and a lower quality of life, show less compliance, and have longer hospital stays, thus inducing greater costs.

The presentation is based on the one hand on a review of corresponding comorbidity studies from the psycho-oncological research of the past 20 years, and on the other hand on current results from a questionnaire-based study involving more than 1000 breast cancer patients performed at the Institute for Medical Psychology of the Hamburg-Eppendorf University Clinic.

The results indicate a considerable risk of comorbidity for psychological disorders in breast cancer patients. This primarily relates to anxiety disorders and depression, in each of which rates of incidence differing between 10% and 30% have been determined. The frequency of psychological disorders requiring treatment appears to be dependent on numerous factors. In addition to socio-demographic variables, these factors include illness oriented variables such as the stage and prognosis of the illness, the severity of the physical impairment and negative effects on self-perception, as well as psycho-social variables such as the available coping resources, and support from the familial and social environment.

The results show that a qualified treatment of the psychological symptoms (anxiety, depression) is necessary for certain subgroups of breast cancer patients. This can be psychotherapeutic, psychopharmacological, or combined in nature, and requires corresponding specialist training and experience (for example, medical or clinical psychologists or psychiatrists).

A specific problem can be seen however in the fact that the psychological comorbidity in breast cancer patients frequently goes without being recognized by those responsible for primary treatment. This is due in part to the diversity of the psychopathology, the overlapping of somatic and psychological symptoms, the underestimation of psychological disorders in light of dominant physical symptoms, and to the lacking knowledge of the pathology of psychological disorders and their ability to be treated. On this basis, the conclusion can be drawn that oncologists responsible for the primary care of breast cancer patients must be better educated in the diagnosis of psychological comorbidity in the course of their studies and training.

Keywords: Psycho-oncology, psychological comorbidity.

43 INVITED

Psychological response to breast cancer and its impact on survival

L. Fallowfield. *Cancer Research UK, Psychosocial Oncology Group, Brighton, East Sussex, UK*

There have been many attempts over the years to establish the types of pre-morbid personality patterns that either predisposed women to develop cancer or to influence their survival. Findings from much of this early work stimulated considerable interest in the possibility of improving not just the quality but the quantity of women's lives through psychological approaches. In this talk I will briefly review some of the data that both supports and refutes the likelihood that psychological factors influence survival. None of the research findings will impact significantly on most clinicians or clinical care until the complex biological pathways mediating and mind-body interactions are established.

44 INVITED

Who is the patient? Psychological distress of breast cancer couples

L. Baider. *Hadassah University Hospital, Director, Psycho-Oncology Unit, Jerusalem, Israel*

The purpose of this randomized prospective study was to identify factors influencing the psychological distress of breast cancer patients and their husbands during remission. Background variables and distress levels of 172 couples from two populations (Graz, Austria and Jerusalem, Israel) were assessed, using three standardized instruments, during two time periods 6 to 8 months apart. In both geographic-cultural groups, women whose partners refused to participate reported significantly less perceived family support ($P<0.01$ for Graz; $P<0.05$ for Jerusalem). It may be suggested that partner participation serves as an indication of how patients appraise their own perception of family support. The Grand Severity Index (GSI) (measuring total psychological distress) reflected minor changes in psychological distress of both patients and husbands over time. Although findings on the relative distress of healthy partners and patients are not always consistent and are mostly restricted to the first years after diagnosis, the majority of studies support a consistent tendency in the relative but similar psychological distress levels of the patient and spouse. Implications for psychological intervention are discussed.

45 INVITED

Psychological intervention with breast cancer patients: an update

Abstract not received.

Wednesday, 17 March 2004 16:00–17:15

PROFFERED PAPERS

Adjuvant and neo-adjuvant therapy

46 ORAL

Efficacy of Pre-operative Arimidex (anastrozole) compared with Tamoxifen (PROACT) as neoadjuvant therapy in postmenopausal women with hormone receptor-positive breast cancer

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Background: In selected patients both cytotoxic and endocrine treatments (eg tamoxifen) given for a short period prior to breast cancer surgery have been shown to cause tumour shrinkage. This enables mastectomy, where a tumour was previously considered inoperable, or breast conserving surgery (BCS) when only a mastectomy was feasible prior to treatment.

Materials & Methods: The PROACT trial evaluated the efficacy of anastrozole (AN) versus tamoxifen (TAM) as neoadjuvant therapy in postmenopausal women with large, operable or potentially operable, locally-advanced, hormone receptor-positive breast tumours. Patients were randomised to double-blind treatment for 12 weeks prior to surgery. Additional chemotherapy was optional and was decided prior to randomisation. The primary objective was a comparison of objective response (OR) rates as assessed by ultrasound at 12 weeks. Secondary objectives included changes in both planned and actual surgery (inoperable at baseline to mastectomy/BCS, or mastectomy at baseline to BCS) from baseline to 12 weeks and tolerability.

Results: 451 patients (mean age 67 years) were randomised to treatment with AN (n=228) or TAM (n=223). At baseline, 14.2% of the patients had tumours assessed as suitable for BCS, 78.3% for mastectomy and 7.3% had inoperable tumours. OR rates by ultrasound are shown in table 1.

Table 1

Patient population	N	OR (% patients)			
		AN	TAM	Odds ratio (95%CI)	P value
All patients	451	39.5	35.4	1.24 (0.84–1.83)	0.29
Hormonal therapy only	314	36.2	26.5	1.57 (0.97–2.55)	0.07
Hormonal therapy +*	262	36.6	24.2	1.81 (1.06–3.11)	0.03

*Also requiring mastectomy/inoperable at baseline.

Considering those patients receiving hormonal therapy alone, more of the AN than TAM treated patients had an improvement in their planned surgical option (47% versus 38% respectively, 1.44 [0.88–2.36] p=0.15) and significantly more of the AN treated patients had an improvement in their actual surgery (43% versus 31% respectively, 1.69 [1.01–2.81] p=0.04). Both treatments were well tolerated.

Conclusions: AN is an effective and well-tolerated neoadjuvant treatment for postmenopausal women with hormone receptor-positive breast cancer whose large tumours necessitate a mastectomy or who have locally-advanced, inoperable disease. These data are consistent with previous findings for AN.

47 ORAL

Anastrozole versus tamoxifen as neoadjuvant therapy for oestrogen receptor-positive breast cancer in postmenopausal women: the IMPACT and PROACT trials

I. Smith[1], L. Cataliotti[2]. *On behalf of the IMPACT and PROACT Trialists.* [1]*Royal Marsden Hospital, London, UK;* [2]*University degli Studi di Firenze, Firenze, Italy*

Background: Two large trials have evaluated anastrozole (AN) vs tamoxifen (TAM) as neoadjuvant therapy in postmenopausal women with hormone-sensitive breast cancer. In contrast to most previous randomised neoadjuvant trials, patients eligible for breast-conserving surgery (BCS) at entry were included. The PROACT (PReOperative Arimidex (anastrozole) Compared with Tamoxifen) trial (N=451) evaluated AN vs TAM, while the IMPACT (IMmediate Preoperative Arimidex, tamoxifen or Combined with Tamoxifen) trial (N=330) compared AN vs TAM alone and in combination.

Results of a prospectively planned combined analysis of these trials are presented.

Methods: In both trials, patients were randomised double-blind to treatment for 12 weeks prior to surgery. In the PROACT trial, additional chemotherapy was optional, whereas IMPACT patients did not receive chemotherapy. Therefore, the results from patients who received either AN or TAM alone have been combined for the primary endpoint of objective response (OR), assessed by calliper and ultrasound. OR rates are also reported for patients whose tumours were inoperable, or were scheduled to have mastectomy at baseline, the population reported in most previous studies. Surgical improvement was assessed in those patients who were inoperable or required mastectomy at baseline (improvement to any surgery/BCS at 12 weeks), defined by improvement in feasible surgery and actual surgery.

Results:

Patient population	OR (% patients)			
	AN	TAM	Odds ratio (95% CI)	p-value
Total (N=535, 69%)				
Calliper	45	36	1.42 (1.00–2.02)	0.052
Ultrasound	32	27	1.28 (0.88–1.87)	0.191
Inoperable/requiring mastectomy at baseline (N=344, 44%)				
Calliper	47	35	1.65 (1.06–2.56)	0.026
Ultrasound	36	26	1.60 (1.00–2.55)	0.048

Significant improvements were seen in both feasible surgery (47% vs 35% [1.67 (1.08–2.60); p=0.021]), and actual surgery (43% vs 31% [1.70 (1.09–2.66); p=0.019]) for AN vs TAM, respectively.

Conclusions: AN is an effective neoadjuvant treatment for post-menopausal women with hormone receptor-positive breast cancer. Overall, AN showed a strong trend towards greater efficacy than TAM, and in patients requiring mastectomy or those with locally advanced inoperable disease, AN was significantly more effective than TAM for all endpoints assessed.

48 ORAL

Correlation between response to neoadjuvant chemotherapy (NACT) with single agent taxanes and HER-2 gene amplification in patients with breast carcinoma

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Background: Taxanes are mitotic poisons that play an important role in the treatment of breast cancer. Identification of patient-specific tumor characteristics may predict response to treatment. The use of NACT is the optimal setting to observe these predictions. The objective of this study was to determine whether HER-2 gene amplification was associated with pathologic response to NACT with taxanes in patients with early-stage breast cancer.

Methods: 71 consecutive patients with stage II and III breast cancer from whom tissue was available were included. Fifty-seven patients (80%) received paclitaxel as part of a randomized clinical trial of NACT for patients with operable breast cancer (Buzdar AU et al. JCO 1999;17:3412–7). Fourteen patients (20%) received neoadjuvant docetaxel off protocol. All 71 patients received FAC postoperatively. HER-2 gene amplification was determined using fluorescence in situ hybridization (FISH). Pathologic complete response (PCR) was defined as no evidence of invasive breast cancer in the breast and the axillary lymph nodes. Breast pathologic response (BPR) was defined as no evidence of invasive breast cancer in the breast only. The association between HER-2 status and pathologic response was evaluated using the Chi Square method. The Kaplan-Meier survival analysis was used to calculate disease free survival (DFS).

Results: The median patient age was 49 years (range, 21 to 70 years). Forty-eight patients (68%) had stage II breast cancer and 23 patients (32%) had stage III breast cancer. HER-2 amplification was detected in 19 (28%) of tumors. Hormone receptor (estrogen and/or progesterone) were detected in 11 (58%) of HER-2 amplified tumors (HER-2[+]) and 31 (65%) of HER-2 non-amplified tumors (HER-2[−]). Median number of NACT cycles was 4. There were 8 PCR, 3 (16%) in patients with HER-2[+] tumors and 5 (10%) in patients with HER-2[−] tumors, (p=0.5). There were 12 BPR, 5 (26%) in patients with HER-2[+] tumors and 7 (15%) in patients with HER-2[−] tumors, (p=0.2). At a median follow up of 53.7 months there have been 17 recurrences. None of the patients who achieved pCR developed recurrent disease, regardless of HER-2 status of the primary tumor. The DFS was 89 months in both groups (HER-2[+] and HER-2[−]) (p=0.1).

Conclusion: HER-2 gene amplification was not predictive of PCR or BPR to neoadjuvant single agent taxanes in patients with early-stage breast cancer.

49 ORAL

Postoperative adjuvant chemotherapy followed by adjuvant tamoxifen versus nil for patients with operable breast cancer. First results of a randomized phase III trial EORTC 10901

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Introduction: Adjuvant Tamoxifen as monotherapy reduces recurrence and mortality in patients with hormone receptor positive operable breast cancer. However, its contribution is less established in patients receiving adjuvant chemotherapy. Experimental data suggest that Tamoxifen and chemotherapy may in fact be partially antagonistic, and recently published clinical trials confirm that concomitant administration of Tamoxifen with chemotherapy yield inferior results than chemotherapy alone. This trial, initiated by the EORTC Breast Group in 1991, investigates the impact of Tamoxifen, given sequentially after completion of adjuvant chemotherapy in patients with operable breast cancer.

Methods: Female patients with stage I–IIIA operable breast cancer receiving after surgery 6 cycles of adjuvant combination chemotherapy with either CMF, CAF, CEF, FAC or FEC were eligible, irrespective of their menstrual status and of the hormone receptor status of their primary tumor. Patients with any other malignant disease including contralateral breast cancer were excluded, except those with adequately treated cervix carcinoma or basal cell carcinoma of the skin. Patients consenting to participate were stratified by institute, chemotherapy scheme and age (above 50y or younger) and were randomized at the start of their last cycle of chemotherapy to receive either Tamoxifen 20mg daily during 3 years or no further treatment. The main endpoint of the trial was to detect a 5% increase in the 5 year survival (from 80% to 85%) in favor of antiestrogen therapy, which required to observe at least 159 deaths in each treatment arm. Secondary endpoints were relapse free survival, local control, incidence of second primary breast cancer and correlation of results with receptor status.

Results: Between 03/1991 and 05/1999, 1863 patients were randomized by 51 institutions from 14 countries. At a median follow-up to date of 6.3 years, 359 deaths and 551 events (relapse and/or death) have been observed.

Conclusions: The number of events needed to perform the first analysis has recently been reached and the data base is in its final stage of cleaning. A full report of the results of this trial will be presented at the meeting.

50 ORAL

Docetaxel-based regimen (TAC) improves DFS and OS over FAC in node positive early breast cancer patients: Efficacy, safety and quality of life at 55 month follow-up

M. Martin, T. Pienkowski, J. Mackey, M. Pawlicki, J. Guastalla, C. Weaver, E. Tomiak, M. Murawsky, J. Nabholtz, A. Riva, C. Vogel. *On behalf of BCIRG 001 Investigators. Hospital Universitario San Carlos, Servicio de Oncologia Medica, Madrid, Spain*

The BCIRG001 trial comparing the docetaxel (Taxotere®)-based regimen TAC (75/50/500 mg/m2 q3wk ×6) with FAC (500/50/500 mg/m2 q3wk×6) accrued 1491 patients with node positive early breast cancer from June 1997 to June 1999. The 2nd planned interim analysis with a median follow-up of 55 months and 399 events showed that TAC improves disease free survival (TAC/FAC Hazard Ratio: 0.72, p=.0010) and overall survival (TAC/FAC Hazard Ratio: 0.70, p=.0080) over FAC (Table 1).

Among hematological toxicities, febrile neutropenia was more frequent in the TAC arm (24.7% vs 2.5%), but with no increased incidence of grade 3/4 infection (3.9% vs 2.2%) and no septic deaths. Non-hematological toxicities (grade 3/4) with incidence >5% of pts were nausea (9.5%), vomiting (7.3%), asthenia (5.6%) in the FAC arm and, asthenia (11.2%), stomatitis (7.1%), nausea (5.1%) in the TAC arm. 91% of patients in the TAC arm and 97% in the FAC arm completed the planned 6 cycles of treatment. Quality of life (QoL), a secondary endpoint of this trial, was assessed using the EORTC QLQC30 (version 2.0) and QLQBR23 (version 1.0). The two treatment groups were well-balanced for baseline scores in