social activities, mental health, change in health status perception) showed significant improvement ($p<0.05$). The cost of the intervention per woman was meanly 40 euros, but costs could be lowered to 20, if non medical personnel should be employed.

This kind of approach is worth of being considered, because of its low costs, safety, and observed results.

357 INVITED

The validity of research/clinical trials of CAM

E. Winer. *Dana Farber Cancer Center, Boston, USA*

Women with breast cancer use a variety of complimentary and alternative approaches (CAMS), both during active treatment and following the completion of therapy. The percentage of women using CAMs varies from study to study,depending to a large extent on the patient population and the definition of CAM. Women cite a variety of reasons for pursuing CAMs including a desire to improve quality of life, take control over their illness, relieve symptoms, and improve overall survival. Some studies have found that women who use CAMs are more likely to have either physical and/or psychological symptoms compared to non-users.

Unfortunately, there are relatively few studies that have demonstrated unequivocal benefits for many of the commonly used CAMs. Many studies suffer from methodological problems including: inadequate sample size; lack of randomization; failure to blind; and poorly defined interventions and measures of outcome. It is not necessary that all therapies, particularly CAMs, show a survival benefit. However, if any CAM is to be used widely, it should be shown to be safe, particularly if it being used concurrently with other therapy, and that it has some beneficial impact on the user. Recent studies will be highlighted to demonstrate which CAMs have been adequately evaluated to justify common use and which are in need of further investigation.

358 INVITED

Does CAM have a place in breast cancer treatment?

E. Ernst. *Peninsula Medical School, Universities of Exeter&Plymouth, Complementary Medicine, Exeter, UK*

Most breast cancer patients try one form of complementary and alternative medicine (CAM) or another, often out of desperation. In evaluating CAM, one has to consider foremost its proven effectiveness and its potential risks. It is sensible to differentiate between CAM for prevention, treatment and palliation of cancer.

Prevention: Many forms of CAM are promoted for (breast) cancer prevention. The scientific data in support are usually scarce. Some promising (albeit not compelling) evidence exists for the regular use of garlic, green tea, phytoestrogens and panax ginseng. None of these relate specifically to breast cancer.

Treatment: An increasing number of CAM treatments are promoted as cancer 'cures', often supported by quasi-scientific data. Essiac, Di Bella therapy, Hoxley formula, mistletoe, laetrile and shark cartilage are just some examples. For none of these therapies is there sufficiently sound evidence to recommend them to breast cancer patients. Several of these alleged cancer 'cures' are associated with significant risks.

Palliation: Several forms of CAM are not aimed at prevention or treatment but at increasing the quality of life of cancer patients, often through relaxation and reduction of stress, e.g. reflexology, aromatherapy. Other treatments can ease the adverse effects of orthodox cancer therapies, e.g. acupuncture can reduce nausea and vomiting after chemotherapy. Even though the scientific data are often weak, CAM's role in palliative and supportive care is potentially important.

Friday, 19 March 2004 16:00–17:15

PROFFERED PAPERS

Breast conservation

359 ORAL

Gene expression profiling of patients at risk for local recurrence after breast conserving therapy

B. Kreike, H. Halfwerk, P.M.P. Kristel, A. Velds, A.M. Glas, T. Van Der Velde, H. Peterse, G. Hart, H. Bartelink, B. Van De Vijver. *Netherlands Cancer Institute, Radiotherapy, Amsterdam, The Netherlands*

Background: A limited number of risk factors for developing local recurrence after breast conserving therapy have been identified. The most important risk factors appear to be incomplete resection of the tumor and young age. The identification of additional risk factors would be very useful in guiding optimal therapy and also improve understanding of the mechanisms underlying local recurrence. We used cDNA microarray analysis to identify gene expression profiles associated with local recurrence after breast conserving therapy.

Material and Methods: Gene expression profiles were obtained from 60 patients who were under the age of 51 years at diagnosis of a primary invasive breast carcinoma and underwent breast conserving therapy. Of these 60 patients 26 developed a local recurrence and 34 controls were free of local recurrence at 11 years after therapy. From 10 patients with a local recurrence the RNA of the recurrence was isolated and used for analysis. In total 70 samples were analyzed; 60 primary tumors and 10 recurrences. Gene expression profiling was performed using a glass array containing 18,000 cDNAs. Unsupervised and supervised methods of classification were used to separate the patients in groups corresponding to their disease outcome and to analyze the differences between primary tumors and their recurrences.

Results: Hierarchical clustering of patients did not show any grouping reflecting local recurrence status. Supervised analysis revealed a possible classifier consisting of three genes; these data need to be validated. Paired-data analysis showed no set of genes that is consistently different in expression between primary tumors and recurrences. Co-clustering of the primary tumors and their local recurrence in the hierarchical cluster analysis also reflects this.

Conclusions: There are no great differences in gene expression patterns between breast carcinomas with and without a local recurrence after breast conserving therapy. The gene expression pattern in primary tumors and local recurrences is very similar. Preliminary results suggest that there may be a classifier for local recurrence after breast conserving therapy.

360 ORAL

Update of the BASO II trial of primary treatment of tumours of excellent prognosis

R. Blamey[2], U. Chetti[2], D. George[2], D. Morgan[2], M. Mitchell[2]. [1]*Nottingham City Hospital, Breast Institute, UK;* [2]*BASO Breast Group Trialists*

This trial examined additional treatments to Wide Local Excision with clear margins, in Grade I, node negative tumours of 2 cm or less with clear margins. Between 1992 and 2000, 1172 patients were randomised to a 2×2 design. The primary outcome measure is local recurrence (LR), defined as tumour in the treated breast. The median follow-up is 54 months. Survival is excellent, only 7 deaths from breast cancer.

LR by randomisation are:

Randomisation	n	LR	LR%PA
Radiotherapy (RT) to intact breast	584	8	0.3
No RT	574	21	0.8
Tamoxifen	200	2	0.2
No Tamoxifen	208	8	0.9
RT plus Tamoxifen	96	0	Nil
No RT, no Tamoxifen	95	6	1.5

Since for those entering only to the RT or the Tamoxifen comparisons, the other therapy could be given electively by centres, the results by treatment received:

Received	n	LR	LR%PA
Neither therapy	174	15	2.0
RT only	191	6	0.72
Tamoxifen only	411	8	0.44
RT plus Tamoxifen	396	2	0.12

It appears that % LR PA is too high from surgery alone but that Tamoxifen is as effective as RT in lowering LR to very acceptable levels. This would have important cost and waiting time implications for RT in the NHS, if borne out by longer follow up.

361 ORAL

Surgical outcomes for clinically occult breast lesions: comparing radioguided occult lesion localisation (ROLL) vs. wire guided lumpectomy (WGL)

R. Nadeem[1], L. Chagla[1], C. Titterrell[2], R. Audisio[1]. [1]*Whiston Hospital, Prescot, Surgery, UK;* [2]*University of Liverpool, Surgery, UK*

Introduction: Widespread screening has resulted in an increased incidence of clinically occult breast lesions. The surgical management

of impalpable lesions has become a daily challenge. Various localisation techniques were developed and tested but none can be considered ideal. ROLL was pioneered in Milan at EIO, we modified the technique and implemented at our Breast Unit, we have compared our ROLL and WGL series to provide sufficient data to demonstrate the efficacy of ROLL vs. WGL.

Methods: We have treated 100 consecutive impalpable breast cancers between January 2002 to September 2003, and ROLL was introduced in December 2002: this series represents a comparison between the last 50 WGL patients and the first 50 ROLL (Technetium^{99} labelled colloidal albumin). Data was collected in relation to age, radiological abnormality, pre-operative core biopsy, type of primary surgery, length of localisation/excision, hospital stay, cancer size, weight and volume of the excised specimen, clearance margins, for both groups. Tumour volume (*Vt*) was calculated and compared with the volume of the excised specimen: *Vt* was theoretically computed with the formula $(\pi/6)d^3$ by assuming the cancer was spherical. The theoretical volume of an ideal specimen with 1 cm safe margins (*Vis*) was also computed; finally the volume of the excised specimen was calculated (*Vexs*). The following equations were then computed:

R^* = *Vexs*/*Vis* (ratio of the excised specimen's volume to the volume of the ideal excised specimen); and

R^{**} = *Vexs*/*Vt* (ratio of the excised specimen's volume to the tumour volume).

Results: The two groups proved comparable with respect to median age, radiological findings, type of surgery, and pathological findings. Median hospital stay (2 days) and operative time (30 min) were similar in both groups. Median localisation time with US or stereotactic technique was 6 min (5–7) and 12 min (10–15) respectively in the ROLL group, as compared to 15 min (15–17) and 20 min (20–25) respectively in WGL. Median pathological tumour size was larger in the ROLL group (15 mm) than WGL (10 mm); consequently, *Vt* was larger in the ROLL group (1768 mm^3 vs. 696 mm^3 for WGL). Conversely, median weight of the excised specimen was smaller in ROLL (39 g; range 6–128 g vs. 45 g in the WGL; range 7–167 g), and median volume of the excised specimen was similar in both groups (107,250 mm^3 vs. 115,500 mm^3). Although median minimal clearance was similar for the 2 groups, more ROLL patients had clear margins (78% vs. 62%). Amongst patients with clear margins, R^* and R^{**} were higher in WGL than ROLL (6.56 vs. 4.17, and 98.38 vs. 66.65) respectively: this implies that a larger amount of normal breast tissue was excised with WGL, without achieving a better cancer clearance. Average cost of ^{99m}Tc is £28/patient, compared to £35/patient for wire insertion. Cosmetic results were excellent (70%) or good (30%) in ROLL group vs. (58%) and (42%) respectively in WGL. No major complication/technical fault was recorded.

Conclusions: ROLL localises the lesion very precisely, surgical removal is easy and margins clearance is better than with WGL, size of the excised specimen is smaller resulting in better cosmetic results.

Radiological localisation is quick and cost-effective.

362 ORAL

Surgical approaches to early breast cancer in the Intergroup Exemestane Study: large differences by country and geographical region

J. Jassem[1], E. Hall[2], R. Coombes[3], J. Bliss[2], L. Gibson[4]. *For the Intergroup Exemestane Study – IES – Steering Committee / ICCG Data Centre / Imperial College – London, UK. [1]Medical University of Gdansk, Poland; [2]Clinical Trials and Statistics Unit, Institute of Cancer Research, Sutton, UK; [3]Imperial College, London, UK; [4]ICCG Data Centre, London, UK*

Background: Breast conserving therapy (BCT) has been widely accepted as a valuable alternative to mastectomy in early breast cancer. Despite that, in many countries mastectomy continues to be used as a main surgical approach. Our aim was to analyse the rate of mastectomy in various geographical regions in a large group of breast cancer patients entered into a global randomised study.

Patients and methods: The objective of the IES (96OEXE031-C/13/96-BIG02/97) was to compare the efficacy and safety of continued adjuvant tamoxifen versus exemestane in postmenopausal women with operable breast cancer after having received adjuvant tamoxifen for 2–3 years. Major eligibility criteria included positive or unknown steroid receptor status and adequate surgical treatment (both breast conserving and mastectomy were allowed) with or without postoperative chemotherapy and/or radiotherapy. Patients were randomised to subsequent exemestane, 25 mg daily or further tamoxifen, 20 mg daily for a total of 5 years adjuvant endocrine therapy period.

Results: Between February 1998 and February 2003, 4743 patients from 35 countries and 5 continents were enrolled into the study. Surgery data are currently available for 4689 patients. Of those, 2411 patients (51%) underwent mastectomy, 1810 (39%) – wide local excision and 465 (10%) – other types of breast-conserving surgical procedures. Main clinical and therapeutic characteristics were well balanced between the study arms. However, there were large differences in surgical approaches between particular countries and geographical regions. Mastectomy rate was highest in Central and Eastern Europe (77%), followed by USA (56%), Western and Northern Europe (46%), Southern Europe (42%), and Australia and New Zealand (34%). Among countries with representative number of patients (>150), mastectomy rates were as follows: Belgium: 37%, France: 28%, Germany: 43%, Italy: 41%, the Netherlands: 48%, Poland: 98%, Spain: 66%, Switzerland: 47%, UK: 31% and USA: 56%.

Conclusions: The results of this analysis demonstrate substantial differences in surgical approaches to early breast cancer in various geographical regions and countries. A retrospective multivariate analysis of factors predictive for the extent of surgery will be presented.

363 ORAL

Quadrantectomy and axillary dissection vs quadrantectomy alone as surgical treatment for T1a,b,c N0 breast cancer. Early results of Milan V: a randomised clinical trial

M. Gennaro, C. Ferraris, A.R. Conti, L. Balzarotti, M. Greco. *Ist Nazionale Tumori, Breast Unit, Milan, Italy*

Introduction and Study design: Currently, tumor size and nodal status, which represent the most important prognostic factors, are combined with several independent predictive and prognostic factors to assess the risk of relapse and to plan adjuvant treatment.

Several findings underscore the fact that in clinically node-negative patients, treatment of regional lymph node metastases does not seem to be a determiningfactor in the outcome of breast cancer. Nevertheless axillary dissection, which is nowadays performed in case of positive sentinel node, has maintained its role in prevention of regional relapse. The integration of additional tumour features with those commonly used may allow a more reliable selection of patients for adjuvant chemotherapy without performing axillary surgery. Toward this end, a randomised clinical trial comparing surgical staging of axillary lymph nodes at primary treatment (control arm) with a surgical treatment only in case of relapse (study arm) is currently in progress at the National Cancer Institute in Milan. Adjuvant treatment of patients who received quadrantectomy alone without nodal staging was determined through a prognostic panel including only morphological and biological features of the primary tumour while traditional criteria was applied to the control arm.

The primary end point of this study was to verify if the Overall Survival (OS) of the patients enrolled in the study arm is equal or improved when compared with the control group.

Results: Starting from May 1998, accrual was completed on May 2003. 527 patients with T1a,b,c clinically node negative were enrolled: 262 and 265 patients were assigned to the study and control arm respectively. Median follow up was 30 months. According to the prognostic panel, in the first group 88 patients (33.6%) were eligible for adjuvant chemotherapy compared to 135 (51.0%) of the control group by means of traditional criteria. Ten patients of the study group (3.8%) developed axillary lymph node relapse and was subsequently operated. Analysis of first unfavourable event (regardless of axillary relapse) did not show any significant difference between the two groups.

Conclusion: We can't argue any conclusion concerning the primary end point, but our early results suggest that a prognostic panel obtained by the primary tumour characteristics without lymph node surgery may represents a reliable method affected by a low rate of nodal relapses to select patients for adjuvant therapies.

364 POSTER HIGHLIGHT

Breast Cancer Units can significantly improve surgical management of early invasive breast cancer

P. Fenaroli[1], L. Giuliano[1], U. Guerra[2], E. Candiago[3], M. Valentini[4], M. Belfiglio[4], A. Bettini[5], R. Labianca[5], R. Guzzetti[6], C. Tondini[5]. *[1]Ospedali Riuniti, Senology, Bergamo, Italy; [2]Ospedali Riuniti, Nuclear Medicine, Bergamo, Italy; [3]Ospedali Riuniti, Pathology, Bergamo, Italy; [4]Consorzio Mario Negri Sud, Biostatistics, Chieti, Italy; [5]Ospedali Riuniti, Medical Oncology, Bergamo, Italy; [6]Ospedali Riuniti, Radiotherapy, Bergamo, Italy*

Breast cancer research has significantly contributed to reduce aggressiveness of surgical treatment of early invasive cancer (EIBC). Long term results have confirmed safety and acceptability of breast conserving surgery (BCS) as a standard of care for T1–T2 tumours. More recently, the introduction of sentinel node biopsy (SLNB) for nodal staging has allowed the reduction of unnecessary axillary dissection (AD) for node-negative pts. Breast Cancer Units (BCU) with dedicated teams of surgical senologist and a multidisciplinary approach to this disease have been advocated for optimal disease management, and such a Unit is active at our Centre. In the present study, we retrospectively analyse all consecutive cases of EIBC referred for post-operative evaluation and adjuvant therapy to our Oncology