3021 POSTER

The extent of psychological distress in patients with advanced lung cancer at the end of life

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Background: Psychological distress diminishes quality of life in patients with incurable malignancies. Although it has been stated that psychological distress increases towards death, it could also result from a patient's individual susceptibility. To study this hypothesis, the course of psychological distress in lung cancer patients who participated in the Dutch Bone Metastasis Study (DBMS) was investigated with regard to baseline characteristics.
Material and Methods: From March 1996 to September 1998, 1157 patients with painful bone metastases from solid tumours were randomised between single or multiple fraction radiotherapy in the DBMS. Equal effectiveness of both radiotherapy regimens for painful bone metastasis was assessed.
For this analysis, all patients with lung cancer were selected. At randomisation and during follow-up, patients filled out 13 weekly and thereafter monthly questionnaires. The Rotterdam Symptom Checklist psychological subscale of 7 items was used to assess psychological distress on a 4-point scale ranging from 1 = not at all, to 4 = very much for each item. The minimal sum score is 7 (no distress), the maximum sum score 28. A score $\geqslant$17 is valued as needing further psychological assessment. At randomisation, three risk groups for distress were identified: low risk LR (7−11), intermediate risk IR (12−16), and high risk HR (17−28). Psychological distress was analysed as a function of remaining lifetime in patients who died within the study period. The influence of baseline characteristics age, sex, time since primary diagnosis, performance score and pain score on psychological distress was investigated.
Results: Mean age of the 287 patients (47 female, 240 male) at randomisation was 66 years (SD 9.5), mean time since diagnosis was 9.6 (SD 18.1) months. Mean survival after randomisation was 4.6 months (SD 4.5).
At baseline, 46% was LR, 32% IR and 22% HR. In the HR group, mean psychological distress fluctuated with a considerable increase towards death. Both LR and IR groups showed an increase towards death, but stayed below threshold level.
HR patients had a mean performance score of 60, whereas IR and LR had a score of 70 (ns). Time since diagnosis was shorter in the IR group compared to HR and LR (5.9 vs. 10.8 vs. 13.3 months, p = 0.032).
Conclusion: Towards their death, lung cancer patients with bone metastases showed increasing psychological distress. Interventions should be provided to patients identified as high risk early on in their disease.

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Neutropenia and hematologic sequelae in patients receiving casopitant-containing antiemetic therapy for cisplatin-based highly emetogenic chemotherapy

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Background: Casopitant, a novel neurokinin (NK)-1 receptor antagonist (RA) in development for prevention of chemotherapy-induced nausea and vomiting (CINV), is a mild to moderate CYP3A inhibitor. Data from 2 randomized double-blind HEC studies were analyzed to assess impact of casopitant coadministration on hematologic parameters.
Methods: Phase III study (n = 802): Patients received placebo, single-dose 150 mg oral (SDO) casopitant, or 3-day 90 mg IV/50 mg oral/50 mg oral casopitant plus standard antiemetic therapy. Phase II study (n = 488): Patients received placebo, 3-day oral casopitant (50, 100, or 150 mg) or aprepitant (125/80/80 mg), or SDO casopitant plus standard therapy. Adverse events (AEs) were reported for all cycles (maximum 4−6). Phase III study included comprehensive laboratory assessments at screening/day (d) 1, d 6 to 10, d 12 to 17 (cycle 1 [C1] only), and at the end of each cycle. The C1 d 12 to d 17 assessment around anticipated neutrophil nadir allowed more comprehensive assessment of hematologic effects than with previous NK-1 RAs.
Results: Integrated AE data from both studies showed no imbalance in incidence of grade 4 (G4) neutropenia with casopitant (any dose, 11%) vs controls (7%). In phase III, rates of G4 neutrophil count toxicities (NCTs) were higher in C1 with casopitant (control 10%; SDO 16%; 3-day IV/oral 17%). This seemed primarily due to increased incidence of G4 NCTs in patients treated with CYP3A-metabolized drugs vinorelbine or etoposide (34% each casopitant arm vs 18% control). Febrile neutropenia AEs were rare (2% all arms) in C1. In phase II, more patients in the combined casopitant arms (27%) who received vinorelbine (but not etoposide) had G4 NCTs vs control subjects (15%). Chemotherapy dose intensity, assessed in phase III, was similar across treatments in all cycles.
Conclusions: Casopitant in combination with cisplatin and certain CYP3A-metabolized chemotherapy led to an increase in G4 neutropenia; however, overall incidence remained within expectations for cisplatin doublets. The neutropenia was not associated with increased sequelae. Blinded treating physicians did not alter their practice of maintaining chemotherapy dose intensity when casopitant was administered.

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Cardioprotective effect of telmisartan in cancer patients treated with epirubicin

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Background: We previously showed on 31 cancer patients (pts) that early cardiac abnormalities occurred at epirubicin (EPI) doses of 200 mg/m^2 and persisted throughout subsequent EPI doses and even up to 18 months. Early contractility impairment, i.e. Strain rate (SR) reduction was detected by tissue doppler imaging (TDI) associated with high levels of inflammatory/oxidative stress markers. R enin-angiotensin system activation has been suggested to play an important role in the pathogenesis of Anthracycline-induced cardiotoxicity.
Methods: A phase II placebo-controlled study was designed to investigate the possible role of Telmisartan (an antagonist of angiotensine II type I receptor) in preventing both early preclinical and late myocardial damage induced by EPI. The correlation with changes of biochemical/inflammatory markers was also assessed. Planned sample size was 100 pts (50 pts per arm). Inclusion criteria: 18–70 y, histologically confirmed cancer, previously untreated and candidates for an EPI-based regimen; LVEF = 55%; ECOG PS 0−2, no history of cardiac disease and previous mediastinal irradiation. Eligible pts were randomized to receive Telmisartan 40 mg (1 tablet)/day or placebo starting 1 week before EPI until 6 months after the end of EPI administration. TDI as well as inflammatory/oxidative stress markers were assessed at baseline, 24 hours and 7 days at EPI doses of 100, 200, 300, and 400 mg/m^2.
Results: At December 2008 we enrolled 27 pts (M/F: 7/20, mean$\pm$SD age 58$\pm$14 years): 14 Telmisartan and 13 placebo. 15 pts completed EPI treatment (8 Telmisartan and 7 placebo). A significant reduction of SR peak was observed at 200 mg/m^2 of EPI in the placebo arm. *Viceversa* no significant TDI changes occurred in the treatment arm. Proinflammatory cytokines did not change in both arms whilst reactive oxygen species increased significantly in the placebo arm.
Conclusions: The study is in progress.

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Randomised phase III clinical trial of 5 different arms of treatment for patients with cancer-related anorexia/cachexia syndrome (CACS)

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Background: Cancer-related anorexia/cachexia syndrome (CACS) is a multifactorial syndrome characterized by tissue wasting, loss of body weight, particularly of lean body mass (LBM), metabolic alterations, fatigue, reduced performance status, very often accompanied by anorexia.
Patients and Methods: In April 2005 we started a phase III randomised study to establish the most effective and safest treatment of CACS addressing as primary endpoints: LBM, resting energy expenditure (REE), total daily physical activity, serum IL-6, TNF-a and fatigue. Fatigue has been evaluated by the Multidimensional Fatigue Symptom Inventory − Short Form (MFSI-SF). The sample size was 475 patients (pts). Eligibility criteria: hystologically confirmed tumors of any site; weight loss = 5% in the last 3 months and/or abnormal values of proinflammatory cytokines and oxidative stress parameters predictive of the onset of CACS; life expectancy >4 months, patients treated with either antineoplastic therapy or supportive care. All pts enrolled received as basic oral treatment: