

down to 50 nM O₂ corresponding to 0.025% of the saturated concentration prevalent on the surface of the overlaying medium (196 μ M O₂).

Conclusion: These data strongly suggest that severe hypoxia (in terms of very low intracellular oxygen concentrations) is a normal situation for some tumour cells cultivated under standard conditions due to their elevated nutrient and oxygen consumption rates. On the other hand, a strong oxygen gradient built up by mitochondrial respiration increases the oxygen flux via enhanced diffusion rates thereby continuously providing oxygen.

Supportive care & quality of life

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ORAL

Improving the quality of pain treatment by a tailored Pain Education Program for cancer patients in chronic pain

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It has become increasingly evident that patients' knowledge and attitudes regarding pain is important for cancer pain relief. Educational interventions can affect pain treatment. However, the lack of well-established outcome measures to evaluate adequacy of pain treatment hampers the evaluation of educational pain programs.

In this study, the effectiveness of a Pain Education Program (PEP) in cancer patients with chronic pain was investigated in a randomized controlled clinical trial. The main purpose of this study was: 1) to assess the adequacy of pain treatment; and 2) to evaluate the effects of the PEP. The PEP was tailored to the needs of the individual patient and consisted of three elements: 1) educating patients about the basic principles regarding pain and pain management; 2) instructing patients how to report their pain in a pain diary; and 3) instructing patients how to communicate about pain and how to contact health care providers. Intervention group patients received the PEP in the hospital and postdischarge by nurses who were specially trained as pain counselors. Follow-up assessments were till 8 weeks postdischarge.

A total of 313 pain patients were studied. Adequacy of pain treatment was evaluated by means of the Amsterdam Pain Management Index, a measure that compares the aggregated scores of patients' Present Pain Intensity, Average Pain Intensity, and Worst Pain Intensity, corrected for patients' Tolerable Present Pain, with the analgesics used by the patient.

In the hospital, 59.8% received less than optimal analgesic treatment. Results showed that the PEP proved to be feasible, showed a significant increase in pain knowledge in patients who received the PEP, and a significant decrease in pain intensity. Postdischarge, the intervention group patients were significantly more adequately treated than the control group patients. These findings suggest that quality of pain treatment in cancer patients with chronic pain can be enhanced by educating patients about pain and improving active participation in their own pain treatment. The benefit from the PEP, however, decreases slightly over time, pointing at a need for ongoing education.

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ORAL

Patients treated with an NK1 receptor antagonist report less hardship due to chemotherapy-induced nausea & vomiting compared to those on standard antiemetic therapy

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While the antiemetic properties of NK-1 receptor antagonists have been reported in the literature, little information exists on the positive impact of these compounds on patient-reported outcomes. Specifically, the ability to avoid personal hardship and hardship on others due to nausea and vomiting is likely to be an important benefit to patients. In an international randomized double-blind Phase IIb trial, 228 cisplatin-naïve patients (47% female, mean age 55) treated with cisplatin + 70mg/m² received either triple antiemetic therapy (MK-0869 125mg+dexamethasone (D) 20mg+ondansetron (O) 32mg on day 1 followed by MK-0869 80mg+D 8mg on days 2-5) or standard therapy (D 20mg + O 32mg on day 1 followed by D 8mg on days 2-5). Patients recorded vomiting episodes, nausea rat-

ings and rescue medications in a daily diary. Five days post-chemotherapy, patients completed the Functional Living Index-Emeris (FLIE), a measure of the impact of nausea and vomiting on daily life. Cross-culturally validated translations of the diary and FLIE were used in all international sites. "No impact on daily life" (NIDL) is defined as a FLIE average item score >6 on a 7-point scale. The % of patients reporting NIDL from nausea and vomiting in each treatment group (MK-0869 vs standard therapy) was assessed by the FLIE total score (85** vs 67), Nausea domain score (76* vs 60), and Vomiting domain score (93** vs 68). Additionally, the % of patients in each treatment group reporting NIDL from nausea, specifically related to personal hardship (80* vs 64) and hardship on others (83 vs. 74), and the % reporting NIDL from vomiting, specifically related to personal hardship (93** vs 68) and hardship on others, (96** vs 71) was assessed. (*p<0.05, **p<0.01). Nearly 20% more patients treated with MK-0869 reported NIDL as assessed by the FLIE total score over the 5 days post-chemotherapy compared to those on standard antiemetic therapy. Likewise, significantly more patients treated with MK0869 reported no impact of nausea on daily life specifically related to personal hardship and no impact of vomiting on daily life specifically related to both personal hardship and hardship on others. Patients treated with MK-0869 are better able to maintain daily life and avoid hardship following highly emetogenic chemotherapy.

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ORAL

Cancer clinical trials within Europe – An examination into EORTC QL studies

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Purpose: For cancer patients, Quality of Life (QL) is now becoming an increasingly accepted endpoint in cancer clinical trials. However, reports in published literature suggest that fewer than 10% of all clinical trials have quality of life assessment, although it is believed such reports may be biased by time lag factors in the new and emerging field of QL. This paper therefore examines the extent of quality of life studies that are conducted within one of the largest cancer clinical trials organizations in Europe, the EORTC, investigating both completed and ongoing clinical trials.

Method: An examination of all clinical trials conducted by the EORTC (between January 1990 and January 2000) was undertaken, by reviewing data from various databases, publications and records. Trials were systematically selected if they involved any aspect of QL, as clearly specified in the protocol.

Results: In total, some 112 EORTC clinical trials were identified as having a QL sub-study. Over 10,000 patients had been entered into active trials. All of the trials involved multinational patient recruitment, with the highest recruitment from The Netherlands, France and Germany and the lowest from Malta, Estonia and Slovakia. Approximately 14 disease groups have been actively recruiting patients over the last decade, with the major number of patients being from disease groups of Genitourinary, Breast and Lung cancers. A clear linear trend was noted, with increasing numbers of clinical trials involving QL components over this ten-year period. Of all the trials, 74 studies were phase III design, 15 were phase II design, and the remainders were feasibility studies. Presently, 45 trials are ongoing, and open to patient entry, 19 are nearly mature for data analysis, 15 have now been published and 10 are now being analyzed. In the last year, 30 new studies have been submitted for research involving QL, suggesting quality of life is a highly important endpoint in present day trials across the European setting.

Conclusion: While QL was not a major component of EORTC clinical trials in the early 1990's, it is now highly integrated into EORTC cancer clinical trials, and almost a standard secondary endpoint. This suggests that clinicians and researchers alike in the European context are increasingly seeing the importance of patient based outcome assessment methods for assessing the value of cancer therapeutic modalities.

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ORAL

Neuroprotective effect of glutathione (GSH) on oxaliplatin (L-OHP)-based chemotherapy in advanced colorectal cancer patients (pts): a randomized double-blind placebo-controlled trial

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Purpose: L-OHP is a platinum compound active in colorectal cancer and

other malignancies; its dose-limiting toxicity is sensory peripheral neuropathy. GSH, a thiol tripeptide, has been shown to provide protection against cisplatin neurotoxicity. In a phase III randomized placebo-controlled trial we evaluated the efficacy of GSH in the prevention of L-OHP-induced neurotoxicity.

Methods: 52 pts with colorectal cancer were randomized to receive GSH 1500 mg/m² over 15-minute immediately before L-OHP 100 mg/m² 2-h infusion d1, leucovorin 250 mg/m² 2-h infusion followed by 5-fluorouracil 1500 mg/m² 24-h infusion d1-2 (GSH arm), or normal saline solution followed by the same regimen (placebo arm), q 2 weeks. At baseline, after 4 and 6-8 cycles, a clinical neurological evaluation according to NCI-CTC was performed, in addition to electrophysiologic investigations of latency (lat), motor and sensory amplitude potential (map, sap), conduction velocity (cv) of motor (peroneal, tibial) and sensory (sural) nerves.

Results: 26 pts for each arm were randomized into the study, M/F 31/21, median age, 64 years (range 40-77), ECOG performance status 0/1 37/15. After 4 cycles, clinical and electrophysiologic evaluations showed no difference among the treatment arms. After 6-8 cycles, pts (n=21) in the GSH arm had neurotoxicity NCI-CTC gr. 1/2/3/4 16/2/0/0, whereas pts (n=19) in the placebo arm suffered from neurotoxicity gr. 1/2/3/4 5/7/4/1. Remarkably, 63% of pts had grade 2-4 neurotoxicity in the placebo arm compared to 9.5% of pts in the GSH arm (p=0.001). After 6-8 cycles, we observed a significant impairment of lat (p=0.035), sap (p=0.05), and cv (p=0.017) of the sural nerves of pts in the placebo arm, but not in the GSH arm.

Conclusions: This study suggests the efficacy of GSH in reducing the incidence of moderate-to-severe neurotoxicity and the damage to sensory nerves after treatment with L-OHP; these effects are particularly evident for L-OHP cumulative dose of more than 400 mg/m².

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ORAL

A prospective cohort study to examine the risk factors for the development of arm oedema following breast cancer treatment

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Purpose: Arm oedema is a common side effect of breast cancer treatment and it is important to identify the risk factors which may precipitate the onset of the condition. Reports of venepuncture precipitating oedema have prompted warnings against the use of any IV interventions in the ipsilateral (treatment side) arm but the statistical risk of this complication is not known. The aim of this prospective cohort study was to examine the importance of possible risk factors, in particular, to estimate the relative risk of developing arm oedema when venepuncture occurs.

Methods: 252 women undergoing breast surgery which involved axillary node sampling, excision or biopsy were recruited. Limb volumes were measured prior to treatment and at two weeks, three months and six months post-operatively. Volume difference between the ipsilateral and contralateral arms was calculated, adjusted for the natural (pre-treatment) difference in arm volumes, and systemic changes in weight and fluid balance. The occurrence of venepuncture or non-accidental skin puncture was recorded daily throughout the patient's hospital stay.

Results: Six months post surgery 66% of the sample had oedema of the ipsilateral arm. Women who had venepuncture on the ipsilateral side were 1.2 times more likely to develop arm oedema than women who did not have venepuncture on the ipsilateral side. The 90% confidence interval for this result is 0.97 to 1.50. Age and weight were not found to be significant factors. (Interim results of 169 data sets; complete results will be presented at the conference).

Conclusion: These results confirm previous subjective reports of an association between venepuncture and the onset of arm oedema. The management of the arm during treatment for breast cancer and the management of arm oedema after treatment should be informed by the results of this study.

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ORAL

Outcome analysis of cancer patients admitted to the intensive care unit (ICU) in an emergency

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Purpose: ICU treatment for cancer patients has been subject to critical reconsideration or was explicitly discouraged. We were interested to evaluate the outcome of intensive care treatment in cancer patients admitted for an emergency.

Patients and Methods: Retrospective analysis in 189 consecutive cancer pts. referred to the intensive care units (ICU) in an emergency during a two-year period. Parameters evaluated were: patient characteristics, type of emergency causing ICU referral, and ICU treatment modalities. For statistical analysis we used a regression analysis as well as the decision tree learning method acc to Ripley. Data were analyzed with respect to death during ICU stay, after transfer from ICU, and after discharge from hospital. Underlying diseases were solid tumor (55.1%), lymphoma (17.1%), acute leukemia (15.0%), myeloma (4.3%), or other malignancy (8.6%).

Results: Chemotherapy in 46% (HD+SCT in 14%) and surgery in 27% of the pts. were the most recent interventions prior to referral. Reasons for ICU referral were pneumonia (29.6%), sepsis (27.0%), fungal infection (11.1%), another infection (9.5%), gastrointestinal emergency (16.9%), treatment-related organ toxicity (6.9%), or another, non-infectious complication (43.9%). Vasopressor support was required in 50.3%, mechanical ventilation in 49.7%, and hemodialysis or hemofiltration in 26.5% of pts. Overall, 41.3% died during ICU treatment, 12.2% died after transfer from ICU to a non-ICU ward, and 35.5% were discharged alive. Vasopressor support and mechanical ventilation were independent risk factors for fatal outcome, whereas treatment-related organ toxicity and surgical pretreatment predicted favorable outcome. No single risk factor was found to be unequivocally predictable for death. All patients with fungal infections complicated by sepsis and vasopressor support or the need for mechanical ventilation and vasopressor support died during ICU treatment. Non-septic patients who did not require mechanical ventilation, were younger than 74 years of age and had a non-infectious underlying complication, had a survival rate of 100%.

Conclusion: Cancer patients who have not recently given their explicit statement to refuse ICU treatment, should be considered for referral to the intensive care unit in an emergency. A prospective documentation based upon the most significant prognostic parameters seems warranted.

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ORAL

Attitudes towards nutritional aspects among cancer patients- a nation wide survey

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Nutrition is seen as an important issue in relation to having a cancer disease by most patient. There are many myths about the relation between nutrition and disease course. Nutrition is seen as a way of influencing the disease course. At the same time, eating is a very important social concept.

Methods: On three days, all patients coming for treatment with either chemotherapy or radiotherapy at the department of oncology where ask to participate in this questionnaire study. The questionnaire consisted of questions about attitudes, knowledge about nutrition, and how an eventually weight loss influenced their daily living and quality of life.

Material: A total of 1036 patient agreed to participate, 739 (71%) women and 289 (29%) men, from the six Danish cancer centres.

Results: Of these 1036 patient 63% had changes their eating habits, and 71% were having some form of nutritional supplements. Significantly more women than men were taking dietary supplements (p>0.005). While 20% thought that nutrition was very important for the course of a cancer disease, only 8.5% did not think that nutrition had any influence at all. Significantly more women and younger patients emphasised the importance of nutrition. However regarding the patients actual knowledge about food, there was substantial misconception about which food was reasonable for cancer patients, as a majority favored vegetables and food with low-calorie content.

Patients in the age group between 40 and 60 years of age, where significantly more information seeking than the younger and older age groups. 59% of the patients, and significantly more women than men, where less than satisfied with the information offered at the hospitals.

Conclusion: Nutritional aspects are seen as very important by cancer patients, and the nutrition is seen as a way to influence the disease course. However, despite the high information seeking behaviour, there is a lack of knowledge of what would constitute reasonable eating habits. So, the quality of the counselling offered at the hospitals concerning nutritional aspects need improvements, as this would a way of improving every day life of the cancer patients.