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.
Supported by F. Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany

1274 POSTER

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

MGA parameters and awareness of disease, family interference, reading of CF by proxy and probability of receiving less information, as follows:

	PS	Charlson's score	MMS	GDS	ADL	IADL
Awareness of disease	p = 0.036	ns	p < 0.001	p = 0.013	ns	ns
Family interference	p = 0.003	ns	p = 0.022	ns	p = 0.025	p = 0.031
Reading of CF by proxy	p < 0.001	ns	ns	p = 0.033	p = 0.033	p < 0.001
Less information	p < 0.001	ns	p = 0.041	ns	p < 0.001	p < 0.001

ns = non significant

Conclusions: Our prospective cohort shows that limited and/or attenuated information is still a relevant modality of relation with elderly cancer patients undergoing chemotherapy in Italy, often in connivance with their family. Limited awareness of disease correlates with poor PS and cognitive/affective problems, while family interference is more frequent in patients with cognitive deficit and low functional status. Comorbidity does not appear to play a relevant role in the informed consent process.

1276 POSTER

Duration of onset of metastatic bone pain relief with ibandronate: phase III and phase II trial results

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Background: Bone pain is the most common reason for patients with skeletal metastases to seek treatment from their physician. This symptom is difficult to manage and often persists despite bone radiotherapy or analgesic consumption. The onset of metastatic bone pain relief with ibandronate has been evaluated in clinical trials.
Materials and methods: In a 96-week, randomized, phase III trial, ibandronate 6mg (n = 154) or placebo (n = 158) was infused over 1–2 hours every 3–4 weeks. In two phase III studies (data pooled), patients received oral ibandronate 50mg (n = 287) or placebo (n = 277) once daily. Bone pain was assessed on a 5-point scale (0 = none to 4 = intolerable). In phase II studies of patients with bone pain due to metastatic urologic cancer (n = 55) or hormone refractory prostate cancer (HRPCA; n = 45), ibandronate 6mg was infused on 3 consecutive days (18mg loading dose), followed by a single 6 mg infusion every 4 weeks. Bone pain was assessed on a visual analog scale (VAS) from 0 = no pain to 10 = maximum pain. Analgesic use was recorded in a diary and functioning by the Karnofsky index.
Results: In a phase III trial, intravenous ibandronate 6mg reduced bone pain below baseline within 4 weeks (maximal effect by Week 12). At endpoint, the mean change from baseline was −0.28 vs +0.21 with placebo ($p < 0.001$). Oral ibandronate 50 mg also reduced bone pain below baseline within a few weeks; this was maintained for 2 years (−0.20 vs +0.10 with placebo at Week 96; $p = 0.001$). In the urologic cancer study, 73% of patients (40/55) had pain relief (≥ 3-point VAS reduction) by Day 2 following loading-dose ibandronate, reaching statistical significance on Day 3 (2.5 vs 6.8 at baseline, $p < 0.001$). Eleven patients (20%) became pain-free. Analgesic use reduced by ≥50% in 64% of patients (35/55). In the HRPCA study, 40 patients (89%) had pain relief by Day 3 ($p < 0.001$). In both phase II studies pain scores remained below baseline for >20 weeks with ibandronate maintenance dosing; performance status also improved (regained mobility and independence).
Conclusions: Standard-dose ibandronate alleviated bone pain within several weeks, and for up to 2 years. Severe symptoms were reduced within days of the intravenous loading dose, suggesting that ibandronate offers rapid relief to patients who need it the most. Trial findings are corroborated by case report data. Large-scale comparative trials of oral ibandronate and intravenous zoledronic acid for metastatic bone pain are planned.

1277 POSTER

Quality of life in patients with painful bone metastases: results from the randomized Dutch Bone Metastasis Study on single fraction versus multiple fraction radiotherapy

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Background: The prospectively randomized Dutch Bone Metastasis Study evaluated the palliative effect of 8 Gy single fraction radiotherapy versus 24 Gy in 6 fractions in patients with painful bone metastases. In previous Publication onlyns, the equal effectiveness of both radiotherapy treatment schedules for treating pain was reported. Here, we focus on three specific quality of life (QOL) domains in patients with painful bone metastases.
Material and methods: 1157 patients were randomized into the study. Median overall survival was 7 months. Patients filled out 13 weekly and then monthly questionnaires for two years or until death. Questionnaires contained 48 items from EORTC QLQ-C30, Rotterdam Symptom Check List and EURO-QOL. Item scores were summarized by three component scores: physical symptoms, psychological symptoms and functional status. Mixed modeling was used to model the course of QOL during follow up, and to test differences between the two randomization groups, and between primary tumor groups (breast cancer, lung cancer, prostate cancer versus other types of cancer). Differences were expressed as effect sizes d, which can be interpreted as small (d = 0.2), medium (d = 0.5), or large (d = 0.8).
Results: In general, patients deteriorated immediately after treatment, subsequently recovered and temporarily improved, but deteriorated sharply in the last months before death. Recovery and improvement were larger in patients with a more prolonged survival. For example, patients with 18 months survival reported less physical symptoms than patients with 6 months survival (figure 1). In addition, patients who received multiple fractions reported more physical symptoms than after a single fraction (d = 0.11, $P < 0.01$), but not more psychological symptoms (d = 0.05, $P = 0.20$) or worse functioning (d = 0.01, $P = 0.80$). Patients with breast cancer reported more psychological symptoms (d = 0.20, $P = 0.02$) and worse functioning (d = 0.19, $P = 0.04$).

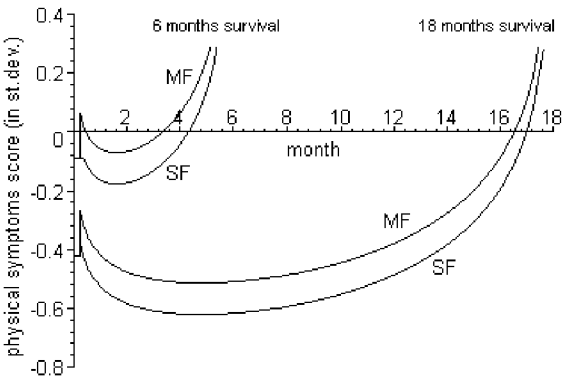

Fig. 1: Mean curve estimates of physical symptoms scores of patients who recieved either single fraction (SF) or multiple fraction (MF) radiotherapy and who survived either 6 or 18 months.

Conclusions: The course of QOL of patients receiving single fraction radiotherapy is at least as good as the QOL of patients receiving multiple fractions. Because single fraction radiotherapy provides equal palliation for treating pain it should be the standard palliative treatment for the majority of patients with painful bone metastases. Patients with breast cancer reported worse QOL than others, for that reason, further analyses of specific QOL domains related to direct treatment side effects will be presented at ECCO.

1278 POSTER

The efficacy of interleukin-6 and hypothalamus-pituitary-adrenal (HPA) axis function as predictors for the presence of depression in cancer patients

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Background: Inflammation and perturbation of the hypothalamic-pituitary-adrenal (HPA) axis function play a putative role in the ethiology of depression. Patients (pts) with metastatic cancer show elevated prevalence rates for depression. The objective of this study was to illustrate the efficacy of interleukin-6 (IL-6) and HPA axis function in predicting the presence of depression in pts with cancer.
Methods: 114 patients with metastatic cancer were assessed by the Hospital Anxiety and Depression Scale (HADS) for Depression and diagnoses was established according to the DSM-IV criteria. A level of ≥ 11 was considered significant on the HADS-D axes for Depression. Plasma concentrations of IL-6 were measured in addition to cortisol levels (8AM and 8PM). The relative diurnal variation of cortisol (cortisol VAR), expressed in percent, was calculated as measure of the circadian function of the HPA