by 5-Fluorouracil (5FU) has been investigated.
Materials and Methods: Rats (5/group) were given ATL-104 orally (200 mg/kg) once daily for up to 3 days (day −1, days −1 & −2 or days −1, −2 & −3), single dose 5FU (150 mg/kg, ip) on day 0 and euthanased and small intestine collected up to 4 days post-5FU. Standard histology was done.
Results: Rapid loss of crypt cells and collapse of the crypts and villi occurred after dosing with 5FU. At 2 days, few dividing cells were present and crypts were not readily discernible. The sub-epithelial myofibroblast sheath [ISEMF] was also severely disrupted. Cell division re-started at around 3 days and an extensive dividing cell population was re-established by 4 days. However, the ISEMF was not restored. As a result, the regenerating crypts and villi remained disorganised.
Pre-treatment with ATL-104 ameliorated the effects of 5FU. Crypt epithelial cell loss and villus collapse occurred as with 5FU alone, but was less marked. By 2 days, micro-crypts (clusters of dividing, goblet & Paneth cells in a myofibroblast sheath) were evident. By 4 days, the crypt epithelium and ISEMF had expanded and villi were returning to normal.
Conclusions: Treatment of rats with ATL-104 caused adaptative changes to intestinal epithelial and sub-epithelial metabolism. In combination, these enabled the gut to deal more effectively with 5FU. Thus, damage caused by 5FU was reduced and restoration of normal gut structure was facilitated. Pre-treatment with ATL-104 for 1 day (day −1 only) gave protection. However, treatment for 2 or 3 days was more effective (3 d >2 d >1 d >0 d).
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3085 POSTER

Management of chest wall pain after breast cancer surgery and radiotherapy. What is the evidence?

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Background: Mastectomy or Breast conserving surgery (BCS) is the usual method of surgical management of breast cancer. However with BCS Radiotherapy (DXT) is usually indicated either for invasive or in-situ disease. Even in patients undergoing mastectomy radiotherapy may be indicated. Up to 50% of patients undergoing radiotherapy following BCS or mastectomy complain of chest wall pain/discomfort. The exact cause is unknown and may be multifactorial. Most cases of chronic pain in post radiotherapy patients with breast cancer is considered as a part of sequelae of radiotherapy by inducing neural damage and fibrosis. There is no effective management and patients are advised to use analgesia with little effect. The aim of the study was to evaluate the literature about the chest wall pain after breast cancer surgery and radiotherapy and assess the evidence if any to correctly manage this problem.
Material and Methods: The authors reviewed MEDLINE, COCHRANE database, EMBASE databases, and online resources published in English between January 1960 and April 2009 as well as relevant pain management books available were searched. Local Breast Nurse Specialists were contacted with regards to management of this problem. All the literature was reviewed by the authors.
Results: There exists little if any reference in literature to address this issue. Local signs are frequent after chest wall DXT but rarely severe (9% of patients). Chronic moderate to severe pain occurs in 12% of BCS and radiotherapy patients compared to 12−51% of the breast cancer survivors independently of management option. The extent of axillary dissection was found as main factor predicting pain. There are no designated tools for assessment of this pain or record database kept by Breast Care Nurses team in most hospitals.
Conclusion: There is no management protocol for patients with such pain. Chest wall pain after Breast cancer surgery and radiotherapy seems to be frequent but not debilitating side effect. However, further clinical studies or prospective trials are needed to address this issue for definite conclusions.

3086 POSTER

Efficacy of casopitant, a novel NK-1 receptor antagonist, for antiemesis over repeated cycles of moderately emetogenic therapy

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Background: Casopitant, a novel neurokinin (NK)-1 receptor antagonist, is in development for prevention of chemotherapy-induced nausea and vomiting (CINV). Phase II and phase III studies have shown that casopitant is effective in patients receiving highly and moderately emetogenic chemotherapy (HEC, MEC). Data from a phase III, randomized, double-blind, placebo-controlled study in MEC was used to evaluate whether the efficacy of casopitant in cycle 1 was maintained during 3 subsequent cycles.
Methods: Patients received antiemetic therapy including ondansetron and dexamethasone, alone or together with one of the following casopitant doses: single-dose 150 mg oral; 3-day intravenous (IV)/oral (90 mg IV/50 mg oral/50 mg oral); or 3-day oral (150 mg/50 mg/50 mg). The primary endpoint was complete response (CR, defined as no vomiting/retching or rescue medications) over the first 120 hours [CR(0–120)] after initiation of MEC. Post hoc analysis of CR data from the first 4 cycles was used to evaluate treatment effect over repeated cycles.
Results: In patients receiving anthracycline/cyclophosphamide-based MEC (N = 1933), the higher overall CR(0–120) rates observed in cycle 1 were maintained for at least 3 subsequent cycles with the single-dose oral (odds ratio [OR] 2.02; 98.3% confidence interval [CI] 1.53−2.68); 3-day IV/oral (OR 2.05; 98.3% CI 1.55−2.7); and 3-day oral (OR 1.98; 98.3% CI 1.50−2.61) casopitant regimens. In addition, for patients who did not respond in the previous chemotherapy cycle, CR(0–120) was achieved in 35% to 44% of patients receiving single-dose casopitant in the subsequent cycle; 37% to 49% of those receiving the 3-day IV/oral regimen; and 35% to 39% of those receiving the 3-day oral regimen vs 26% to 33% of control subjects.
Conclusions: The higher overall CR(0–120) rates of CINV achieved with casopitant in cycle 1 of MEC were maintained over repeated chemotherapy cycles. The improved CR rate associated with casopitant treatment was not dependent on results of the previous cycle.

3087 POSTER

The NK-1 antagonist aprepitant (APR) in combination with granisetron and dexamethasone in high dose chemotherapy (HDC)

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Background: 5-HT_3 receptor antagonists (RA) plus dexamethasone (DEX) are still the standard antiemetic therapy in patients receiving HDC. However, in the few available small studies complete protection from nausea and vomiting was only achieved in a small proportion of patients. The role of aprepitant in HDC remains to be defined.
Methods: In this study, pts. with HDC received APR orally 125 mg d1, 80 mg consecutive days, granisetron (GRAN) 1 mg i.v. daily and DEX 8 mg i.v. daily for prevention of acute chemotherapy induced nausea and vomiting (CINV) and APR 80 mg and DEX 8 mg for 2 days for delayed CINV. Endpoints were complete response (CR, no vomiting & no use of rescue therapy) in the acute (during days of HDC) delayed (day 1 until 5 days after end of HDC) and overall (acute and delayed) phase. Acute and delayed nausea were also evaluated.
Results: To date 42 pts. (f/m 10/32 pts.; median age 39.4 y) with various types of cancers (testicular cancer 26 pts., sarcoma 9 pts., multiple myeloma 6 pts. and CUP 1 pt.) were included. 26 pts. (62%) received High dose (HD)-PICE (paclitaxel, ifosfamide, carboplatin, etoposide; d1−3), 10 pts. (23.7%) HD-ICE (ifosfamide, carboplatin, etoposide; d1−3) and 6 pts. (14.3%) HD melphalan; d1−2. The median duration of HDC was 2.9 days.