Table. adverse events (CTCAE v3.0)

	Grade0	1	2−4	Grade 1 (%)
fatigue	31	20	0	39.2%
nausea	48	3	0	5.9%
vomiting	51	0	0	0
anorexia	45	6	0	11.8%
dermatitis	4	47	0	92.2%
dry skin	48	3	0	5.9%
skin pigmentation	35	16	0	31.4%
Skin depigmentation	51	0	0	0
edema	30	21	0	41.2%
pain	32	19	0	37.3%
pneumonitis	51	0	0	0

5131 POSTER

Hypofractionated radiotherapy after conservative surgery for breast cancer: analysis of acute and late toxicity in a mono-institutional series

L. Deantonio[1], G. Gambaro[1], D. Beldì[1], E. Negri[2], S. Tunesi[3], C. Magnani[3], M. Krengli[1]. *[1]Radiotherapy, University Hospital Maggiore della Carità, Novara, Italy; [2]Medical Phisics, University Hospital Maggiore della Carità, Novara, Italy; [3]Epidemiology and biostatistics, University Hospital Maggiore della Carità, Novara, Italy*

Background: To assess acute and late toxicity after hypofractionated radiotherapy (RT) following breast conserving surgery in a mono-institutional series.
Materials and Methods: A group of 85 women operated by conservative surgery for breast cancer (pT1−2 pN0−1 M0) was treated with postoperative hypofractionated RT to a total dose of 45 Gy in 20 fractions of 2.25 Gy to the whole breast followed by 9 Gy boost in 3 fractions (BED = 55 for acute toxicity, alfa/beta = 10; BED = 78 for late toxicity, alfa/beta = 3). Acute and late toxicity were scored according to the RTOG/EORTC criteria. These results were analyzed and compared with those observed in a group of 70 patients with similar characteristics and treated with RT to the same treatment volumes to a total dose of 50 Gy in 25 fractions followed by 10 Gy boost in 5 fractions (BED = 60 for acute toxicity, alfa/beta = 10; BED = 83 for late toxicity, alfa/beta = 3). Statistical analysis was performed using the chi-square test to compare acute and late toxicity between patients treated with hypofractionation and those treated with conventional fractionation.
Results: Early reactions were observed in 72/85 (85%) patients treated with hypofractionation and in 67/70 (96%) patients treated with conventional fractionation. Acute toxicity was classified as grade 1 in 60%, as grade 2 in 22% and as grade 3 in 2% of patients in the group treated with hypofractionation. Early reactions were classified as grade 1 in 49%, as grade 2 in 41% and as grade 3 in 5% of patients in the group treated with conventional fractionation. The difference between the two fractionation groups resulted to be statistically significant ($p = 0.01$).
Late toxicity was observed in 8 patients (10%) in the group treated with hypofractionation with a mean of follow up of 435 days and in 10 patients (15%) in the group treated with conventional fractionation with a mean follow up of 854 days, respectively. The difference in frequency of late toxicity was not statistical significant ($p = 0.4$).
Conclusions: In our experience, a radiation hypofractionated schedule delivering 45 Gy in 20 fractions offered a significant reduction of skin acute toxicity ($p = 0.01$) and not significant difference of late effects ($p = 0.4$) compared to the conventional schedule. The reduction in acute toxicity in patients treated with hypofractionated RT could be explained by the BED values and by the dosimetric data that are still under analysis and could differ in the two treatment groups.

5132 POSTER

Targeted intraoperative radiotherapy and sentinel node biopsy enable breast and axillary lymph node preservation

J. Mielko[1], A. Kurylcio[1], M. Jankiewicz[1], J. Romanek[1], B. Winkler[1], M. Lewicka[1], B. Chrapko[1], W.P. Polkowski[1]. *[1]Medical University Hospital of Lublin, Surgical Oncology, Lublin, Poland*

Background: The purpose of the study is: 1) to analyse results of the breast conserving treatment (BCT) in patients with breast carcinoma using both intraoperative radiotherpy (IORT) and sentinel node biopsy (SNB) simultaneously; and 2) to estimate breast and axillary lymph nodes preservation with this approach.
Material and Methods: The treatment protocol was approved by Ethical Committee. The BCT using combined SNB, wide local excision (WLE) and IORT was performed in 138 patients who signed the informed consent. Patients with primary tumour $\leqslant 2$ cm and clinically negative axillary lymph nodes were eligible. The SNB was done using isotope-dye technique with preoperative lymphoscintigraphy. The INTRABEAM® PRS 500 system (Carl Zeiss, Oberkochen, G) was used for irradiation of the tumour bed with the dose of 20 Gy (boost; energy 18 keV). After completion of the adjuvant treatment, whole breast external beam irradiation was performed with a total dose of 50 Gy, omitting the tumour bed. Objective computerized aesthetic effect assessment was done using BCCT.core® software (University of Porto, PT). Follow-up time ranged from 9 to 38 months (mean 22 months).
Results: Minor early postoperative complications (reddening of the skin wound; seroma) did not prolong hospitalization. In 14 patients (10%), surgical specimen pathology revealed positive margin. Re-excision of the margins was performed all in of these patients. In one patient mastectomy was necessary because neoplastic cells in re-excison specimen. In 27 (20%) patients (selective) lymphadenectomy was performed following positive SNB. In one patient both positive SNB and positive margins necessitated mastectomy; whereas in another patient after selective lymphadenectomy, mastectomy was necessary because of margins' infiltration by comedo type carcinoma. Altogether breast and axillary lymph node preservation was possible in 108 (78%) of patients. Fifteen patients (11%) had fibrosis of the treated breast quadrant. In patients after breast conservation who reached 1 year follow-up, the BCCT.core® general aesthetic score was excellent in 52%, good in 42%, and fair in 6% of patients. There was neither poor aesthetic outcome. In one patient pulmonary metastases were detected prior to local recurrence in the breast.
Conclusions: The combination of SNB, WLE and IORT is a safe surgical procedure leading both to breast and axillary lymph nodes preservation with improved patients' satisfaction by excellent or good aesthetic effect and shortening the time of treatment in majority of patients.

5133 POSTER

Incidence of distant metastasis (DM) in elderly postmenopausal women with operable breast cancer treated with tamoxifen (TAM)

J. Doughty[1], J. Mansell[1], I. Monypenny[2], A. Skene[3], P. Abram[4], R. Carpenter[5], J. Gattuso[5], C. Wilson[1], W. Angerson[1]. *[1]Western Infirmary, University Department of Surgery, Glasgow, United Kingdom; [2]University of Wales College of Medicine, University Department of Surgery, Cardiff, United Kingdom; [3]Royal Bournemouth Hospital, Department of Endocrine and Surgery, Bournemouth, United Kingdom; [4]Belfast City Hospital, Northern Ireland Cancer Centre, Belfast, Ireland; [5]St. Bartholomew's Hospital, Breast and Endocrine Unit, London, United Kingdom*

Background: Breast cancer recurrence risk is greatest during the first 2 years following surgery, and DM recurrences predominate during this early peak (Mansell J et al. *Breast Cancer Res Treat.* 2008; Dec [Epub ahead of print]). DM has been associated with poor survival and breast cancer-related death (Lamerato L et al. *J Clin Oncol*. 2005;23(16S):62s. Abstract 738). Elderly women ($\geqslant 75$ yr) with early breast cancer are often less likely to receive chemotherapy (CT) due to comorbid conditions (pulmonary, cardiovascular), yet they remain at risk for early DM and are good candidates for adjuvant hormonal treatment (Crivellari D et al. *J Clin Oncol.* 2008;26:1972−9; Rao VSR et al. *Int J Cancer.* 2007;120:1155−60).
Methods: We stratified a cohort of 3614 women treated with TAM following surgery for early breast cancer by age, identified CT status, and the incidence of DM and calculated the Kaplan-Meier-estimated 2.5- and 5-year recurrence rates.

	N	Patients with DM, n (%)	CT received, n (%)	CT status unknown, n (%)
All pts	3614	344 (9.5)	713 (21.9)	360 (10)
<75 yr	2992	272 (9.1)	690 (25.1)	248 (8.3)
$\geqslant$75 yr	622	72 (11.6)	23 (4.5)	112 (18.0)

Results: Elderly patients (pts) $\geqslant 75$ yr were less likely to receive CT, and the incidence of DM was higher than in younger pts <75 yr (Table). The 2.5-yr and 5-yr cumulative DM (95% CI) for pts <75 yr vs $\geqslant 75$ yr, respectively, were 4.0% (3.2−4.8) and 8.7% (8.5−10.9) versus 9.0% (6.5−11.5) and 14.8% (11.3−18.3). Of the 344 pts with DM, 75.6% died during follow-up.
Conclusions: Elderly pts with breast cancer are frequently undertreated for their disease, despite being at risk for DM, and are good candidates for adjuvant hormonal therapy. The aromatase inhibitors are superior to TAM, and results from the BIG 1−98 trial show that letrozole (LET) significantly reduces recurrences, regardless of age (Crivellari et al 2008). Early reductions in DM recurrence, as observed with initial adjuvant LET (Thurlimann B et al. *N Engl J Med.* 2005;353:2747−57; Mauriac L et al. *Ann Oncol.* 2007;18:859−67] may translate to the observed survival advantage

(Mouridsen H et al. *Cancer Res.* 2009;69[suppl]:66s. Abstract 13) with well characterized adverse events.

5134 POSTER

The cariatide study: evaluation of the impact of educational material on the compliance and persistence rates to adjuvant aromatase inhibitor medication in postmenopausal breast cancer patients

A. Chioti[1], P. Neven[2], C.I. Markopoulos[3], M. Tanner[4], R. Kreienberg[5], L. Atkins[6], M. Marty[7]. *[1]Astrazeneca, Medical, Brussels, Belgium; [2]UZLeuven, Gynecology Oncology, Leuven, Belgium; [3]Athens University Medical School, Breast Unit, Athen, Greece; [4]Tampere University, Chemo and Onco, Tamper, Finland; [5]Universitats-Frauenklinik, Onco, Ulm, Germany; [6]St Thomas Hospital, Institute of Psychiatry, Sussex, United Kingdom; [7]Hopital St Louis, Citoh, Paris, France*

Rationale: Approximately 430,000 women are diagnosed with breast cancer each year in Europe and recurrence occurs in 20−30% of patients who have undergone surgery with curative intent. Patient adherence to the long-term medication is a multidimensional problem despite the demonstrated efficacy of adjuvant Aromatase Inhibitor (AI) treatment of early breast cancer. Providing educational material may help patients to be more compliant to their treatment; subsequently, understanding the reasons of non-adherence may lead to the design of more adequate interventions aiming to improve patients' compliance to long term hormonal therapy.
Methods: This global, observational study (NCT00681122) will be conducted in 2,732 patients from 350 centres in 18 countries. Impact of educational material (EM) on compliance and adherence of post-menopausal women with hormone sensitive early breast cancer treated or planned to be treated with upfront adjuvant AI will be evaluated. This study investigates whether educational information provided to patient could influence patient's motivation and behaviour, resulting in improved treatment adherence. Adherence on upfront AI medication will be followed for two years of adjuvant hormonal treatment. Patients will be randomised to Group A: Standard Therapy and GroupB: Standard Therapy+EM. Patients in Group B will be supplied with a total of 9 educational packages, including information on the characteristics of early breast cancer, risk of recurrence, hormonal treatment options, benefits and risks of upfront adjuvant endocrine treatment, coping with and adherence to long-term hormonal medication and supporting of active and healthy female lifestyle.
Outcome variables: (1) *Compliance rate* (% number of subjects being 'compliant') for the adjuvant AI medication will be analysed at one year based on the subject's assessment. (2) *Persistence rate* (% number of subjects with a 'persistent' use of adjuvant AI medication) will be evaluated for the first time after one year and a second time after two years. (3) *Time to treatment* and *reasons for discontinuation* of AI will be analysed. Specialized questionnaires will be used to evaluate medication adherence and the patient's feelings and beliefs on the disease and therapy (EORTC-INPATSAT-32, OPTIMA-X, GHQ-12, FACT-ES, compliance questionnaire, and EM feedback questionnaire in Group B patients).
Results: Study accrual has been completed on March 2009; preliminary results after one-year follow-up are expected early 2010 and the study is expected to finish March 2011.

5135 POSTER

Half of breast cancer patients starting on tamoxifen complete five years of endocrinetreatment

A.C. Voogd[1], M.P.P. van Herk-Sukel[2], G.A.P. Nieuwenhuijzen[3], R.M.C. Herings[2], J.W.W. Coebergh[4], L.V. van de Poll-Franse[4]. *[1]Maastricht University, Department of Epidemiology, Maastricht, The Netherlands; [2]PHARMO, Institute for Drug Outcomes Research, Utrecht, The Netherlands; [3]Catharina Hospital, Department of Surgery, Eindhoven, The Netherlands; [4]Comprehensive Cancer Centre South, Eindhoven Cancer Registry, Eindhoven, The Netherlands*

Background: Adjuvant endocrine therapy in women with early stage breast cancer prolongs disease free and overall survival. The aim of the study was to determine first treatment switch and discontinuation in breast cancer patients starting on tamoxifen and to analyze the predictors of discontinuation.
Patients and Methods: Patients with early stage breast cancer were selected from the Eindhoven Cancer Registry from 1998 to 2006 and linked to the PHARMO Network to select drug use during follow-up. Patients starting on tamoxifen were included in the study cohort. Continuous use of endocrine treatment was determined as the time between start and stop of therapy, allowing a 60 days gap between refills. The switch from tamoxifen to an aromatase inhibitor (anastrozole, exemestane or letrozole) was determined. Cox regression was used to identify independent determinants of discontinuation of any endocrine treatment (tamoxifen and/or aromatase inhibitor use) during five years of follow-up.
Results: A total of 1,451 new breast cancer patients started on tamoxifen. Of those, 26% had a treatment switch to: anastrozole (n = 203), exemestane (n = 113) or letrozole (N = 64) with a mean duration until first switch of 2.0 (SD = 1.3) years. Of the patients followed for five years, 51% discontinued any endocrine treatment before the completion of five years (see table). Multivariate analyses showed that discontinuers were less likely to be aged 50−69 years (versus 70 years; HR = 0.74; 95%CI: 0.60−0.91) and were more likely to have 2 or more concomitant diseases (versus no comorbidity; HR = 1.54; 95% CI: 1.06−2.26).

Table. Continuous use of any endocrine treatment of patients who start tamoxifen

Treatment	Start	Continuous use at . . . *									
		1 year		2 years		3 years		4 years		5 years	
	N	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)
Hormonal	1,451	1,336	1,168 (87)	1,120	872 (78)	896	621 (69)	676	423 (63)	499	245 (49)

* % calculated as number of continuous users, "n" (still on therapy) at a specific day of follow-up, divided by "N" total number of patients in study population at start of interval.

Conclusions: Only half of the breast cancer patients starting tamoxifen continued five years of endocrine treatment. Identification of patients at risk of discontinuation will assist in the development of interventions to improve adherence.

5136 POSTER

Tamoxifen and exemestane adjuvant multinational (TEAM) trial; findings from the Dutch/belgian subset

C. Seynaeve[1], C.J.H. van de Velde[2], E. Maartense[3], R.M.H. Roumen[4], J.W.R. Nortier[5], E.T.M. Hille[6], J.G.H. Nes van[2], H. Putter[7], R. Paridaens[8], L.Y. Dirix[9]. *[1]Erasmus MC Daniel den Hoed Cancer Center, Medical Oncology, Rotterdam, The Netherlands; [2]Leiden University Medical Center, Surgical Oncology, Leiden, The Netherlands; [3]Reinier de Graaf Gasthuis, Medical Oncology, Delft, The Netherlands; [4]Maxima Medical Center, Surgical Oncology, Veldhoven, The Netherlands; [5]Leiden University Medical Center, Medical Oncology, Leiden, The Netherlands; [6]Leiden University Medical Center, Datacenter, Leiden, The Netherlands; [7]Leiden University Medical Center, Statistics, Leiden, The Netherlands; [8]UZ Gasthuisberg, Medical Oncology, Leuven, Belgium; [9]General Hospital Sint-Augustinus, Medical Oncology, Antwerp, Belgium*

Background: At 2.75 years of follow-up, the multinational TEAM trial (N = 9779) showed that upfront adjuvant therapy with exemestane (E) in postmenopausal, hormone-sensitive breast cancer (BC) patients may be more effective than tamoxifen (T) (DFS (ITT) HR 0.89; 95% CI 0.77−1.03, p = 0.12). Subgroup analyses suggested that some patient categories (i.e. age $\geqslant$70 years, N1) might benefit more from upfront E. To further explore the effectiveness of E as upfront strategy and in specific subgroups, the Dutch/Belgian TEAM data were analysed as there was a high inclusion rate throughout these countries (N = 3167), and this population was very homogeneous and representative for the real-world of patients being given adjuvant hormonal therapy.
Methods: Postmenopausal, hormone-sensitive early BC patients being eligible for adjuvant endocrine therapy were randomized to open-label E or T. After 2.5−3 years, T patients switched to E; endocrine therapy was given for 5 years in both arms. The first co-primary endpoint was DFS of T versus E at median follow-up of 2.75 years. Cox regresion stratified for important prognostic variables was used to compare treatments.
Results: Comparing the Dutch/Belgian with the Global study cohort, the first group consisted of significantly more high-risk patients (70% N+ vs 48% N+) and patients $\geqslant$70 years (30% vs 27%), explaining the different event rate (10.3% and 7.6%, resp.). DFS at 2.75 yrs was 90.7% in E and 88.1% in T patients (HR T/E 0.77; 95%CI 0.62−0.96, p = 0.02). RFS, DFS on study drug, and time to distant metastases significantly favored E; HRs (95%CI; p-value) were 0.74 (0.58−0.94; 0.015), 0.72 (0.57−0.92; 0.008), and 0.68 (0.52−0.90; 0.006), respectively, all stronger than in the main study. In patients $\geqslant$70 years (HR 0.59; p = 0.005, numbers needed to treat (NNT) 15.7) and with 1−3 positive nodes (N1) (HR 0.67; p = 0.008, NNT = 26.5) the HRs were even stronger than the overall Dutch/Belgian results, but not significantly different.
Conclusions: In the Dutch/Belgian cohort of the TEAM study, being at high risk of disease recurrence, E was more effective than T after 2.75 years. Although the Dutch/Belgian data show stronger HRs, the data are in line with the results of the main study. Further, the Dutch/Belgian data suggest more benefit from upfront E for patients $\geqslant$70 years and with N1 disease. However, the identification of specific subgroups potentially benefiting from an aromatase inhibitor upfront remains to be analysed in larger study cohorts.