cancer. Here we report the efficacy of AIs and the effects on the expression of hormone receptors and Ki67 in breast cancer tissues.

Patients and Methods: Twenty-nine postmenopausal patients with stage I (n = 3), IIA (n = 11), IIB (n = 5), IIIA (n = 2) and IIIB (n = 9) ER-positive breast cancers were treated with anastrozole, letrozole or exemestane as neoadjuvant treatment. One patient had bilateral breast cancer. The median age of the patients was 73 years, with a range of 48 to 87 years old. Expression of hormone receptors and Ki67 was assessed before and after the treatment.

Results: One of 30 tumors showed complete response (CR), 15 showed partial response (PR) and 14 showed stable disease (SD). Objective response rate was 53%. The median duration of treatment was 6 months. All treatments were generally well tolerated. There was a significant positive relationship between hormone receptors expression and tumor response (ER; 0.037, PgR; 0.033). After the treatment, a decrease of PgR expression was more frequent in responding tumors (93.8%) than in non-responding tumors (35.7%). Percentage change in Ki67 expression from baseline after treatment was −76.6±4.2% in responding tumors and −8.7±24.5% in non-responding tumors, respectively. Suppression of the proliferation marker Ki67 after treatment was significantly greater in responding tumors than in non-responding tumors ($P = 0.002$, Mann–Whitney U test). With a median follow up of 69 months, there was no significant difference in overall survival between patients with CR or PR and those with SD.

Conclusions: Neoadjuvant AI provided satisfactory efficacy and safety profiles in breast cancer. The main biological effects of AI consisted of a decrease in Ki67 expression for responders.

No conflicts of interest

Wednesday, 19 March 2014

POSTER SESSION

Bone and Other Organ Targeted Therapy

64 Poster

The best timing of using strontium-89 combing with zoledronic acid for breast cancer patients with painful bone metastases

K. Yamada[1], H. Kaise[1], S. Komatsu[1], M. Matsumura[1], Y. Nakamura[1], M. Hosonaga[1], T. Kawate[1], K. Miyahara[1], A. Ueda[1], N. Kohno[1]. [1]*Tokyo Medical university, Breast Oncology, Tokyo, Japan*

Background: Strontium-89 is recognized to relieve radiation-induced pain, as demonstrated in cases of external irradiation. This agent reaches metastatic bone sites throughout the whole body when intravenously administered as a single dose, and is therefore often employed to treat multiple bone metastases. However, Sr-89 induces bone marrow suppression as an adverse effect. In relation to this, the guidelines established in the United States and Europe emphasize that physicians must carefully consider the use chemotherapeutic agents and external irradiation in relation to the development and treatment of metastatic bone pain. However, there are no restrictions regarding combinations such as with endocrine therapy agents, analgesic agents, or adjuvant analgesic agents (e.g., bisphosphonates). The purpose of this study was to examine the safety and efficacy of the concurrent use of the radiopharmaceutical strontium-89 (Sr-89) chloride with zoledronic acid in standard anticancer therapy for breast cancer patients with painful multifocal bone metastases.

Material and Methods: The subjects were 38 breast cancer Japanese women with painful bone metastases detected by bone scintigraphy, computed tomography or magnetic resonance imaging, in whom Sr-89 was added to zoledronic acid continuous therapy, or was added after an initial administration of zoledronic acid at the Department of Radiology in our hospital, between October 2007 and October 2013. The median age of the subjects was 56 y-o (39−77 y-o). The average period of using zoledronic acid before Sr-89 administration is 15.8 months (0−64months).

Results: In this study, the median survival period after Sr-89 administration was 15.1 months. When evaluating the efficacy of this combination with respect to changes in the doses of analgesic agents, 29 (76%) of the 38 patients responded to this therapy. In this study, we also reviewed chemotherapeutic regimens combined before and after Sr-89 administration. Chemotherapy with vinorelbine, gemcitabine, capecitabine, and nab-paclitaxel, which may cause bone marrow suppression, was performed before and/or after Sr-89 administration. Adverse events were tolerable, suggesting that simultaneous combination therapy with chemotherapy before or after Sr-89 administration, or combination therapy early after Sr-89 administration is possible in patients with bone metastasis from breast cancer.

Conclusions: The use of Sr-89 with zoledronic acid in breast cancer patients with painful bone metastases was safe and effective when administered concurrently with other standard therapies. Our Japanese group (JONIE) is currently trying a large-scale clinical study of treatment with Sr-89 at the early stage. The results of this trial (JONIE-2 trial) are expected soon.

No conflicts of interest

65 Poster

Feasibility and improvements in quality of life for patients with metastatic breast cancer changing from intravenous pamidronate to subcutaneous denosumab

A. McCormack[1], S.A. Kelly[1], J. Oliver[1], M. Campbell[1]. [1]*Plymouth Hospitals Nhs Trust, Oncology, Plymouth Devon, United Kingdom*

Background: Following NICE approval of subcutaneous denosumab (Xgeva®) for use in patients with bony metastases from breast cancer, we converted all suitable cancer patients from iv pamidronate to sc denosumab and measured changes in quality of life (QOL); the percentage able to self-administer; how many could receive treatment in the community, and improvement in capacity in our chemotherapy outpatient department.

Materials and Methods: An outpatient, hospital based nurse led clinic was set up to administer denosumab, with the aim that all patients should eventually receive treatment in the community. The first 3 monthly injections were given in hospital, and patients or their relatives were offered the opportunity to learn how to administer the treatment at home. QOL questionnaires were completed before starting, after the third and following three injections in the community. Patients were reviewed monthly initially and three-monthly thereafter. Capacity within the outpatient chemotherapy department was assessed in terms of 'chair-time' before and after the regime change.

Results: 71 patients commenced denosumab between 1st Jan and 31st Oct 2013. 17 patients were excluded from the analysis; 1 moved out of area, 12 died, and 4 patients discontinued treatment. 90% of patients received treatment within the community. Of these, 39.5% self-administered, 14.5% relied on a relative or friend, 23.3% attended their GP practice, 6% were visited by the district nurse and 16.7% attended chemotherapy outreach services.

Patients found treatment with denosumab was less troublesome than pamidronate, with more patients reporting treatment was convenient (64% vs 27%); fewer having their day disrupted (12% vs 33%); and more were able to plan future events (52% vs 33%). Denosumab was more comfortable to administer (48% vs 37%). In addition fewer patients were bothered that they had to be accompanied for treatment (12% vs 33%). However patients receiving pamidronate enjoyed the company with more reporting that they enjoyed meeting other people at treatment (50% vs 20%). 152 hours of 'chair-time' was liberated by the change to denosumab in a single month.

Conclusion: We demonstrated that it is relatively simple to set up a system to administer treatment for bone metastases in the community. Patients found denosumab tolerable, easy to administer and more convenient than bisphosphonates. In addition, by utilising an outpatient-based system, capacity within the department was increased.

Conflict of interest: Corporate-sponsored research: A grant was provided by Amgen to fund a nurse to set up an outpatient-based clinic to administer denosumab

Wednesday, 19 March 2014

POSTER SESSION

Detection, Diagnosis and Imaging

66 Poster

Immune targets on circulating epithelial cells in early and late breast cancer

L. Habets[1], B. Frenken[1], I. El Ghali[1], M. Danaei[2], M. Kusche[2], U. Peisker[3], K. Pachmann[4]. [1]*Metares e.V., CEC research, Aachen, Germany;* [2]*Brustzentrum Aachen Kreis Heinsberg, Senologie Aachen, Aachen, Germany;* [3]*Brustzentrum Aachen Kreis Heinsberg, Senologie Erkelenz, Erkelenz, Germany;* [4]*TZB bayreuth, Bayreuth, Germany*

Background: The main differences between the MAINTRAC method in comparison to enrichment based methods are the higher counts of EPCAM+ cells and that not mere existence but rise or fall of cell counts

are prognostic. It could be shown that these cells have markers of epithelial–mesenchymal transition and stem cell characteristics. So far 2 intriguing observations emerged from our continued exploration of CEC. (1) The cell type with EMT and stem cell characteristics can be found also in non-cancer conditions, e.g. metabolic liver disease. (2) Cell counts disappear in progressing patients or are negative a priori in aggressive subtypes. These findings urged for an extended characterization of CEC.

Materials and Methods: We adapted the MAINTRAC Basic procedure (RBC Lysis, immunofluorescent analysis and detection on Olympus Scan R) for flowcytometric detection of CEC on the AMNIS FlowSight (EMD − Millipore). Besides the addition of a fourth colour not only single cells but also subcellular particles and cell aggregates can be detected and analyzed.

The basic 4 colour panel consists of EPCAM, CD45, DAPI and ALDH1. In parallel we ran a second panel were ALDH1 was substituted by PDL1 or phosphatidylserine (PS). The basic panel defines living or dead EPCAM+ ALDH1+ cells. In the second panel coexpression of PDL1 or PS can be analyzed on the EPCAM+ CD45neg population.

Results: We examined 1 ml of blood from 88 patients with early and 58 patients with late breast cancer. The control population consisted of 30 persons. We found the following counts of living EPCAM+ cells in early breast cancer patients: 0 (n = 44), 100 (n = 8), 250–500 (n = 120), >1000 (n = 7). In advanced breast cancer patients: 0 (n = 9), 250–500 (n = 20), 500–1000 (n = 11), >1000 (n = 18). In the defined control: 0 (n = 28), 100 (n = 2). In a group of non-healthy non-cancer patients higher cell counts can be found, especially in patients with signs of metabolic liver afflictions. The percentage of living cells within the EPCAM+ population varied from 0% to 28%. ALDH1 is nearly exclusively expressed on EPCAM+ cells and shows no overlap in the CD45 population. The same holds true for the expression of PDL1 and phosphatidylserine. The expression of PDL1 and PS is also detectable on the CEC in non-cancer situations. Besides HER2 all the markers we tested so far (estrogen receptor, EGFR2, metabolic markers like HIF1 or CA9 or several cytokeratin markers) were not able to differentiate between 'liver derived' and real CTC.

Conclusion: We could demonstrate the upregulation of the targetable immune markers PDL1 and phosphatidylserine on CEC in early and late breast cancer as well as in non-cancer conditions. This upregulation serves to guarantee a better survival of cells in epithelial–mesenchymal transition during their passage through the bloodstream. The MAINTRAC defined CEC phenomenon shows that cells in EMT are not a rare event. Though not exclusively tumor derived it opens extended possibilities to investigate the biology and targetability of these cells in different disease situations.

No conflicts of interest

67 Poster

Discordance in estrogen, progesterone and HER2/neu status between primary and recurrent breast tumours: A systematic review

I. Yeung[1], M. Clemons[2], B. Hutton[3], F. Haggar[3], C.L. Addison[3], I. Kuchuk[2], X. Zhu[2], S. Mazzarello[2], A. Arnaout[1]. *[1]The Ottawa Hospital, General Surgery, Ottawa, ON, Canada; [2]The Ottawa Hospital Cancer Centre, Medical Oncology, Ottawa, ON, Canada; [3]Ottawa Hospital Research Institute, Medicine, Ottawa, ON, Canada*

Background: In breast cancer patients, estrogen (ER), progesterone (PR), and epidermal growth factor receptor (HER2) discordance between primary and metastatic disease is well recognized and can have important therapeutic implications. A systematic review was conducted to assess the extent of receptor discordance between primary tumors and their paired recurrences.

Methods: EMBASE, Medline and Cochrane Central Register of Controlled Trials were searched for English-language cohort studies reporting ER, PR, and HER2 expression for matching primary and recurrences. Using pre-defined criteria, two reviewers independently performed data extraction. QUADAS-2 was used to assess risk of bias and study applicability of the included studies. Median discordance and ranges between primary and recurrence for each biomarker were calculated. Associations between receptor discordance and the site of recurrence were also explored.

Results: Of 7,359 citations identified, 46 studies (representing 3,328 total samples) met the inclusion criteria. Studies were generally small with a median of 42 matched pairs. Median discordance rates for ER, PR, and HER2 were 15% (range 0−67%, IQR 10−29%), 21% (range 0−62%, IQR 16−43%), and 10% (range 0−44%, IQR 4−14%) respectively. Discordance rates were higher at bone site of metastases [ER: 53% (IQR 42−67%); PR: 50% (IQR 46−50%); HER2: 20% (IQR 11−38%)] compared to all other sites (brain, liver, lung, lymph node, GI). The general trend was for a loss of receptor. HER2 tend to be more stable than the hormone receptors.

Conclusion: Discordance rates vary for both the biomarker and the site of recurrence. When discordance occurs, loss of a biomarker expression is more common than gain, and is observed most frequently with PR. Bone metastasis had the highest rate of discordance compared to other sites. Discordance amongst receptors can have important treatment implications. Future studies evaluating the impact of discordance on patient outcome and management are recommended.

No conflicts of interest

68 Poster

MRI screening in women at average risk for breast cancer

S. Schrading[1], C.K. Kuhl[1]. *[1]RWTH Aachen University Hospital, Department of Diagnostic and Interventional Radiology, Aachen, Germany*

Background: In asymptomatic women at average-risk, mammography alone, possibly amended by ultrasound (US), is recommended for screening. MRI is established for screening women at high-risk, but there are no data available to support its use in women at average-risk. Therefore, we systematically offered breast MRI (DCE) to asymptomatic women at average-risk who had normal screening mammograms and (in dense breasts) normal screening ultrasound, in order to investigate the added cancer yield and accuracy of breast MRI in the average-risk screening situation.

Materials and Methods: Between January 2005 and December 2012, 1516 women at average-risk, i.e. without personal or family history of breast or ovarian cancer or tissue diagnosis of atypias underwent 2574 annual MRI screening studies. Mean/median age was 55/56 years, range 40−79. All women had normal clinical breast examination and normal double-read 2-view digital screening mammograms. In women with breast densities, additional US had been performed and women were included if also US was normal. Patients underwent bilateral DCE MRI at 1.5 T using a 2D GE pulse sequence.

Results: A total of 132 MRIs were rated positive (MR-BI-RADS 4/5) (132/2574; 5.1%). Biopsies performed in these women were positive for breast cancer or DCIS in 48, and revealed high risk lesions in another 27 patients, yielding an additional cancer yield of 18.6/1000. In 50 women (38%), biopsy revealed benign changes only. This translates into a PPV of 36% (48/132), or 57% (75/132) if high risk lesions are included. Of the 48 cancers, 31 (65%) were invasive and 17 (35%) DCIS. Mean size of invasive cancers was 12 mm (median 11, range 4−25). Invasive cancers were intermediate or high grade in 26/31, DCIS in 13/17. Invasive cancers were staged pN0, M0 in 94% (29/31). Minimal cancer rate was 34/48 (71%). Distribution of mammographic breast densities in women with MRI-diagnosed cancer was as follows: ACR I in 2 (11%), ACR II in 3 (17%), ACR III in 8 (44%), ACR IV in 5 (28%). This was equivalent to the distribution of breast densities in the entire cohort.

Conclusion: In this cohort of heavily pre-screened women at average-risk, the additional cancer yield achieved through MRI was high (18/1000). The biologic profile of MRI-only detected additional cancers was indicative of prognostically relevant disease and stage distribution of cancers was favorable. Mammographic breast density did not predict the likelihood with which additional cancers were identified through MRI.

No conflicts of interest

69 Poster

Quantitative MTL-HEP test for breast cancer diagnostic and monitoring of advanced patients treatment

E. Filinova[1], A.N. Galkin[2], I.B. Baranova[2], G.A. Kuznetsov[3], I.V. Romanenko[3]. *[1]Advanced Biomedical Researches Laboratory, Moscow, Russian Federation; [2]Advanced Biomedical Research Laboratory, Molecular Genetics, Moscow, Russian Federation; [3]Advanced Biomedical Research Laboratory, Physics Methods of Analysis, Moscow, Russian Federation*

Antibodies-based immunohistochemistry diagnostics are routinely made test for the expression absence-presence of hormone receptors and other cancer-associated antigens. However, these methods are not quantitative and cannot be applied in monitoring advanced patients and the adjustment of individual aromatase inhibitors/chemo- and radiotherapy regimes.

Method: Quantitative TaqMan single-tube five-primer-pairs RealTime-RT-PCR with fluorimetric RNA concentration measurement test system [1] (MTL-HEP) was developed for measuring the presence of malignant-specific forms of Muc1 antigens and levels of expression of estrogen (ER1), progesterone (PR), and HER2-neu (ERBB2) receptors, and for monitoring breast cancer patients' hormone resistance/progression status while they are undergoing hormone- or chemotherapy.

Results: Samples of 97 breast cancer patients subjected to surgery (38 in 2008–2009 and 59 in 2010) were studied using the MTL-HEP test. 80% of all patients showed Muc1 hyperexpression (17 times higher