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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.

422 Poster discussion

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