420 Proffered paper oral

Real Time Assessment of Axillary Nodes Based On Molecular Differences Using Raman Spectroscopy

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Background: Raman Spectroscopy, based on the inelastic scattering of laser light, has been seen as a potential new modality in cancer diagnostics. The scattered light is collected and used to produce a tissue 'finger print', or spectra. The scattering of light and thus the spectra produced is influenced by the molecular composition of the tissue. Raman spectroscopy confers a number of advantages over more traditional histopathological techniques as it is simple, quick, cost effective and can be performed on fresh tissue. This potentially allows for its use in real time settings such as the operating theatre. In this study we aim to demonstrate that the technique can identify molecular differences between lymph nodes with and without metastases that have been excised during axillary surgery in breast cancer.

Material and Methods: Following ethical approval and patient consent, 192 lymph node samples from 52 patients undergoing axillary surgery were assessed using a portable Raman spectroscopy device (MiniRam II, B&W Tek, Newark, DE, USA). All patients had a recent diagnosis of invasive breast cancer. Tissue assessment took place in real time within the operating theatres using fresh tissue. Spectral acquisition took 90 seconds for each sample. All tissue underwent subsequent standard histopathological assessment following local guidelines. Interpretation of the spectra obtained was performed using Matlab software.

Results: 160 of the samples (from 39 patients) were reported as being negative for metastatases and 32 (from 13 patients) were reported as positive for macrometastases following standard histopathological assessment. None of the samples were damaged by Raman assessment. Spectral assessment was performed using T-test statistical analysis of the spectral peaks. This demonstrated 35 peaks that had significant differences ($p < 0.01$). These peaks were attributable to lipid, protein and DNA components within the tissue. The negative nodes demonstrated an increased contribution from peaks attributable to lipids and the positive nodes demonstrated increased contributions from peaks assigned to protein and DNA. Based on these differences principal component fed linear discriminant analysis achieved a sensitivity of 96.4% (31/32) and a specificity of 99.4% (159/160) at distinguishing between the two groups.

Conclusions: This work for the first time uses Raman spectroscopy to demonstrate, in real time using fresh tissue, the molecular differences between negative and positive axillary nodes. These differences allow for the differentiation of tissue types in a clinically relevant time frame. Based on this information diagnostic models can be created that would allow assessment of axillary lymph nodes in a non destructive way within the operating theatre.

Friday, 23 March 2012 12:45–14:00

POSTER SESSION

Adjuvant and Neo-Adjuvant Therapy

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ER Allred Score Predicts Outcome of Adjuvant Endocrine Therapy in Postmenopausal Breast Cancer – a TEAM Study Analysis

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Background: Multiple studies suggest better efficacy of endocrine therapy in patients with endocrine sensitive metastatic breast cancer with high compared to low estrogen receptor (ER) levels. The present investigation assessed efficacy of endocrine therapy in the adjuvant setting, by semi-quantitative ER expression in postmenopausal patients with early breast cancer.

Materials and Methods: Patients enrolled in the Tamoxifen Exemestane Adjuvant Multinational (TEAM) trial were randomized to exemestane (25 mg daily) for 5 years or to tamoxifen (20 mg daily) for 2.5–3 years followed by exemestane for a total of 5 years. Inclusion in the present study was restricted to Dutch and Belgian patients with either infiltrating ductal or lobular breast cancer. ER expression was centrally reviewed according to Allred score (<3 ER-negative, 3–6 ER-poor, ⩾7 ER-rich). Primary endpoint was relapse-free survival (RFS), which was defined as time from randomization to disease relapse or contralateral breast cancer.

Results: Overall, 2603 patients were included, of which 2169 (83%) had ER-rich tumors, 291 (11%) ER-poor and 178 (6%) had unknown ER-expression. At a median follow up of 5.2 years, patients with ER-rich Allred scores allocated to exemestane alone had an improved RFS (multivariable hazard ratio 0.71 (95% CI 0.56–0.89)) (Table 1). In contrast, patients with ER-poor Allred scores showed an improved RFS for sequential treatment (multivariable hazard ratio 2.33 (95% CI 1.32–4.11)). Significant effect modification by ER-Allred score was confirmed (multivariable $p = 0.001$).

Conclusions: ER-rich patients showed superior efficacy to upfront exemestane, while ER-poor patients had better outcomes with sequential therapy, emphasizing the relevance of quantification of ER expression. In view of the retrospective, unplanned nature of this analysis, these results need to be validated through further prospective investigation.

Table 1. Efficacy of endocrine therapy by ER Allred score

	5-year	Univariate		Multivariable	
	survival	HR (95% CI)	p value	HR (95% CI)	p value
ER-rich			**0.001**		**0.003**
Tam→Exe*	84%	1 (reference)		1 (reference)	
Exemestane	88%	0.69 (0.56–0.86)		0.71 (0.56–0.89)	
ER-poor			**0.023**		**0.004**
Tam→Exe*	82%	1 (reference)		1 (reference)	
Exemestane	74%	1.78 (1.08–2.93)		2.33 (1.32–4.11)	

*Tam→Exe: Tamoxifen followed by exemestane; **HR adjusted for age, histological grade, histological subtype, T stage, nodal stage, PR Allred score, most extensive surgery, radiotherapy, and chemotherapy.

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Final Safety Data From a Randomised Phase III Trial (CIBOMA/2004–01_GEICAM/2003–11) Assessing Adjuvant Capecitabine Maintenance Therapy After Standard Chemotherapy for Triple-negative Early Breast Cancer. a Study From Coalicion Iberoamericana De Investigacion En Oncologia Mamaria (CIBOMA) and Grupo Español De Investigacion En Cancer De Mama (GEICAM)

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Background: CIBOMA/2004–01_GEICAM/2003–11 is a multicenter, international randomised phase III trial that focuses on adjuvant capecitabine (C) maintenance therapy after conventional induction chemotherapy in triple-negative early breast cancer (EBC). This is the only adjuvant trial exploring C in a specific subset of EBC. Here we report the final safety data from the trial.

Materials and Methods: Patients (pts) with operable, node-positive (or node-negative with tumour diameter ⩾1 cm), hormone receptor-negative, HER2-negative EBC (central laboratory confirmation) who have received standard anthracycline- and/or taxane-containing chemotherapy in the (neo) adjuvant setting are eligible. Pts are randomised to receive 8 cycles of C (1000 mg/m^2 bid, d1–14 q21d) (Arm A) or observation (Arm B). The primary endpoint is disease-free survival (DFS). Assuming 30% risk reduction in DFS rate at 5 years (from 64.7% to 73.7%, HR of 0.701) with a power of 80% and a two-tailed log-rank test at 0.05, 834 evaluable pts will be needed. With an expected dropout rate of 5%, 876 pts were included. The recruitment was completed on September 2011. Efficacy analysis will be triggered after 255 events.

Results: Here we report the safety data from 853 pts (435 in Arm A and 418 in Arm B). Baseline characteristics are well balanced between the treatment arms (table). In total, 2,938 cycles of C were administered

(median 8, range 1−8). All 8 cycles were completed by 72.4% of pts (15 pts were still on treatment). Median relative dose-intensity of C was 89.9%. The most common grade 3/4 clinical AEs related to C were: hand-foot syndrome (Grade 3 18.6%), diarrhoea (3.5%), fatigue (2.8%), irregular menses (2.4%), neutropenia (1.9%), nausea (0.9%), vomiting (0.7%), bilirubin elevation (0.7%), sensory neuropathy (0.7%) and nail changes (0.5%).

Conclusions: The safety profile of adjuvant C as maintenance therapy is consistent with its known toxicity profile. This analysis will be updated at the meeting with safety data from all randomised pts (876).

	Arm A, C (n = 435)	Arm B, Observation (n = 418)
Median age, years	50	49
KPS, %		
80	1.8	4.1
90	12.9	15.8
100	85.3	80.1
Node-positive (post-surgery), %	45.2	43.0
Basal phenotype, %	72.0	72.7
Histology, %		
ductal	88.1	86.8
lobular	1.8	2.2
other	10.1	11.0
Median tumor size, cm (range)	2.7 (0.8–11.0)	2.7 (0.5–14.0)
Post-menopausal, %	70.1	67.0
Prior standard chemotherapy, %		
Anthracyclines without taxanes	32.1	31.8
Anthracyclines and taxanes	67.9	68.2

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Can Surgery Be Avoided in Patients with Breast Cancer Who Achieve a Complete Clinical Response to Neoadjuvant Chemotherapy?

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Background: The objective of this study was to evaluate the local recurrence rates in patients with primary breast cancer who achieved a complete clinical response (cCR) to neoadjuvant chemotherapy and did not have surgery.

Materials and Methods: 148 women who achieved a cCR to neoadjuvant chemotherapy were identified from a prospectively maintained database (1995–2011) of 667 patients. 122 patients went on to have surgery (either wide local excision or mastectomy) followed by radiotherapy. 26 patients (median age 49, range 35−72 years; T2-T4, N0-N3, M0) did not undergo surgery but instead received radical external beam radiotherapy. Surgery was avoided due to either physician or patient choice. Recurrence was defined as first relapse of disease, either local (ipsilateral breast and/or axilla) or distant.

Results: All 26 patients who did not have surgery received neoadjuvant chemotherapy with 20 patients (77%) receiving anthracycline-based (FEC, FAC, ECF), 5 (19%) MMM and 1 (4%) CMF chemotherapy. The median number of cycles was 6 (range 4−8). Chemotherapy was followed by radical external beam radiotherapy to the breast +/− supraclavicular fossa and axilla (median dose delivered, 60 Gy in 2 Gy fractions). All were identified as operable at diagnosis including 3 patients who had supraclavicular lymphadenopathy. All 26 patients achieved a final cCR in the breast to chemotherapy. 21 patients had imaging with mammography and/or ultrasonography to assess radiological response at the end of neoadjuvant chemotherapy, of which 19 had a complete response and 2, a partial response. After a median follow-up of 144 months, 10/26 (39%) patients experienced local disease recurrence (2 also had distant recurrence) and 4/26 (15%) patients with distant metastases only. Patients with local recurrence only, went on to have a mastectomy whilst those with distant disease received systemic therapy. There were 10 deaths, 9 of which were breast cancer related (35%).

Conclusions: In patients achieving a cCR following neoadjuvant chemotherapy and who avoided surgery, local recurrence rates were high. As a result, practice in our institution has changed to include insertion of clips and surgical excision on completion of chemotherapy. With increasing pathological complete response rates to more active chemotherapy schedules (including taxanes +/− trastuzumab), it has been proposed that surgery could potentially be avoided in certain patients. However, our results demonstrate that caution should be exercised.

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The Role of Cyclin D1 in Planning of Endocrine Therapy for Women of Postmenopausal Age with Breast Cancer

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Background: Nowadays tamoxifen still remains the primary drug in breast cancer endocrine therapy. However, its application is limited due to the resistance of tumor cells. The search of adequate biomarkers is one of the most actual problems in prognosis of effectiveness of tamoxifen adjuvant therapy. The most perspective biomarker is cell cycle regulator cyclin D1. The objective of our work was to evaluate the effectiveness of tamoxifen in adjuvant therapy of hormone-receptor-positive breast cancer in women of postmenopausal age with cyclin D1 expression and to compare the effectiveness of tamoxifen and anastrosole in adjuvant therapy of hormone-receptor-positive breast cancer in women with cyclin D1 expression more than 30%.

Material and Methods: To evaluate the effectiveness of tamoxifen we have researched 2 retrospective groups of 70 patients with hormone-receptor-positive T1−4N0−3M0 breast cancer that have been on regular medical check-up for a period of 5 years or that had previously undergone treatment. On the basis of the archive histological material we have revealed cyclin D1 in tumor cells. To compare the effectiveness of tamoxifen and anastrosole we have additionally researched 1 additional group of 50 patients with breast cancer and cyclin D1 expression more than 30% that have been on regular anastrozole treatment for a period of 27 months.

Results: Patients with lack of cyclin D1 expression or with low quantitative value (according to our data less than 30%) have no neoplastic process progression throughout the 5 years of tamoxifen adjuvant therapy. On the contrary, women with moderate and high cyclin D1 expression (more than 30%) had a relapse of tumor. Thus, distant metastasis is prognosed in 5 years of observation in this patient's group. Moderate level of cyclin D1 expression was observed in 45 (64%) patients and 28 (62%) of them had progression with metastasis in bones, 9 (20%) metastasis in soft tissues, 2 (4%) metastasis in lungs and 6 (14%) relapse in postoperative scar. High expression was revealed in 25 (35%) women and 17 (68%) of them had bone affection, 7 (28%) soft tissue metastasis and 2 (4%) tumor relapse in postoperative scar. The average period of tumor relapse and progression of neoplastic process in patients with cyclin D1-positive breast cancer is 20 months. Patients who have cyclnin expression more than 30% and receive anastrosole in adjuvant have no tumor relapse and progression throuhgh out 27 months of observation.

Conclusion: Women with hormone-receptor-positive cyclin D1-negative breast cancer on early stages have more prolonged non-relapse period during the tamoxifen adjuvant therapy. Patients with cyclin D1-positive breast cancer are less sensitive to tamoxifen treatment and in adjuvant regime should receive therapy with other effective equivalent drugs (aromatase inhibitors). It is necessary to continue the research of cyclin D1 as biomarker that could influence on the choice of treatment between tamoxifen and aromatase inhibitors.

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Prognostic Factors for Triple Negative Breast Cancer Patients with Preoperative Systemic Chemotherapy

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Background: Triple negative breast cancer (TNBC), which is immunohistochemically characterized by lack of expression of the estrogen receptor (ER), progesterone receptor (PgR), and HER2, tends to show visceral metastasis and aggressive clinical behavior. The aim of this study is to identify the prognostic factors for patients with TNBC after receiving preoperative systemic chemotherapy (PST).

Materials and Methods: Among 4195 operable primary breast cancer patients, 135 TNBC patients who underwent preoperative systemic therapy between 2000 and 2009 were investigated. The significant prognostic factors among clinicopathological characteristics including familial history, menopausal status, body mass index (BMI), UICC staging before PST, chemotherapy regimen, completion of scheduled chemotherapy, clinical response, surgical procedure, radiotherapy, histological grades, pathological invasive size, pathological nodal status, lymphatic invasion, vascular invasion, HER2 status (0 or 1), pathological complete remission,