the 2 arms was 25.5 (HTX) and 23.5 (HT) months. PFS and TTP favoured the HTX regimen (Table). Overall survival data are immature.

	HTX (n = 112)	HT (n = 110)	Hazard ratio	p value
ORR, %	71	73		0.72
Complete response, %	23	16		
Partial response, %	47	56		
Stable disease, %	25	16		
Progressive disease, %	4	9		
Median DoR, months	15.9	13.4		NC
Median PFS, months	17.9	12.8	0.72	0.04
Median TTP, months	18.6	13.6	0.70	0.03
1-year survival rates, % (95% CI)	91 (86, 96)	85 (79, 92)		
2-year survival rates, % (95% CI)	75 (66, 83)	66 (56, 75)		

NC, not calculated.

Most non-haematological adverse events (AEs) were grade 1 or 2. The most common grade 3/4 AEs were hand-foot syndrome (HTX 17%; HT <1%) and diarrhoea (HTX 11%; HT 4%). There was a lower incidence of grade 3/4 neutropenia in the HTX arm compared with HT (54% vs 77%). 12% of pts experienced mild to moderate cardiac AEs; 2 pts in each arm had left ventricular ejection fraction declines to <40%. Symptomatic congestive heart failure was experienced by 1 pt in each arm. No pt died due to a cardiac event. 4 deaths recorded during the study were considered to be treatment related (HTX 1 pt; HT 3 pts).

Conclusions: Both regimens demonstrated high ORR, with HTX achieving significant improvement in TTP and PFS compared with HT in HER2-positive LABC/MBC. Both treatments were manageable and cardiac safety was consistent with other H-based trials.

Thursday, 17 April 2008 16:00–17:30

CLINICAL SCIENCE SYMPOSIUM

Lifestyle and survival after treatment for breast cancer

210 Invited

What breast cancer survivors want to know about lifestyle after breast cancer

C. Murphy-Whyte[1]. [1]*Europa Donna Ireland, N/A, Co. Dublin, Ireland*

Awareness of cancer survival has increased greatly since the 1990's due largely to increasing numbers and the work of advocates. If prevalence of and survival with cancer worldwide continues to increase and follows predictions made in the USA, the number of recorded cancer survivors worldwide in 2025 will approach 50 million and in 2050 will approach 70 million. With a European prevalence rate of 34% for breast cancer – the most prevalent cancer in women – issues for breast cancer survivors will of necessity gain more attention.

From the point of diagnosis, breast cancer survivors have to deal with a confusing and disturbing array of conflicting studies and advice, reinforced by media hype regarding cancer scares and cures, so key issues for them are what and who to believe and where to find reliable evidence.

Most survivors will want to know the chances of their breast cancer progressing or recurring and what they can do to minimise those chances. Survivors are living longer and therefore long enough to develop new primary cancers or other chronic diseases.

Together with those who are closest to them, survivors want to learn about and act on helpful recommendations in terms of lifestyle based on sound evidence. They need recommendations on lifestyle that will not do them harm, that help limit the progress of breast cancer and help prevent a recurrence of breast cancer or any other cancer, and help prevent other diseases as well as improve the quality of their lives.

Studies and advice have traditionally focussed on significant components of lifestyle such as food, nutrition, and physical activity as applied to cancer risk and prevention and according to the WCRF/AICR report published in 2007, on the available evidence it is not yet possible to make judgements that apply specifically to survivors.

In tandem with the shift from life-threatening to life-changing disease, survivors want to know more about the changes that women are making in their lives following breast cancer. Apart from understanding more about maintaining a healthy immune system, survivors will increasingly want to extend the focus to address psycho-social aspects of lifestyle including working life, relationships, sexuality, the use of complementary therapies and supports and the complex interactions of stress and fatigue, on lifestyle choices. The challenge for advocates will increasingly be to find ways of getting these issues and appropriate methodologies onto the research agenda.

211 Invited

Stress, distress and support groups – are they important?

D. Kissane[1], B. Grabsch[2], D.M. Clarke[3], R.D. Snyder[4], Y. Li[1]. [1]*Memorial Sloan Kettering Cancer Center, Psychiatry & Behavioral Sciences, New York, USA;* [2]*University of Melbourne, Center for Palliative Care, Melbourne, Australia;* [3]*Monash University, Psychological Medicine, Melbourne, Australia;* [4]*St Vincent's Hospital, Medical Oncology, Melbourne, Australia*

Background: The sustained debate about group therapy and survival across the past decade distracted clinicians from the consistent evidence of quality of life benefits in reducing distress and depression when women with breast cancer attend support groups. A series of prospective, randomized, group therapy studies using larger cohort sizes failed to prolong survival in women with both metastatic (Canadian 235; Australian 227 and American 125) and early stage (Australian 303) breast cancer.

Material and Methods: DSM-IV diagnoses for psychiatric disorders and dimensional measures of anxiety, depression and quality of life were obtained in both Australian trials, where survival was the primary outcome; psychosocial well being was appraised secondarily.

Results: Anxiety was effectively relieved by group therapy in early breast cancer. Clinical depression was both actively ameliorated and new cases prevented across the course of the group therapy for advanced breast cancer compared to controls. Survival was not extended by either intervention.

Conclusions: These studies have consistently reduced distress and significantly prevented onset of new cases of depression in advanced breast cancer. The preponderance of systematic evidence supports the relief of distress, with the strongest evidence for anxiety-related outcomes (fear of recurrence) in early stage cancer. New evidence for the prophylactic benefit in preventing depression in advanced cancer argues for group support being offered to all interested subjects. Psycho-oncology needs to promote behaviors leading to health promotion (smoking cessation, obesity reduction and exercise), preventive screening and early detection, the relief of distress and culturally sensitive interventions to encourage adherence to anti-cancer treatments. Issues of medical mistrust and fatalism leading to anti-cancer treatment drop-outs could be addressed through these interventions.

212 Invited

Lifestyle interventions in breast cancer – what do we know and what do we need to know?

P.J. Goodwin[1]. [1]*Samuel Lunenfeld Research Institute at Mount Sinai Hospital University of Toronto, Medicine, Toronto, Ontario, Canada*

There is increasing recognition of the importance of lifestyle factors (e.g. obesity/body size, diet, physical activity) after breast cancer (BC) diagnosis. Over 50 studies have investigated obesity as a prognostic factor – the majority have identified an adverse prognostic effect. One meta-analysis identified a hazard ratio (HR) of 1.91 for distant recurrence and 1.60 for death for obese vs. non-obese women. Observational data have suggested that some dietary practices (e.g. increased intake of saturated fat in postmenopausal women) may increase risk of recurrence. Recent research has also suggested that low levels of physical activity around the time of BC diagnosis may also worsen prognosis.

Two randomized trials of lifestyle interventions have reported disease-free survival outcomes. The Women's Intervention Nutrition Study (WINS) studied the effect of reducing dietary fat intake to 20% of calories. Dietary fat reduction was associated with a relative weight loss of 2.3 kg. Five year relapse-free survival was significantly improved in the intervention arm (HR 0.76, p = 0.034). The effect was greatest in receptor negative (HR 0.58) vs. receptor positive (HR 0.85) BC. The Women's Healthy Eating and Living Study randomized women to a complex dietary intervention that involved fat reduction combined with increased intake of fruit, vegetables and fiber, up to four years post BC diagnosis. There was no effect on 5 year disease-free survival.

Intervention research (both randomized and non-randomized) has demonstrated the feasibility of physical activity after BC diagnosis. Improvements in fitness, quality of life and body composition have been demonstrated. There are no randomized trials of prognostic effects of physical activity. Similarly, the feasibility of weight loss through diet and physical activity has been demonstrated in BC patients. Apart from the WINS Study noted above, there are no randomized data addressing prognostic effects of weight loss.

One major challenge is to understand the biologic basis for the relationship between lifestyle and BC outcomes. Circulating estrogens, insulin and other members of the IGF family of growth factors may play important roles.

Future research should examine prognostic effects of lifestyle interventions using randomized designs. Optimal approaches to weight loss, and types of physical activity most strongly associated with BC outcomes, should also be delineated.

213 Proffered Paper Oral

Factors affecting occupational returning in breast cancer survivors in working age: preliminary analysis from a 131-patient sample

M. Strada[1], M. Frascaroli[1], I. Jedrychowska[1], C. Innaurato[1], A. Bernardo[2], R. Palumbo[2], G. Poggi[2], C. Teragni[2], A. Amatu[2], G. Bernardo[2]. *[1]Fondazione Maugeri, Rehabilitative Oncology, Pavia, Italy; [2]Fondazione Maugeri, Medical Oncology II, Pavia, Italy*

Background: The correlations between survival and returning to work in cancer survivors is an issue of increasing interest, given the actual improvement in treatment strategies, and only a few data are available in the literature. Here we report the preliminary data from an analysis of a sample of 131 patients affected with breast cancer in working age.

Methods: One hundred thirty-one patients with surgically treated breast cancer, all in working age at the time of disease occurrence, were interviewed by a questionnaire including personal data (age at cancer diagnosis, familiarity for cancer, education degree, children, etc.), disease (co-morbidity, sequelae, treatment-related side effects, disease duration, rehabilitative treatment), the type of work (dependent, independent, physical, intellectual, full- or part time, flexibility). Statistical analysis was performed by using ?2 test and univariate/multivariate logistic regression model.

Results: Median age was 45 years (68 patients >45, 63 <45), 9 patients had elementary education, 66 secondary, 24 degree; 26 patients with co-morbidity and 63 with surgical sequelae, 50 referred treatment-related toxicities, 73 had received post-surgical rehabilitation. Working-related factors: independent in 33 patients, public dependent in 50, enterprise dependent in 48; physical work in 54 patients, intellectual in 77; 102 worked full-time and 26 part-time. Overall, 97/131 patients (74%) returned to work (77% dependent, 65% intellectual, 41% reduced duties; 54% flexible hours versus 44% at diagnosis). Thirty-four patients did not go back to work, because of disease/treatment-related sequelae (53%), changed working bent (41%), company policy (6%); 30% of them obtained civil invalidity, 23% old-age pension, 30% disease protraction, 17% remained out of work. The type of work and disease duration (< or >60 days) resulted the only two statistically significant factors; specifically, negative factors for physical work were the loss of technical knowledge and update and the psychological impact, while the flexible hours resulted a stimulating positive factor; no significant effect was found for socio-demographic characteristics, as well as for dependent/independent, full/part time work.

Conclusions: Our preliminary analysis showed a statistically significant impact of both work type and disease duration on working returning in breast cancer patients, but additional aspects of great importance on patient qualify of life are emerging (elaboration of EORTC and FACT-An questionnaires is ongoing).

214 Proffered Paper Oral

Age, clinical and psychological associations with fatigue following radiotherapy for early breast cancer – Results from 2208 women in the UK Standardisation of Breast Radiotherapy Trials (START) on behalf of the START Trial Management Group

J. Mills[1], G. Sumo[1], J. Haviland[1], J.M. Bliss[1], P. Hopwood[2]. *[1]The Institute of Cancer Research, Clinical Trials & Statistics Unit, Sutton, United Kingdom; [2]Christie Hospital NHS Foundation Trust, Psycho-oncology Service, Manchester, United Kingdom*

Background: Fatigue is a frequently reported symptom in women following early breast cancer treatment and may be increased with adjuvant breast radiotherapy. There are conflicting reports on contributing factors and whether fatigue persists in the longer term. The aim of this Quality of Life (QL) sub study is to investigate the effect of a range of other clinical and psychological factors and symptoms on fatigue in women following radiotherapy for early stage breast cancer in the START Trials.

Methods: In the START Trials a subgroup of women were recruited to a QL study and completed standardised questionnaires including the EORTC QLQ C-30, the BR23 and HADS at baseline (after surgery +/−adjuvant systemic therapy but before radiotherapy) and 6, 12, 24 and 60 months. Fatigue was measured as a symptom subscale comprised of 3 individual items. The effect of age, time from surgery, type of surgery, chemotherapy (CT), endocrine therapy and change over time were tested using a GEE model. Associations of fatigue with anxiety, depression, insomnia and physical functioning were estimated using Spearman's rank correlation.

Results: 2208 women consented to the QL study; mean age 56.9 years; 82.9% underwent conservative surgery; 33% had received CT. 2180 (99%) women completed baseline QL. Fatigue levels were highest at baseline (median 33.33) and decreased during follow-up (median 22.2). Feeling tired was the most highly scored individual item with 29% women reporting 'quite a bit'/'very much' at baseline, decreasing to 22% by 1 year and remaining stable to 5 years. The other 2 items showed a similar trend. An early effect of CT on fatigue was seen ($p < 0.001$) but decreased over time. Worse fatigue during follow-up was associated with worse fatigue at baseline ($p < 0.001$), earlier follow-up time ($p < 0.001$) and older age ($p = 0.007$). Worse fatigue scores were moderately to strongly associated with worse depression, anxiety, physical functioning levels and insomnia ($p < 0.001$).

Conclusions: There was no evidence of persistent fatigue after RT although a transient effect due to earlier CT was found. Fatigue improved over time for the majority of women. However, significant associations with older age, mood and physical functioning highlight a subset of patients most at risk of poorer QL that warrant a holistic assessment.

Thursday, 17 April 2008 12:30–14:30

POSTER SESSION

Adjuvant and neo-adjuvant therapy

215 Poster Discussion

The effects of concurrent or sequential administration of trastuzumab on radiation-induced pulmonary fibrosis in rats

C. Umay[1], N.S. Bese[1], S. Serdengecti[2], N. Kepil[3], C. Karaca[4], N. Sut[5], T. Altug[6], A. Ober[1]. *[1]Istanbul University Cerrahpasa Medical School, Department of Radiation Oncology, Istanbul, Turkey; [2]Istanbul University Cerrahpasa Medical School, Department of Medical Oncology, Istanbul, Turkey; [3]Istanbul University Cerrahpasa Medical School, Department of Pathology, Istanbul, Turkey; [4]Istanbul University, Department Experimental Animal Breeding and Research Laboratory, Istanbul, Turkey; [5]Trakya University, Department Biostatistics, Edirne, Turkey; [6]Istanbul University, Department Experimental Animal Breeding and Research Laboratory, Istanbul, Turkey*

Background: There is not enough data regarding the late effects of combination of T with RT. Lung is the most sensitive tissue to observe the late effects of irradiation. In this study we evaluated if concurrent or sequential administration of T has any impact for the development of radiation induced pulmonary fibrosis (RIPF)in rats.

Materials and Methods: 54 female wistar-albino rats were divided into 6 groups (G). The animals in G 1 (concurrent T) had irradiation in two hours of following T administration. G 2 (sequential T-RT) received irradiation, one week after T. G 3 (sequential RT-T) had irradiation first and received T one week after RT. G 4 (T only) had only T. G 5 (RT only) had only irradiation. The rats in G 6 (sham) were only observed. A single dose of 12 Gy was given to both lungs with an anterior field at 2 cm depth after simulation. T dose which was equivalent to 6 mg/kg adult dose was calculated for each rat, and injected by the tail vein. For sequential administration one week interval was given between T and RT which was shown to be the half life of T in rats. Animals were sacrificed 16 weeks after RT which was shown to be a sufficient period for the development of RIPF in rats. Both lungs were fixed by formalin and embedded in paraffin. Five-micrometer thick sections were stained with Masson's trichrome to visualize fibrosis and collagen. As quantative end point the extent of fibrosis for each field was graded on a scale from 0 (normal lung or minimal fibrous thickening of alveolar or bronchial walls) to 4 (total fibrous obliteration of the field). The mean score values were calculated for each group. Normality distribution and linearity were tested, then the One way ANOVA test and Tukey HSD post-hoc test were used to calculate the significance of the differences among groups.

Results: The mean value of fibrosis were 1.44, 1.77, 1.75 and 1.62 for G 1, G 2, G 3 and G 5 respectively, and there were no significant differences among the comparison of these 4 groups ($p > 0.05$). The mean value of fibrosis score was 0.25 for G 4 and 0.33 for G 6. The difference was not significant between these two groups ($p > 0.05$), When the mean value of fibrosis scores of the groups which had thoracic irradiation with or without T, compared with observation arm and the animals which received T only, the differences were statistically significant ($p < 0.05$).