model. We also examined antiangiogenic potential of RL-66 *in vitro* using the endothelial cell tube formation assay and transwell migration assay.
The results showed that RL-66 arrested MDA-MB-468 cells in the G2/M phase of cell cycle. Furthermore, RL-66 increased apoptosis in MDA-MB-468 cells by 4-fold compared to control. Moreover, RL-66 altered the expression and phosphorylation pattern of a variety of proteins which are involved in either cell proliferation or apoptosis. Importantly, treatment of nude mice bearing MDA-MB-468 xenografts with RL-66 (8.5 mg/kg/d, 70d, PO) significantly reduced tumour growth by 50% compared to control. In addition, RL-66 showed antiangiogenic properties by inhibiting endothelial cell invasion and the ability of these cells to form a capillary like tube network.
Thus our findings provide evidence that RL-66 has promising anticancer activity *in vitro and in vivo* in ER negative breast cancer in addition to antiangiogenic activity *in vitro* and thus it has potential clinical application.

5086 POSTER

Quality of Life − Patient-reported Outcomes in Patients With Advanced Hormone Receptor Positive Breast Cancer

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Background: Quality of life/patient-reported outcomes (PRO) are an important consideration in the care of patients with advanced breast cancer (BC). Approximately 75% of invasive BCs are hormone receptor positive (HR+). HR+ BC is distinct from HR negative BC in its pathological, clinical, and prognostic features. The aim of this study is to identify PRO instruments that are fit for purpose in these patients and meet regulatory standards for PRO claims of new medicines.
Materials and Methods: Data were obtained from a systematic literature review and interviews with 2 clinical experts (1 US, 1 EU). Literature search was conducted using OVID (EMBASE & Medline) for publications from 2000–2010.
Results: The literature search yielded 636 abstracts; of these, 33 assessed PRO in advanced HR+ BC. Symptoms and functional impacts of the disease and treatments identified through literature and expert input include bone pain due to bone metastasis, weakness, fatigue, abdominal fullness and dyspnea due to liver and lung metastases respectively, and endocrine symptoms related to hormone treatments. The most commonly used PRO instruments included the EORTC and Functional Assessment of Cancer Therapy (FACT) questionnaires core and BC-specific modules (EORTC QLQ-C30, QLQ-BR23, FACT-B). These instruments however do not capture the key issues important to these patients. Symptom-specific instruments such as bone pain or bone metastasis specific instruments EORTC QLQ-BM22, BOMET-QOL10, and FACT-Bone Pain, and endocrine symptom-specific instrument FACT-ES are not widely used and not BC specific. All of the instruments failed to show that input from advanced HR+ BC patients is solicited in the development of the questionnaires. Their validity, sensitivity, and reliability in this patient population are unclear. To address all aspects of PRO in this patient population, it would seem necessary to use multiple instruments with redundant questions of varying validity and reliability. No single instrument is fit for purpose in this patient population by regulatory standards.
Conclusions: Symptoms and functional impacts important to these patients need to be confirmed with patient input. New medicines interested in claims of PRO benefits would need a single instrument that captures all key issues confronting this patient population with sensitivity, validity, and reliability and without undue burden to the patients.

5087 POSTER

An Integrated Approach for Causal Association Among Gene Expression, Genotype Variation and Chronic Fatigue in Breast Cancer

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Background: Fatigue is the most common late effect of cancer therapy. The etiology of fatigue is still unclear. To elucidate the mechanisms behind fatigue, we have so far applied basic statistical approaches to two data sets including mRNA expression, SNPs, cancer-related information and the fatigue questionnaire (FQ) scored to identify chronic fatigue (CF). Incorporating information of genotype, expression and disease may improve understanding of disease etiologies, we focus on developing an integrated approach. The method of choice is model-based statistical tests [1] that identified causality among specific genotype variation, mRNA expression levels and longitudinal clinical data.
Material and Methods: Women treated for BC stage II/III at the Norwegian Radiumhospitalet were in 2004/2005 invited to attend a primary follow-up study on late effects. 76% of the invited women eligible subjects completed the FQ. RNA and DNA were isolated from peripheral blood and mRNA and SNP were obtained by Illumina platform. Using SNP, mRNA and CF data, we consider possible relationships among them by following three models, causal, reactive and independent models defined in [1]. Each model is represented by a Bayesian model and likelihood-based model selection is applied to select the best-fit-model to each genomic location. After matching these locations to genes, pathway analysis (IPA http://www.ingenuity.com) is performed for the gene lists obtained by the best-fit-model to investigate the biological functional mechanisms.
Results: We applied three models to in-*cis* relationships of mRNA and SNP for ~7,500 genes and 177 samples. The causal model identified ~2,400 genes and the reactive model identified ~5,000 genes. The independent model identified 29 genes. By the gene lists for the causal model, IPA estimated the biological functions related to inflammatory response, infection and inflammatory diseases, hematological system development, cell-mediated immune response and immune cell trafficking, and regulation of the immune response for the canonical pathways. For the reactive model, the biological functions significantly indicated inflammatory mechanisms, B cell receptor signaling and CD40 signaling in the canonical pathways.
Conclusions: The causality and reactive models involving genotype variation, mRNA expression and CF indicated more comprehensive information than only applying statistical procedure to two data combinations. To identify more specific biological characteristics, we plan to look into the genomic region related to immune system and apply specific statistical methodology. We could also involve other clinical variables related to CF such as BMI to these models.

References

[1] Lee et al. Genomics, 2009.

5088 POSTER

Assessment of Burden of Illness in Women With HER2+ Metastatic Breast Cancer: Findings From a Community Web-based Survey

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Background: To better understand burden of illness in women with HER2+ metastatic breast cancer (MBC), we conducted a survey to evaluate their treatment experiences.
Materials and Methods: This one-time, web-based survey was conducted with the help of 4 independent U.S. breast cancer support groups. Respondents were invited to participate via email, and were required to be female, aged 18+ with HER2+ MBC, and to have received active treatment in the past month. Approximately 100 demographic, clinical, employment, quality of life, social and resource use data items were collected.
Results: 130 women with HER2+ MBC completed the survey. The majority of respondents were 45−59 years old (54.6%), white (93.9%), living with a spouse or partner (72.3%) and had at least a college education (70.8%). The most common comorbid conditions were high blood pressure (10.0%), thyroid disease (4.6%), diabetes without complications (4.6%), congestive heart failure (3.9%) and rheumatologic conditions (3.9%). While over 65% were full time employed at the time of MBC diagnosis, only 26% were at the time they completed the survey. 69% were currently taking a trastuzumab containing regimen, commonly with another medication. Frequently used medications included lapatinib and paclitaxel. Symptoms reported as frequently bothersome by at least 20% of women were: tiredness (52%), decreased sexual interest (50%), difficulty sleeping (39%), worry (39%), joint/ muscle pain (34%), difficulty concentrating (27%), alopecia (24%), low back pain (23%), depressed mood (22%), constipation (20%), and tingling of hands or feet (20%). Despite their disease, these women expressed high levels of satisfaction with their lives and relationships (with family, friends, and other women with MBC), but were less satisfied with their employment and their feeling about the future. They expressed higher levels of burden due to pain/discomfort and anxiety/depression than due to usual activities, self-care, and mobility. Fewer than 10% had discussed palliative care options with their doctor.
Conclusions: This community survey of women with HER2+ MBC provides valuable insights into their demographics, work status, treatment, and symptom burden. There were numerous symptoms that were

frequently reported as bothersome; however, women who completed the survey expressed high levels of satisfaction with their lives and relationships demonstrating a resilient ability to cope with their disease.

5089 POSTER

Radiosensitized Treatment of Advanced Breast Cancer

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Background: Currently the methodologies that are used in oncology are quite of limited possibilities Therefore, there is a constant search for new perspective treatment methods, which could prolong the lives of cancer patients and would make them more qualitative One of such methods is sensitized tumour therapy based on quite selective porphyrin accumulation in tumour. This study presents our primary results in − radiosensitized advanced breast cancer therapy using derivatives of hematoporphyrin as a radiosensitizers.
Material and Methods: From 2001 to 2010 a total of 54 female patients with advanced breast cancer underwent radiosensitized treatment (RST). All patients underwent chemotherapy and/or radiotherapy and surgical treatment until RST. In all cases any radical method of treatment was impossible. Multiplex metastatic lesions were established in 53 patients. Brain multiplex metastases were diagnosed in 19 patients, multiplex bones metastases in 27 patients. However 9 patients had both metastases − bones and brain. Lung, liver or soft tissues metastatic lesions were obtained in the rest 17 patients. Hematoporphyrin derivative was injected intravenous; 24, 48 and 72 hours after an injection of the sensitizer tumours were irradiated with gamma rays from radioactive ^{60}Co 2 Gy at a time (6 Gy per course).
Results: As the result of RST complete regression of all treated tumours was observed in 5 patients after two or more RST courses. A significant response − regression of more than 50% of all brain metastases and remission of the disease for over 6 months was established in 17 patients. A partial response was observed in 18 patients with malignant brain tumours. For the rest 14 patients treatment was ineffective. The Karnofsky performance scale index increased immediately in 33 patients following RST treatment. RST was especially effective in the treatment of brain and bones metastatic lesions. As regards brain metastases in one patient all 3 brain metastatic lesions fully disappeared and there were no evidence of any recurrence in brain for 8 months. In 6 patients − regression of more than 50% of all brain metastases and remission of the disease for over 6 months was established. The median survival of 19 patients with multiplex brain metastases was 12 months from the moment of brain metastases detection. As regards bone metastases as the result of RST, all metastatic lesions fully disappeared in 7 patients.
Conclusion: Radiosensitized advanced metastatic breast cancer treatment is a hopeful method, especially when lesions involve the brain and bones.

5090 POSTER

Circulating Tumour Cells or Stem Tumour Cells From Periferal Blood as a Prognostic Marker for the Clinical Course of Patients With Breast Cancer?

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Background: Recently it has been proved and recognized the value of the circulating tumour cells as a predictive entity and marker for various types of neoplasm. This analysis has as a unique purpose to induce the exploration of an entity which is a subgroup of whole cancer disease in a patient called circulating tumour cells which include stemness features, with final purpose their exploitation as a predictive and possible diagnostic marker with relevant value.
Materials and Methods: For the reason of the specific analysis of blood samples from 58 patients with breast cancer has been used in different stages according TNM classification system (between II and IV). From these samples we have perform identification, isolation, quantitation and quality analysis of the circulating tumour cells as well as of the presence of cancer stem cell like cells. The assays that have been followed were on pairs in order to form double platform method in order to avoid false positive or negative results. Parallely, we have requested from the medical centers where the patients were being treated their clinical assessment so far according the commonly accepted response rate classification. From these two groups of data (laboratory and clinical) we have performed a static correlation in order to accept or reject the relevance of the cancer stem cell like cells with the clinical assessment and progress of the disease.
Results: From the whole of the patients a statistic analysis of data has been performed and those samples with enough data have been selected in order to avoid statistical error type I. The statistic analysis showed that there is a strong static correlation and relevance between the existence and the concentration of the cancer stem cell like cells in the blood sample of a patient with breast cancer in relation with the progress of the disease and the response to treatment. The immunphenotype of the cancer stem cell like cells has an additional role to the prognosis of cancer patient, equally important with the previous parameters.
Conclusions: From the present analysis it is shown that the detection of cancer stem cell like cells can have an accurate role as a prognostic marker of the clinical development of the cancer patient disease.

5091 POSTER

Prognostic Significance of Breast Cancer Phenotypes in Patients for Operated Stage IIIC Breast Carcinoma

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Background: Breast cancer is a heterogenous disease with varied clinical behaviour. Aim of this retrospective study was to evaluate prognostic significance of phenotypes in patients for operated breast carcinoma who had $\geqslant$10 lymph node positive before approval of trastuzumab for adjuvant use.
Material and Method: Medical records of 136 breast cancer patients with $\geqslant$10 axillary lymph node involvement diagnosed between 1994–2009 years were evaluated retrospectively. 111 patients whose tumours were known hormon receptor(HR) and HER2 status are included in the study. None of these patients had received neoadjuvant systemic therapy.
Results: Median age was 48 (21−77)years. Median follow-up was 42 (3–155) months. 63 patients were premenopousal. 87% of the patients had invasive ductal carcinoma. Only 9.2% of primary tumours were <2 cm. 95% of the patients had grade 2 or 3 tumours. The proportion of breast cancer phenotypes was 56.8% HR+/HER2−, 32.4% HER2+ and 10.8% triple negative (TN). Nearly all patients underwent modified radical mastectomy and adjuvant radiotherapy. 84 patients received taxan-based adjuvant chemotherapy. At the time of analysis, 75 patients had recurrent disease and 53 patients died due to breast cancer. The percentage of recurrent disease in patient subgroups were as follows: 63.5% for luminal A, 77.8% for HER2+, and 58.3% for TN. Five-year overall survival (OS) and disease-free survival (DFS) rate for entire group was 55% and 22% respectively. Tumour size has shown a negative correlation with OS and DFS (log-rank $p < 0.0001$ and $p = 0.07$ respectively). Although DFS of luminal A was relatively longer than others, it did not reach statistically significance (log-rank $p = 0.2$). Patients with HR+/HER2− tumour had a significantly longer survival time as compared with HER2+ and TN groups (65%, 35% and 37%, respectively; log-rank $p = 0.05$). Univariate analysis showed that larger tumour size, HER2+ and TN subtypes had a negative impact on overall survival. In multivariate analysis these parameters were found independent prognostic factor with a significant negative influence on overall survival in patients who had $\geqslant$10 axillary lymph node metastasis also.
Conclusion: HR+/HER2− breast cancer had better prognosis than TN and HER2+ ones even if they had entensive axillary lymph node metastasis. Prognosis of HER2+ breast cancer was similar TN groups in the absence of adjuvant trastuzumab treatment.

5092 POSTER

DNa Toxicity of Pt(II) and Pd(II) Polyamine Complexes in Human Breast Cancer Cells

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Background: Since the discovery of cisplatin [1], Pt(II) and Pd(II) complexes have become of increasing importance in the design of new anticancer drugs. Among these second and third-generation agents, polyamine chelates have been the target of intense research since they yield DNA adducts with long-distance intra- and interstrand cross-links, not available to the conventional mononuclear platinum compounds [2]. The modified spermidine $H_2N(CH_2)_3NH(CH_2)_3NH_2$ (norspermidine, NorSpd) was used as a ligand to synthesize $Pd_3NorSpd_2$ and $Pt_3NorSpd_2$ chelates.
Material and Methods: Normal human breast epithelial cells MCF-10A and breast cancer cells JIMT-1 and L56Br-C1 were treated for several treatment