3062 POSTER

Significant Pain Relief With Loading Dose Zoledronic Acid in Bone Metastases, Is Only Seen in Patients With Elevated Initial Serum C Telopeptide (CTX)

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Aim: Recent publications [1−3] drew attention to the analgesic effect of loading dose of ibandronate. The analgesic effect of loading dose Zoledronic acid (ZA) is not as well documented and predictive biochemical markers for its analgesic effect are enterily lacking.
Methods: Patients with painful bone metastases requiring analgesics, were treated with loading dose zoledronic acid (4 mg/day on 4 subsequent days). VAS score and analgesic consumption were evaluated. C telopeptide at baseline and on day 5 were evaluated.
Patients: 20 patients were treated from 10/2009 to 10/2010. All patients had diffuse bone metastases and severe pain (VAS >4);initially even resistant to opioids. Median age 74 (range 44−90). Tumour types: prostate 5, lymphoma 2, myeloma 2, breast 3, lung 3, bladder 1, kidney 1. VAS evaluation was done prior to bisphosphonate administration and on day 4 (24 hours after the last administration) serum CTX was determined at start of treatment and at day 4.
Results: Median VAS dropped from 8.0/10 to 3.4/10 after administration of ZA. This effect was seen across tumour types, and also in sites of prior irradiation. There were no side effects noted, nor subsequent renal function deterioration. Best analgesia was seen in patients with highly elevated CTX (>800) initially, in all these responding patients with a mean reduction of 62% from baseline CTX ($p < 0.001$). Three patients with normal CTX had no analgesic effect of this administration nor decrease of CTX.
Conclusion: In symptomatic bone metastases with significant pain, refractory to standard analgesics and radiotherapy, loading dose ZA represents a simple and non toxic treatment to obtain significant pain relief in a very short time. Its analgesic effect is limited to patients with massive osteoclast activation cq. high initial serum CTX. The pain reduction is proportionally correlated with the reduction of CTX.

References

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3063 POSTER

Metabolic Syndrome (MetS) in Metastatic (m) Colorectal Cancer (CRC) Patients (pts) Might Delay the Onset of Cachexia

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Background: It has been proven that the presence of MetS (hypertension, obesity, dyslipidemia, diabetes) increases the risk of CRC recurrence in radically resected pts. We aimed at evaluating whether increased values of MetS parameters also confer a worse prognosis in pts with established mCRC.
Materials and Methods: Consecutive mCRC pts treated at our Institution between March 2006 and December 2009 with standard first line chemotherapy (CT) and available baseline assessment (i.e. within two weeks before starting treatment) of Blood Pressure (BP), Body Mass Index (BMI), cholesterolemia, triglyceridemia and glycemia entered into the study. Primary endpoint was median overall survival (mOS) for both univariate and multivariate analyses.
Results: 152 pts were included (Male:Female, 95:47, median age 64, range 29−85 years). 89% of pts were treated with poly-CT (fluorouracil plus either irinotecan or oxaliplatin), 55% received a monoclonal antibody (bevacizumab or cetuximab). Baseline BP, BMI and cholesterolemia above median values (that were 130/70 mmHg, 25 kg/m^2 and 180 mg/dL, respectively) conferred a nonsignificant favourable prognosis (mOS 25.9 v 20.3, 24.6 v 18.3 and 28.4 v 19.3 months, respectively), whilst triglyceridemia or glycemia above the median (that was 125 mg/dl and 97 mg/dl, respectively) were not associated with improved mOS. When all the MetS parameters were combined together for survival analysis, pts with 4 to 5 parameters with values above the median had a statistically significant longer survival as compared to pts with 0 to 3 above-median values (mOS 34.1 v 19.2 months, respectively, HR 0.49, 95% CI 0.29–0.82, p 0.02). Significance of MetS parameters was retained in the multivariate analysis together with type of CT (mono- v poly-CT), ECOG PS (0−1 v >1), number of metastatic sites (0−1 v >1) and baseline WBC (> v <10000/mm^3).
Conclusions: Unlike what has been seen for radically resected pts, increased values of MetS parameters were associated with improved survival in the mCRC setting. The following possible explanation is under investigation: MetS may confer an additional energetic reserve able to counteract cachexia thus delaying health deterioration and prolonging survival.

3064 POSTER

Malnutrition: a Therapeutic Target in Oncology − Results of a Multicentre Observational Study in 391 Cancer Patients

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Background: In patients with solid tumours, malnutrition increases the risk of chemotherapy-induced neutropenic fever (Alexandre J et al. Ann Oncol, 14(1):36−41, 2003; Alexandre J et al. Ann Oncol, 18(1):168−72, 2007). Moreover, malnutrition participates to performance status deterioration (A Cessot et al., Supportive Care in Cancer, Mar 10, 2011). However, the effects of nutritional interventions in this setting remain poorly documented. The aim of this observational study was to evaluate factors associated with improvement of quality of life in cancer patients treated with a 3-month home enteral nutrition (HEN).
Methods: A prospective multicentre study was conducted in patients with cancer on HEN for a period of at least 3 months. Patients were evaluated at D0 and D90. Body weight (BW), BMI, performance status (PS), albuminemia, and QoL were assessed. Physical and Mental health Composite Scores (PCS & MCS) were completed by patients using a 12-question score, ranging from 0 to 100.
Results: Among the 391 patients included, 243 (62%) achieved the 3 months nutritional program. Male: 84%. Age: 60±10 yrs. Tumours: head and neck (58%), gastro-intestinal (41%) or other (1%). Indications of HEN were malnutrition (43%), swallowing disorders (35%) or both (22%). HEN was exclusive in 25% of pts. At D0, 80% of patients were malnourished (loss of BW >10% and/or BMI <18.5 or <21 in patients aged 75 or over). Over 3 months, HEN improved BW (61±13 to 62±12; $p = 0.0001$) and BMI (21.3±4.5 to 21.7±4.1; $p = 0.0003$; paired t-test). The nutritional gain was associated with improvement in quality of life as measured by PCS (35.0±9.0 to 36.8±8.8, $p = 0.0028$) and MCS (40.3±11.0 to 43.0±9.9, $p = 0.0009$). In multivariate analysis, malnutrition at D0 (OR 3.4, 95% CI [1.06–10.87]; $p < 0.04$) and non-progression of the cancer disease at D90 (OR 2.56, 95% CI [1.04–6.29]; $p < 0.04$) were independently associated with PCS improvement.
Conclusion: Concomitantly to the multidisciplinary therapeutic approach of the tumour progression, a 3-month home enteral nutrition is feasible, participates to the clinical benefit and quality of life improvement.

3065 POSTER

Palonosetron, Aprepitant and Dexamethasone to Prevent Nausea and Vomiting During Multiple Cycles of Cisplatin-Based Chemotherapy in Lung Cancer Patients

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Background: With repeated courses of chemotherapy, chemotherapy induced nausea and vomiting (CINV) is progressively more difficult to control. The aim of our study was to evaluate, for the first time, whether the antiemetic efficacy of the triple combination palonosetron aprepitant, and dexamethasone could be sustained for up to six cycles of highly emetogenic chemotherapy (HEC) in lung cancer patients.
Methods: Chemotherapy-naïve patients receiving cisplatin-based HEC, were treated with palonosetron 0.25 mg/i.v., dexamethasone 20 mg/i.v. and aprepitant 125 mg/p.o., 1-hour before chemotherapy. Aprepitant 80 mg/p.o. and dexamethasone 4 mg p.o. were administered on days 2−3. The primary endpoint was complete response (CR- no vomiting and no use of rescue medication), over five days following HEC in up to six cycles. Secondary

endpoints were emesis-free and nausea-free rates during the five days following HEC in up to six cycles. Safety was also evaluated.
Results: 158 patients with lung cancer were included in the study. Median age was 64 years, most of the patients were male (76.6%), with stage IV lung cancer (74.7%) and all of them were treated with cisplatin dosage of ⩾75 mg/sqm. Efficacy results are reported in the table. The most commonly reported side effects were mild constipation, headache and hickup.

Variable	Cycle					
	1	2	3	4	5	6
CR %	74	77.2	80	79.2	81.8	83.2
No emesis %	92.4	93	91.6	90.3	91.7	94.1
No nausea %	58.9	67.1	65.2	63.6	66.1	69.7

Conclusions: This study shows that, in lung cancer patients, the antiemetic efficacy of the triple combination palonosetron aprepitant, and dexamethasone could be sustained for up to six cycles of cisplatin-based HEC. These data confirm that adequate control in the first cycle of chemotherapy is more likely to be associated with control of CINV in subsequent cycles.

3066 POSTER

Erythropoiesis-stimulating Agents for the Treatment of Chemotherapy-induced Anemia and Mortality: a Meta-analysis of Individual Patient Data From Japanese Randomized Trials

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Background: Erythropoiesis-stimulating agents (ESAs) reduce the need for transfusions and improve quality of life in cancer patients receiving chemotherapy, but several clinical trials have suggested that ESAs may have a negative impact on survival in cancer patients. The FDA and European Medicines Agency have requested a change in the product labels for ESAs and restricted their initiation and target hemoglobin (Hb) levels to minimize the risk when they are used in patients with chemotherapy-induced anemia (CIA).
Materials and Methods: To evaluate the efficacy and safety of ESAs, including the impact on overall survival (OS) and thromboembolic events (TEE), we conducted a meta-analysis of 3 Japanese randomized, placebo-controlled trials (epoetin beta or darbepoetin alfa n = 273, placebo n = 238) in patients with CIA. Individual patient data were provided by Chugai and Kyowa Hakko Kirin. An association between the Hb level achieved during treatment and the risk of mortality was examined using landmark analysis.
Results: ESAs significantly reduced the risk of transfusion (relative risk 0.47, 95% CI 0.29–0.76). No statistically significant effect on OS was observed with ESAs (hazard ratio [HR] 1.00, 95% CI 0.75–1.34). A prespecified subgroup analysis showed no strong interaction between the baseline Hb level and the effect of ESAs on OS. Among ESA-treated patients, a mean Hb level of 11 < to 11.5 g/dL during the 3 month treatment period was associated with the lowest risk of mortality (HR 0.43, 95% CI 0.17–1.07; reference: mean Hb ⩽10 g/dL), but the highest achieved Hb level during the treatment period in each patient had no impact on OS. No increase of TEE was observed in the ESA-treated patients (0.7% vs 1.7% placebo).
Conclusions: Treatment with ESAs reduced the risk of transfusion without a negative impact on OS in Japanese patients with CIA.

3067 POSTER

SAMITAL®: a New Challenge for the Treatment of Oral Mucositis Induced by Chemoradiotherapy

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Background: Oral mucositis constitutes a widely diffused concomitant effect of chemoradiotherapy (CT/RT). The development of oral mucositis is a complex process which starts from tissue damage injury produced by CT/RT and rapidly degenerates in severe ulceration followed by inflammation, pain and infection. Oral mucositis, despite its relevance in worsening the quality of life and the therapeutical chances of oncological patients, is still considered an unmet need. In this framework, SAMITAL® has been developed by rationally combining three highly standardized botanical extracts each one endowed with specific pharmacological properties which can globally contribute to the relief of all the four key stages of mucositis.
Materials and Methods: Five clinical studies have been conducted using SAMITAL®. From 2008 to 2011, a total of 93 oncological patients (73 adults and 20 paediatric subjects) with mucositis induced by CT/RT have been treated with SAMITAL® (oral soluble lozenges or granules for suspension) 3−4 times daily, for almost the entire CT/RT regimen (4−50 days). Primary end-points: reduction of the progression of oral mucositis (according to WHO Scale), clinical tolerability and compliance. Secondary end-points: oropharyngeal pain intensity and continuity of CT/RT program.
Results: SAMITAL® was effective in controlling symptoms of severe mucositis, in improving recovery of lesions and in reducing the progression. A positive effect on dysphagia was also observed associated with an improvement of painful symptoms. An extensive enhancement of the quality of life was observed in all the patients who completed SAMITAL® treatment. Clinical tolerability and compliance were acceptable. Adverse events were infrequent and included mild vomiting and nausea (6/93, <6%), which resolved rapidly. Finally a general clinical advantage has been observed in all these studies, due to the better tolerability of CT/RT resulting in the maintenance of the complete therapeutic regimen.
Conclusions: Clinical evidences accumulated so far demonstrated that SAMITAL® has good tolerability and good efficacy. The effects were particularly relevant in term of reduction of mucositis and pain, recovery of swallowing and nutritional impairment; improvement of life quality, overall clinical advantage with completion of CT/RT regimen. These results encourage and support additional Phase II/III clinical studies on SAMITAL®.

3068 POSTER

Aprepitant is Active in Biological Therapies Induced Severe Pruritus − Final Results of the Italian Proof of Concept Study

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Background: Increasing evidences prove the involvement of keratinocytes NK1 receptors in the pathogenesis of pruritus: this prospective study aims to evaluate the role of aprepitant, a NK1 receptor antagonist, in the treatment of severe pruritus induced by biological therapies.
Materials and Methods: 30 patients (15 Male/15 Female), 63 years as mean age, affected by lung cancer (12), colorectal cancer (13) or other tumours (5), who developed severe pruritus (VAS ⩾7) during treatment with erlotinib (12), cetuximab (13), panitumumab (1), lapatinib (1), sunitinib (2) and imatinib (1) were enrolled. After the onset of severe, steroid or antihistaminic resistant pruritus, aprepitant was administered (125 mg day 1; 80 mg day 3; 80 mg day 5). Pruritus intensity was evaluated by VAS score before and after aprepitant administration (day 7 and every other following week until day 90 or the recurrence moment).
Results: Initial pruritus intensity was 10 in 3 patients, 9 in 6, 8 in 14 and 7 in 7 (median 8). After 1 week of aprepitant therapy the reported pruritus intensity was 0 in 14 patients, 1 in 6, 2 in 4, 3 in 4, 4 in 1 and 6 in 1 (median 1). The median decrease was 88%. Moreover, 93% of patients responded to aprepitant (decrease >50%), 2 did not (respectively, 50% and 30% of intensity reduction). Median duration of one cycle effect was 25 days (7−90 days).
Conclusions: This study assessed aprepitant activity in the management of biological therapies induced severe pruritus. Randomized studies are necessary to compare aprepitant activity with those of standard therapies.