we have examined the association between functional impairments of cancer patients and circulating cytokines using a multiplex technique.
Methods: 50 patients with solid malignancies were registered in the study. Physical and psychological functions were assessed using the QOL questionnaire (QLQ-C30, version 3.0) of the EORTC. Plasma cytokine levels(IL-1beta, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12(p70), IL-13, IL-15, IL-17, basic FGF, eotaxin, G-CSF, GM-CSF, IFN-gamma, IP-10, MCP-1, MIP-1alpha, MIP-1beta, PDGF-BB, RANTES, TNF-alpha, VEGF) were measured in all patients and assessed the relation to functional scale scores. The institutional Ethical Committee approved the study, and each patient gave written informed consent.
Results: Univariate analysis showed circulating levels of IL-6 and VEGF to have a significant negative correlation with physical functioning scales. Levels of IL-6, G-CSF and VEGF were negatively correlated with cognitive and emotional functioning scales in univariate analysis. Multivariate analysis showed that circulating IL-6 level is a significant independent determinant of physical and cognitive functioning and that circulating VEGF level is a significant independent determinant of emotional functioning in patients with cancer.
Conclusion: We have revealed the relationship between multiple circulating cytokines and functional impairment in patients with cancer, and demonstrated that levels of circulating IL-6 and VEGF can be biologic markers of cancer-related functional impairment. IL-6 and VEGF might play pivotal roles in the pathophysiology of cancer symptoms and functional impairments. These cytokines are highly promising candidates for therapeutic interventions to improve functions of patients with advanced cancer.

3040 POSTER

Culture-related Issues in the Translation of Quality of Life Questionnaires for Use in International Cancer Clinical Trials: Example of Classification and Solutions for EORTC Measures

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Background: The questionnaires developed by the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group are widely used to measure quality of life in cancer patients. The expanding geographical coverage of clinical trials implies a continuous need for new translations of these measures. Besides normal linguistic problems, cultural issues arise, especially outside Europe, and have to be addressed to ensure the equivalence and validity of final questionnaires. We examined these issues in this study.
Material and Methods: The EORTC Translation Unit (TU) analyzed the total of 103 translations finalized in 2010, aiming to classify problematic cultural issues and determine solutions. Theoretical background was provided by a literature search (2002–2011) in Translation Studies publications on culture-related problems.
Results: Our analysis showed two main types of culture-bound issues: (1) specific issues related to culturally-dependent activities or phenomena (e.g. driving a car in Western Europe as opposed to Asia); (2) topical issues related to taboos (e.g. sex or death).
The former are addressed using the foreignization theory, retaining cultural concepts unknown to the target culture. Comprehensibility is checked by pilot-testing the translation on patients and, if necessary, adjustments are made and re-checked. For example, the concept of “a heavy suitcase” is retained in translations into Chinese and not replaced with “a bag of rice” and its comprehensibility is tested in patient interviews.
The latter usually involve whole scales (e.g. sexuality or future perspective) and raise suggestions of deleting the entire scale. Yet, the problematic scales are always retained and patients are invited to reword them during the pilot-testing. Their suggestions are then analyzed and used for rephrasing when possible. For example, in the last 15 multiple myeloma module translations, 20 translated items proved problematic. After analysis, we rephrased 6 items and retained the wording in 14, since either the suggestions had to be refused or no options were provided.
Conclusions: Every day the TU encounters culture-related problems in translation, which, if not addressed, could hinder the assessment of QOL results in clinical trials. No ideal solution to translation challenges exists, since they always impact the final translation and its interpretations, but the TU has developed a method based on foreignization supported by pilot-testing to ensure comprehensibility and, if necessary, analyzing possible rephrasing options suggested by patients. Daily practice and validation studies have confirmed that the quality and validity of translated questionnaires are ensured.

3041 POSTER

Oxaliplatin-induced Neurotoxicity − Comparing Four Methods of Assessment

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Background: Dose-limiting neurotoxicity is a major side-effect of adjuvant oxaliplatin treatment, producing initial acute neurotoxicity and chronic neuropathy with increasing exposure [1]. Despite the potential of increased life expectancy, these symptoms may have a profound effect on the quality of life of survivors. This, coupled with findings from clinical studies (i.e. exploring causative mechanisms, the efficacy of neuroprotective agents or decisions about dose reduction) highlights the limitations of currently available symptom assessment tools. To explore these discrepancies four methods of symptom assessment were compared.
Methods: Consecutive symptomatic patients reporting peripheral neuropathy after oxaliplatin chemotherapy for colon cancer were interviewed using a semi-structured clinical interview. Subjects’ verbatim responses were analysed by qualitative methods. Neurotoxicity was also assessed by the National Cancer Institute Common Toxicity Criteria (NCI-CTC) neuropathy sensory subscale (clinician-rated); by patient ‘self-report’ questionnaires (SRQ) and objectively by nerve conduction tests [2].
Results: Twenty patients participated (65% female; mean age 58). Mean cumulative oxaliplatin dose was 789 mg/m^2. In 40% of patients early cessation of treatment was necessitated by neurotoxicity. Mean time since treatment cessation was 39 weeks. Only 2 patients were designated by clinicians with maximum NCI grade 3 (sensory alteration or paresthesia interfering with activities of daily living), the remainder were classified as grade 1 or 2. All patients interviewed described physical limitations due to symptoms and SRQ data supported this (75% reported ‘moderate symptoms’).
Conclusions: Given the discrepancies in symptom prevalence highlighted by findings in this study, the identification and monitoring of oxaliplatin-induced neurotoxicity would benefit from more appropriate and informative clinical assessment. This would be beneficial not only in clinical trials to monitor the efficacy of interventions and research exploring aetiopathology but also in prospective studies of survivors. A method of assessing symptom severity and frequency together with disability, and which provides a cumulative score is proposed.

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3042 POSTER

Does Response Shift Affect the Change in Health Related Quality of Life During Treatment for Childhood Cancer?

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Background: Confrontation with a serious illness changes the person’s internal standards about good or poor Health Related Quality of Life (HRQL) as a result of adaptation to the imperfect health status. This change in internal standards, called response shift, might influence the measures of change in HRQL in longitudinal studies. This study assessed whether response shift affected the change in HRQL during the first three months of treatment for childhood cancer.
Materials and Methods: HRQL was assessed within two weeks after diagnosis (pre-test) and three months later (post-test) using both child- and parent-report of PedsQL and Cantril’s ladder. Health status was assessed with MSAS and Lansky Performance scale. Concurrently with the post-test, a then-test of PedsQL and Cantril’s ladder was administered where child and parent had to give a renewed judgement about the HRQL shortly after diagnosis. A difference between pre- and then-test indicates the presence of response shift. Included were children $\geqslant$8 years (n = 37), their parents, and parents of children $\geqslant$2 years (total number of parents: n = 80). Wilcoxon Signed Rank-Tests were used to compare pre- post- and then-tests.

Results: Both health status and HRQL improved between pre-and post-test. Cantril's then-test was lower than the pre-test both in child- and parent-report, indicating a negative response shift for overall HRQL. Corrected for response shift, the improvement in overall HRQL was greater than based on the conventional pre-test versus post-test design. However, no differences were found between the PedsQL then- and pre-tests.
The response shift of child and parent was moderately related (Spearman's rho 0.55 $p < 0.01$), where children experienced a greater negative response shift than parents.
Conclusions: Three months after diagnosis children and parents were more negative about the HRQL (Cantril) at diagnosis than at the moment itself. This response shift threatened the interpretability of the change in overall HRQL over time. No response shift was demonstrated in the more specific domains of HRQL (PedsQL) despite the improved health status. By explicitly measuring response shift, changes in the perceived overall HRQL of childhood cancer patients will be assessed more validly.

3043 POSTER

Measurement Properties and Equivalence of the English and Chinese Versions of the New 5-level EQ-5D in Asian Breast Cancer Patients

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Background: Recently, a new, 5-level version of the EuroQoL Group's − 5 Dimensions (EQ-5D) questionnaire has been released. This study aimed to examine the measurement properties and equivalence of the English and Chinese versions of the new EQ-5D in assessing self reported outcomes in Asian breast cancer patients.
Materials and Methods: This is an observational validation study of ethnic Chinese breast cancer patients in Singapore. The patients answered either the English or Chinese version of the EQ-5D according to their language preference and another cancer-specific questionnaire at baseline and at follow-up two weeks later. Demographics, performance status and other clinical variables were also obtained. Multivariable regression analysis with adjustment for differences in demographic and clinical background was used to assess measurement equivalence of the two language versions.
Results: The EQ-5D showed known group validity in distinguishing differences in performance status, evidence of disease and treatment status, and the two language versions had similar performance. The utility index and the 5 classifiers showed convergent and divergent validity in relation to the domains of the cancer-specific questionnaire. Based on patients who expressed no change in quality of life and performance status at follow-up, the test-retest reliability of the EQ-5D was high, and comparable between the two language versions.
Conclusions: The new, 5-level EQ-5D is a valid questionnaire in assessing breast cancer patients' self reported outcomes. The English and Chinese versions of the EQ-5D performed similarly in terms of discriminative ability and test-retest reliability.

3044 POSTER

Bone Marker Patterns During Long-term Bisphosphonate Therapy for Patients With Bone Metastases

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Background: Patients (pts) with bone metastases (mets) from breast cancer (BC), prostate cancer (PC), and other solid tumours are routinely treated with bisphosphonates (BPs) to reduce their risk of potentially debilitating skeletal-related events (SREs). Prior studies have shown that zoledronic acid (ZOL) effectively lowers levels of the osteolytic marker N-telopeptide of type I collagen (NTX) in pts with bone mets (Coleman, *JCO*, 2005), and NTX effects are generally observed within 3 mo (Lipton, *Cancer*, 2008). However, long-term NTX effects, especially beyond 2 yr, have not been studied in the clinical practice setting.
Material and Methods: Urinary NTX assessments were performed for pts with bone mets treated at Hospital de Santa Maria in Lisbon. For ZOL-treated pts, NTX levels were assessed at baseline and annually and categorized as elevated (E) if >100, moderate (M) if 50–100, and normal (N) if <50 nmol/mmol creatinine. Medical records were evaluated for SREs and drug safety.
Results: Fifty-eight ZOL-treated pts with a median follow-up of 36 mo were evaluated, mostly with BC (n = 43) or PC (n = 13), but lung, renal, and liver cancer cases were also included. At baseline, mean NTX was 131 (median, 87) overall and 150 (median, 95) nmol/mmol creatinine for BC. With ZOL, most pts transitioned to lower-NTX categories during treatment (table). Median time to first SRE was 31 mo overall; 22 pts (38%) remained SRE-free at last follow-up, 20 of whom were treated for >2 yr. Three pts had serum creatinine elevations (none >3 mg/dL). A total of 4 pts had ONJ; each was treated for a total of $\geqslant$2 yr. One case of ONJ healed to normal; 3 persisted.

NTX parameter	Baseline	1 yr	2 yr	>2 yr
Evaluable, n	58	54	41	30
E/M/N distribution, n	24/23/11	11/6/37	1/4/36	3/3/24
Median NTX, % of baseline	(= 100%)	32%	28%	26%

Conclusions: These analyses illustrate that ZOL produces long-term normalization of NTX levels and in pts with bone mets. Therapy with ZOL produces SRE rates that compare favorably with prior reports in bone mets settings; ZOL therapy for 2 or more years was generally well tolerated.

3045 POSTER

Febrile Neutropenic Patients Admitted for Intravenous Antibiotics − Analysis of 213 Episodes in 201 Patients With Solid Tumours

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Background: Febrile neutropenia (FN) is a serious adverse event of chemotherapy, but a fraction of patients (pts) diagnosed with solid tumours develops serious complications related to a FN episode. We aimed to characterize FN episodes in patients diagnosed with solid tumours admitted for intravenous antibiotics in our institute, and to identify those pts prone to develop serious clinical complications.
Materials and Methods: It is a retrospective study of 213 episodes of FN in 201 pts admitted in our institution from Jan/2009 to Dec/2010 for intravenous antibiotics after a diagnosis of FN. Antibiotics were selected following the current recommendations. Relevant information were collected at admission, and were correlated to selected clinical complications as outcomes (admission at ICU, hypotension, altered mental state, respiratory failure, renal failure, rapid intravenous fluids administration, dialysis, congestive cardiac failure, arrhythmias, bleeding, disseminated intravascular coagulation, death). Exploratory analyses were performed using chi-square test or Fisher exact test, when appropriate, and the optimal cutoff value for differentiation of patient's categories was defined by ROC analysis for each continuous variable.
Results: 213 episodes of FN in 201 pts were analyzed: 51% male, median age 55 y (16−88 y). Most frequent (>5%) primary tumour sites included soft tissue/bone (21%), breast (13%), lung (12%), colorectal (10%), stomach (7%) and testis (6%). 96 (50%) presented stage IV disease. At admission, the median neutrophil count was 300 cells/microliter, and the median MASCC score at admission was 18 (7−26). Cultures were positive in 90 FN (42%) episodes and Gram negative bacilli were identified in 51% of them. Following current recommendations, piperacillin-tazobactam or cefepime, alone or in combination with vancomycin were prescribed in 193 out of the 213 FN episodes. Serious clinical complications were observed in 139 pts and were more frequently observed in those pts aged >40 y ($p = 0.003$), in pts diagnosed with primary tumours located in esophagus, stomach, lung and colo-rectum ($p = 0.002$), previously diagnosed with COPD ($p = 0.009$) and presenting with dehydration at admission ($p = 0.002$).
Conclusion: FN patients is a heterogeneous group and the identification of selected patients with higher risk allows us to better tailoring their supportive care, and clinical parameters remain as important determinants of serious clinical complications.