

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.

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POSTER

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

Y. Su¹, E. Flood², J. Devlen², S. Tsay², K. Beusterien², S. Wagner¹.

¹Bristol-Myers Squibb, Global Health Economics and Outcomes

Research, Princeton NJ, USA; ²Oxford Outcomes, Patient-reported Outcomes, Bethesda MD, USA

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.

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POSTER

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

H.S. Solvang¹, H.L.H. Landmark-Høyvik¹, H.K.R. Reinertsen¹, J.H.L. Loge¹, S.D.F. Fosså¹, A.L.B.D. Borresen-Dale¹, V.N.K. Kristensen¹, H.E. Edvardsen¹. ¹Norwegian Radium Hospitalet, Genetics, Oslo, Norway

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.

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POSTER

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

M. Mayer¹, J. Doan², K. Lang³, S. Hurvitz⁴, D. Lalla², R. Woodward³, M. Brammer⁵, J. Menzin³, D. Tripathy⁶. ¹AdvancedBC.org, Advocacy, New York, USA; ²Genentech Inc., Biometrics Health Outcomes and Payer Support, South San Francisco, USA; ³Boston Health Economics, Health Economics and Outcomes Research, Boston, USA; ⁴UCLA Jonsson Comprehensive Cancer Center, Hematology/Oncology, Los Angeles, USA; ⁵Genentech Inc., Medical Affairs, South San Francisco, USA; ⁶University of Southern California, USC/Norris Comprehensive Cancer Center, Los Angeles, USA

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