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Efficacy of Cognitive Behavioral Therapy and Physical Exercise in Alleviating Treatment-induced Menopausal Symptoms in Patients with Breast Cancer − Results of a Randomized Controlled Multi-center Trial

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Background: To evaluate the effect of cognitive behavioral therapy (CBT), physical exercise (PE) and of these two program elements combined (CBT/PE) on menopausal symptoms (primary outcome), body image, sexual functioning, psychological well-being and health-related quality of life (secondary outcomes) in breast cancer patients experiencing treatment-induced menopause.

Patients and Methods: Four hundred twenty-two breast cancer patients were randomly assigned to a CBT (N = 109), a PE (N = 104), a CBT/PE (N = 106) or a waiting list control group (N = 103). Self-report questionnaires were completed at baseline, 12 weeks (T1) and 6 months (T2) post-study entry. To compare the intervention groups with the control group over time, multilevel procedures were used to model the series of repeated measurements.

Results: Compared to the control group, intervention groups (intention-to-treat) showed overall decrease in levels of menopausal symptoms (FACT-ES; $p < 0.001$), hot flushes (Hfrs; $p < 0.001$), urinary symptoms (Bfluts; $p = 0.002$), and an increase in sexuality (habit; $p = 0.027$) and physical functioning (SF36 PF; $p = 0.002$). Positive effects of the interventions were found at both short- and long-term follow-up.

Conclusions: This multicenter trial demonstrates that cognitive behavioral therapy and physical exercise can have salutary effects on endocrine symptoms, and to a lesser degree on sexuality and HRQoL-related functioning, among breast cancer patients experiencing treatment-induced menopause. Future work is needed to improve the design and the planning of these interventions with an eye toward improving program adherence.

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TACT2 Trial in Early Breast Cancer (EBC): Differential Rates of Amenorrhoea in Premenopausal Women Following Adjuvant Epirubicin (E) or Accelerated Epirubicin (aE) Followed by Capecitabine (X) or CMF (CRUK/05/019)

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Background: TACT2, a multicentre randomised phase III trial with E-CMF as control (Poole NEJM 2006), tests 2 hypotheses in a 2x2 factorial design: A) accelerated chemotherapy (CT) improves outcomes: (B) capecitabine (X) gives similar efficacy but preferential side-effect profile to CMF. Here we focus on impact of treatment on menstruation in premenopausal women (⩽50 years old).

Materials and Methods: Between Dec 2005−08, 4391 pts (4371 women, 20 men) with node +ve or high risk node -ve invasive EBC were randomised to receive either E (100 mg/m^2 x 4) q3wk or aE (100 mg/m^2 x 4 plus pegfilgrastim, 6 mg d2) q2wk followed by classical CMF q4wk x 4 or X (2500 mg/m^2/day x 14) q3wk x 4. Impact on menstruation was assessed 18 months post-randomisation for premenopausal women ⩽50 years old (n = 1622). Use of elective ovarian ablation was taken as evidence of continuing menses, and data analysed by multiple logistic regression.

Results: Data describing menstruation at 18 months were received for 1333 premenopausal pts (Table).

In adjusted analyses, independent predictors of the continuation of periods included treatment with X over CMF and lower age (continuous) (both $p < 0.001$). Epirubicin schedule and ER status were not significant. A significant interaction was seen between age and X ($p < 0.001$), with a protective effect of X on continuation of menses greatest in older pts. aE rather than E resulted in fewer patients menstruating at the end of chemotherapy but this effect was lost by 18 months.

Menstruation at 18 months, by age	E-CMF (N = 348)		aE-CMF (N = 305)		E-X (N = 346)		aE-X (N = 334)	
	n	%	n	%	n	%	n	%
Continuing	82	*24*	76	*25*	202	*58*	196	*59*
⩽35	19	*63*	22	*67*	13	*62*	20	*80*
36−40	33	*47*	26	*39*	53	*72*	45	*68*
41−45	23	*19*	23	*21*	92	*62*	80	*63*
46−50	7	*6*	5	*5*	44	*43*	51	*44*
Stopped	**241**	***69***	**204**	***67***	**98**	***28***	**96**	***29***
⩽35	5	*17*	5	*15*	2	*10*	1	*4*
36−40	28	*40*	29	*44*	12	*16*	9	*14*
41−45	91	*75*	82	*75*	32	*22*	32	*25*
46−50	117	*92*	88	*92*	52	*50*	54	*47*
Stopped & had ovarian ablation	**25**	***7***	**25**	***8***	**46**	***13***	**42**	***13***
⩽35	6	*20*	6	*18*	6	*29*	4	*16*
36−40	9	*13*	11	*17*	9	*12*	12	*18*
41−45	7	*6*	5	*5*	24	*16*	16	*13*
46−50	3	*2*	3	*3*	7	*7*	10	*9*

Conclusions: E followed by X has much lower risk of rate of permanent loss of menstrual function in pre-menopausal EBC women than CMF after E, particularly for those >40 years old. Whilst comparable efficacy data on these regimens are awaited, these data could be important when interpreting future analyses in TACT2.

Thursday, 22 March 2012 13:30–15:00

KEYNOTE SYMPOSIUM

The Biology of Metastasis in Breast Cancer

201 Invited

Mouse Models of Metastatic Breast Cancer

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Metastatic disease is the major cause of death in cancer patients. Metastasis is the result of a complex set of molecular events whose outcome is eventually disseminated disease. Moreover, metastasis development is influenced by a number of host factors, including stromal cells as well as innate and adaptive immune cells. This complexity has made it difficult to identify the molecular mechanisms driving the metastatic process and has confounded our understanding of how and when therapeutic intervention can be effectively used. Delineation of the mechanisms and tumor-host interactions underlying metastasis formation requires realistic animal models for de novo spontaneous tumor development and metastasis.

To establish GEM models of metastatic breast cancer, we have used the Cre/loxP system for time- and tissue-restricted switching of multiple tumor suppressor genes within cells in vivo. This technology enables the induction of defined tumors within a narrow time window, and the correlation of specific genetic lesions with phenotypic characteristics of the tumor. Using this approach, we have established several mouse models for for E-cadherin mutated lobular breast cancer. These mice develop mammary tumors that closely resemble the lobular morphology and the metastatic spectrum of the cognate tumors in humans. These mouse mammary tumor models can be effectively used to study therapy response and acquired drug resistance of primary tumors and their metastases in a physiologically relevant setting.

202 Invited

Imaging and targeting the drivers of invasion and metastasis

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One of the hallmarks of cancer cells is their ability to invade into adjacent tissue and spread to distant sites within the body. We have been studying invasion, metastasis and ingression of host vasculature into tumours, leading to findings that will take forward development of small molecule