1269 POSTER

Pathogenesis of fever related to ibandronate administration.

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Introduction: The most common adverse event typically associated with bisphosphonate therapy is transient fever. The present study has been performed to clarify the role of the main cytokines involved in acute phaze reaction (IL-6 AND TNF-alpha) in the pathogenesis of ibandronate-induced fever.
Patients and methods: 18 consecutive cancer patients with bone metastases treated, for the first time, with a single dose of ibandronate 4mg by infusion were prospectively evaluated for circulating TNF-alpha, gamma-IFN and IL-6 levels at different time points: just before and after 1, 2, 7 and 21 days following ibandronate infusion. Clinical and standard laboratory parameters were recorded at the same time points.
Results: Circulating TNF-alpha levels significantly increased 1 and 2 days after ibandronate infusion (respectively, $p = 0.002$ and $p<0.001$) and then returned to levels similar to basal ones. IL-6 levels significantly increased 1 day after infusion ($p = 0.007$), but they returned to values similar to the median basal values just 2 days after ibandronate administration. Moreover, in patients who experienced fever, TNF-alpha and IL-6 increase was greater than those in patients who did not. Futhermore, in patients with fever who recorded a higher decrease of total plasma calcium levels 21 days after ibandronate infusion ($p = 0.02$). No statistically significant differences in gamma-IFN were identified at the different time points, either in patients with fever or in those without.
Conclusion: Our results suggested that ibandronate induces a transient TNF-alpha and IL-6 increase and that this increase is higher in patients who developed fever, suggesting that these cytokines could be responsible for fever pathogenesis.

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Return to work after pimary treatment for cancer; occupational stress in the job situation.

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Introduction: As more cancer patients survive after primary treatment their job situation and occupational stress has increasingly become a focus for clinical research, but few studies have been done so far. We explored job situation and occupational stress in Norwegian cancer survivors aged 25 to 57 years.
Methods: Our main sample consisted of 269 women with breast cancer, 173 men with testicular cancer and 71 men with prostate cancer who had finished primary treatment one to five years prior to the survey and were without signs of disease. They were compared to 700 gender- and age-matched controls drawn from the general population (382 women and 318 men). Among the survivors 80% of the women and 88% of the men were in full time or part time work. 417 survivors (208 and 209 men) and 579 controls (308 women and 262 men) filled in the Job Demands-Control-Support questionnaire (DCSQ); which contains three subscales: demands, control, and support.
Results: The cancer survivors did not differ significantly from controls as to job situation, and they generally had no more occupational stress than the controls on any of the DSCQ sub-scales. However, breast cancer survivors reported significantly more support compared to their controls.
Conclusions: In general tumour-free cancer survivors, who have finished their primary treatment, have the same job situation and level of occupational stress as matched controls from the general population. These findings can give raise to optimism concerning cancer survivors' return to their workplaces after primary treatment. However, survivors on long-term sick leave and those who show occupational stress should be identified for closer follow-up.

1271 POSTER

Side effects associated with the use of dexamethasone for prophylaxis of delayed emesis after moderately emetogenic chemotherapy

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Background: The role of dexamethasone to reduce delayed emesis following highly emetogenic chemotherapy is proven, but there is less evidence of benefit after mild-moderately emetogenic regimens. Here, we develop and evaluate a Dexamethasone Symptom Questionnaire (DSQ) to assess the side effects of dexamethasone in the week after patients receive moderately emetogenic chemotherapy.
Methods: After optimization with a focus group, 60 patients receiving oral dexamethasone for delayed prophylaxis of emesis after chemotherapy completed and then evaluated the DSQ.
Results: Patients reported that the DSQ was worded clearly and addressed items important to them. Patients receiving dexamethasone reported moderate-severe problems with insomnia (45%), indigestion/epigastric discomfort (27%), agitation (25%), increased appetite (18%), weight gain (17%) and acne (15%) in the week following chemotherapy. (See table).

Moderate-severe symptoms/signs reported during the week after chemotherapy in patients receiving oral dexamethasone (n = 60)

Symptom	Moderate-severe symptoms (%)
Insomnia	45
Anorexia	32
Nausea	28
Indigestion/reflux/epigastric discomfort	27
Agitation	25
Increased appetite	18
Weight gain	17
Facial rash/acne	15
Vomiting	8
Depression on ceasing dexamethasone	7
Hiccups	7
Oral candida	3

Conclusions: The side effects of dexamethasone may outweigh its benefits when used with moderately emetogenic chemotherapy for prophylaxis for delayed nausea and vomiting. A randomized, double-blind crossover trial is underway to determine the effect of dexamethasone on nausea and vomiting, and the impact of side-effects of dexamethasone and of nausea and vomiting, on quality of life.

1272 POSTER

Long-term health-related quality of life in men treated with 125I prostate brachytherapy for clinically localized prostate cancer

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Purpose: Prostate brachytherapy has been reported to have less morbidity for patients than radical prostatectomy or external beam irradiation. However, information regarding long-term treatment-specific quality-of-life (QoL) is scant. We evaluated the impact of permanent implant brachytherapy on general, cancer specific and symptom domains of QoL for up to 6 years using validated patient-administered quality-of-life instruments.
Methods and materials: A total of 295 men consecutively treated in a single academic medical center between June 1998 and Dezember 2003 were mailed two standarized questionnaires (the EORTC prostate cancer quality of life questionnaire QLQ-PR25 and the ICS-male questionnaire) to assess health-related QoL. We subclassified two groups of patients: group 1 with patients younger than 65 years of age (n = 45, median age 62, range 45–64), group 2 with patients 65 years of age or older (n = 186, median age 73, range 65–85). The minimal follow up was 12 month (mean 50.3 months; range 12–78 months). 106 (45.9%) men have also been treated with hormonal therapy.
Results: A total of 231 questionnaires were returned (78.3% response rate), 221 were suitable for analysis, 12.9% of the patient had died. 76.7% of group 1 and 73.2% of group 2 reported that they were in good, very good or excellent health. 53.5% (group 1) and 70.7% (group 2) refered strong or moderate pollakisuria, 39.2% reported nocturia, without relevant differences between both groups and 5.5% of patients suffered from strong or moderate dysuria ($p > 0.05$). 2.3% patients reported strong stress incontinence; 24.7% reported moderate and 22.0% strong urge incontinence. A total of 13% used pads. There was no evidence of severe rectal dysfunction. 75.6% (group 1) and 60.9% (group 2) had sex during the last four weeks. The most common problems were erectile dysfunction (48.6% vs. 75%, $p < 0.001$) and decrease in ejaculation (39.4% vs. 59.6%,

p<0.001). Whereas sexual complaints were ageassociated, this was not the case for urinary and bowel complaints. Most patients (95.9%) would recommend (125) I seed brachytherapy to others.
Conclusions: Our data substantiate the favorable long-term QoL outcomes associated with modern brachytherapy techniques. Significant age differences were observed in all quality of life measures, with the largest occurring in sexual and urinary symptoms. Sexual function was significantly worse in patients 65 years of age and older ($p < 0.05$).

1273 POSTER

Differential diagnosis and therapy of iron restricted erythropoiesis in anaemic cancer patients: data from the TANDEM study

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Background: Iron restricted erythropoiesis in patients with anaemia of chronic disease (ACD) is often caused by disturbances in iron metabolism and distribution. Thomas et al. developed a diagnostic plot (Thomas-Plot, TP) for the differential diagnosis of iron supply in ACD patients (Thomas C. et.al., Clin. Chemistry 48; 7: 1066–76 (2002)). This plot combines the hemoglobin content of reticulocytes with the ferritin index (the quotient of soluble transferrin receptor and logarithm of ferritin). The aim of the plot is to identify the cause for the anaemia and to provide a therapeutic solution for the most efficacious treatment combination of erythropoiesis stimulating factors (ESF) and iron supplementation. In order to validate the TP in cancer patients we started a phase II trial (TANDEM) in which the anaemia therapy in cancer patients is given based on the differential diagnosis by the TP.
Material and methods: Patients with non-myeloid tumors, > 18 years old, expected to receive at least 3 more cycles of chemotherapy (> 6 weeks), with ferritin >20 ng/ml, and an indication for ESF therapy as per EORTC guidelines are initially analyzed using the TP (screening). TP classifies pts. in 1 of 4 quadrants (Q1–Q4). Pts. in Q2+Q3 receive no ESF but oral iron (3 × 100 mg Fe II/d). Pts. in Q1+Q4 receive 30,000 IU Epoetin beta (NeoRecormon®) sc. once weekly. In addition, pts. in Q4 receive 200 mg Fe-saccharat per week iv. up to 1 g. During the study pts. are monitored by TP every two weeks and anaemia therapy is adjusted accordingly.
Results: Up to now (April 2005), 59 pts. have been recruited by 8 centers. After screening, 8 pts. fell in Q2 and 7 pts. in Q3. These 15 pts. (25%) received oral iron therapy due to a prevalent iron deficiency. 35 pts. (75%) fell in Q1+Q4 and received ESF therapy with Epoetin beta. Those 4 pts. in Q4 received additionally i.v. Fe-saccharat, and subsequently moved to Q1 within the first 2 weeks of treatment. 25% of pts. under EPO-Therapy (Q1+Q4) moved to Q2 or Q3 after 2 weeks of treatment and then received oral iron in addition to ESF. The analyzable pts. receiving ESF therapy with Epoetin beta had an average hemoglobin increase of 0.7 g/dl from baseline after 4 weeks.
Conclusions: Our preliminary results indicate that the TP is a simple and useful tool for optimizing anemia management with ESF and iron in patients with cancer related and chemotherapy induced anemia.
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Impact of bevacizumab plus 5-FU/LV with or without irinotecan on quality of life in patients with metastatic colorectal cancer

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Background: In a phase III trial, patients were treated first line with irinotecan, 5-FU, LV (IFL) plus placebo (n = 411) or bevacizumab (BV; Avastin), a monoclonal antibody to VEGF, plus IFL (n = 402). The addition of BV to IFL significantly prolonged progression-free survival (PFS) by 71% and overall survival (OS) by 30% [Hurwitz et al. J Clin Oncol 2004;22:2335–42]. In a phase II study, 209 subjects were randomized to 5-FU/LV+placebo (105) or 5-FU/LV+BV (104); addition of BV to 5-FU/LV significantly prolonged PFS [Kabbinavar et al. J Clin Oncol 2005;23: epub ahead of print February 28]. Evaluating changes in quality of life (QOL) was a secondary objective in both studies.
Methods: QOL endpoints were pre-specified; these included time to deterioration in QOL (TDQ), measured by the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) colon cancer subscale (CCS); Trial Outcome Index (TOI-C); and FACT-C score. QOL deterioration was prospectively defined based on a clinically meaningful decrease in scores: 3 points (CCS), 7 points (TOI-C), and 9 points (FACT-C). Median TDQ was evaluated for subjects with baseline and post-baseline assessments using the stratified log-rank test. Those who progressed or died before QOL declined were assigned TDQ of time to progression or death. Those who did not die or experience documented QOL deterioration or disease progression/death were censored at time of last QOL assessment. Those who discontinued without a post-baseline assessment or disease progression were censored at date of randomization.
Results: In the pivotal trial, baseline scores were available for 127/122 (CCS), 125/122 (TOI-C), and 124/121 (FACT-C) patients in the IFL and IFL+BV arms, respectively. There were no statistically significant differences in TDQ (CCS, TOI-C, or FACT-C) between treatment arms (Table 1). In the phase II study, baseline scores were available for 77/89 patients in the 5-FU/LV and 5-FU/LV + BV arms, respectively. Median TDQ as measured by TOI-C ($p = 0.0477$) and FACT-C score ($p = 0.0159$) was significantly prolonged for patients treated with 5-FU plus BV.

Table 1

	Median TDQ (months)		
	CCS	TOI-C	FACT-C
Pivotal trial			
IFL+placebo	2.73	3.29	3.94
IFL+BV	2.89	2.76	3.98
Phase II trial			
FL+placebo	3.02	2.30	2.63
FL+BV	3.12	3.22	3.61

Conclusions: When added to IFL, BV significantly prolonged OS and PFS without compromising QOL. Analyses of secondary measures of TDQ (TOI-C and FACT-C score) suggest a QOL gain with an increase in PFS for subjects receiving BV with 5-FU/LV.

1275 POSTER

Multidimensional geriatric parameters, family interference and awareness of disease during the obtainment of informed consent from elderly cancer patients: a prospective analysis

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Background: Limited awareness of disease in elderly cancer patients may be attributed to various patient-related factors (assessable through the multidimensional geriatric assessment-MGA) as well as to family opposition and physician's reluctance to disclose a dismal prognosis. Signature of widespread consent forms (CF) is not a reliable proof of adequate information.
Objective and Methods: To assess prospectively the degree of information given to elderly cancer patients (⩾ 65 years) and to evaluate how baseline MGA parameters (ECOG Performance Status-PS 0 vs ⩾ 1, Mini-Mental State-MMS ⩾ 24 vs < 23, Geriatric Depression Scale-GDS ⩽ 5 vs > 6, Activities of Daily Living-ADL = 6 vs ⩽ 5, Instrumental ADL = 8 vs ⩽ 7 and Charlson's score of comorbidity = 0 vs ⩾ 1) and family attitudes might interfere with the informed consent process. A short interview of the treating physician was performed after first prescription of chemotherapy; patients' frequencies were compared by means of Chi-squared test.
Results: From March 2004 to April 2005, 135 pts (56.3% males, median age 75, range 65–90 years) were eligible. Sixty-three percent of them had PS 0, 86% were independent in ADL and 77.8% in IADL, 84.5% had no signs of depression, 78.5% had no cognitive impairment and 50.3% had no relevant comorbidities. Six patients were not able to sign the CF, and 16 (12.4%) delegated a relative to read it. Seventy-seven percent of patients were fully aware of cancer according to the treating oncologist; yet, only 23% overtly asked for detailed information and estimation of prognosis. The physician admitted not having given the same level of information of younger patients to about 35.5% of patients, and particularly to those with advanced/incurable disease ($p = 0.004$). The family asked to hide the diagnosis in almost one fourth of cases, and expectedly, family opposition predicted unawareness of disease ($p < 0.001$) and attenuated information from the oncologist ($p < 0.001$). Significant association was found among