irradiated with CT-based planning. After completetion of Radiotherapy, hormonal agent was continued unless the patient has to be withdrawn earlier owing to progressive disease (as per RECIST criteria).

Results: Tumor response was evaluated by monthly clinical examination till Radiotherapy begins (to asses the response to the hormonal agent alone) and after completion of Radiotherapy (to find the final response to hormone + concurrent Radiotherapy as per RECIST criteria). More than 50% tumor shrinkage was noted prior to Radiotherapy in 48/156 (31%) patients on tamoxifen and 18/65 (27%) on letrozole. Complete remission was achieved in 137/217 (63%) patients at a median interval of 3 months after completion of Radiotherapy i.e. about 7−8 months of commencement of hormonal therapy. Partial response was recorded in 64/217 and Stable disease in remaining 16/217 patients. Median time to progression was found to be a median 13 months for those having overall response and 8 months for those having stable disease. Although 2 year DFS was noted in only 42/217 patients, 2 year OS was recorded in 203/221 patients − 13/17 deaths were of unrelated causes. Surprisingly systemic metastasis was recorded in only 6/217 patients who completed Radiotherapy.

Conclusion: For estrogen receptor positive inoperable locally advanced elderly patients or those who refuse surgery, primary radio-hormone therapy proves to be a non-toxic well-tolerated inexpensive patient-compliant treatment option, which, till date remains nearly untrodden ground in world literature.

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Monthly versus three-monthly goserelin treatment in premenopausal patients with oestrogen receptor-positive early breast cancer

Y. Rai[1], H. Iwata[2], N. Masuda[3], K. Anan[4], T. Takeuchi[5], N. Kohno[6], H. Takei[7], Y. Yanagita[8], S. Noguchi[9]. *[1]Sagara Hospital, Breast Surgery, Kagoshima, Japan; [2]Aichi Cancer Center Hospital, Breast Oncology, Aichi, Japan; [3]National Hospital Organization Osaka National Hospital, Surgery, Osaka, Japan; [4]Kitakyusyu Municipal Medical Center, Surgery, Fukuoka, Japan; [5]Marumo Hospital, Surgery, Aichi, Japan; [6]Tokyo Medical University Hospital, Breast Oncology, Tokyo, Japan; [7]Saitama Cancer Center, Breast Surgery, Saitama, Japan; [8]Gunma Cancer Center, Breast Oncology, Gunma, Japan; [9]Osaka University Hospital, Breast and Endocrine Surgery, Osaka, Japan*

Background: Goserelin is a luteinising hormone-releasing hormone agonist often used in combination with tamoxifen to treat premenopausal women with oestrogen receptor-positive (ER+) breast cancer. Due to its less-frequent administration schedule, a three-month goserelin 10.8 mg depot may provide a more convenient treatment option versus the current 3.6 mg monthly depot.

Materials and Methods: This multicentre, open-label, randomised study of premenopausal Japanese women with ER+ early breast cancer compared patients receiving goserelin 3.6 mg once every 4 weeks with patients receiving 10.8 mg once every 12 weeks. All patients received concomitant tamoxifen (20 mg/day). The primary endpoint was oestradiol suppression occurring over the first 24 weeks (area under the concentration time curve [AUC]). Secondary endpoints included: oestradiol and follicle-stimulating hormone (FSH) levels; the proportion of patients with oestradiol levels <30 pg/mL; menstruation; disease-free survival (DFS); and safety/tolerability. Treatment continued for 96 weeks or until discontinuation criteria were met.

Results: A total of 170 patients were randomised (84 to the 3.6 mg group; 86 to the 10.8 mg group). The mean AUCs for oestradiol serum concentration were 18.95 pg/mL·week (3.6 mg group) and 18.32 pg/mL·week (10.8 mg group). The baseline adjusted AUC ratio (10.8 mg/3.6 mg) was 0.974 (95% CI: 0.8, 1.19). Oestradiol and FSH levels were suppressed in both treatment groups; $\geqslant$98.8% of patients had oestradiol-serum concentrations <30 pg/mL by Week 4. Menstruation had ceased by Week 16 in both groups. Median follow-up periods for DFS were 675.5 days (3.6 mg group) and 675.0 days (10.8 mg group); a total of four recurrence events were observed during the study (one in the 3.6 mg group and three in the 10.8 mg group, respectively); plus one new cancer (in the 10.8 mg group). The incidence of adverse events (AEs) was similar between treatment groups. The most common AEs were hot flushes, nasopharyngitis and headache. No clinically important differences in the safety and tolerability profiles were found between treatment groups.

Conclusions: In terms of oestradiol suppression, goserelin 10.8 mg is non-inferior to goserelin 3.6 mg in premenopausal patients with ER+ early breast cancer. Both treatments have similar efficacy and similar tolerability profiles.

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Gemcitabine, carboplatin and paclitaxel as neoadjuvant combination chemotherapy in patients with locally advanced (stage III) or inflammatory breast cancer − a non-anthracycline alternative

C. Kambye[1], D.L. Nielsen[1], E. Balslev[2]. *[1]Herlev Hospital, Oncology, Herlev, Denmark; [2]Herlev Hospital, Pathology, Herlev, Denmark*

Background: The gemcitabine/paclitaxel combination is a highly effective regimen in metastatic breast cancer. Preclinical studies have demonstrated synergistic action, when combining a platin-derivative and paclitaxel. We examined the activity of combining gemcitabine, carboplatin and paclitaxel (GCP) in patients (pts) with locally advanced or inflammatory breast cancer (LABC or IBC).

Material and Methods: In the period 2002−6, 44 consecutive pts with LABC or IBC entered a phase II protocol of neo-adjuvant GCP (G, 800 mg/m^2 d1+8; C, AUC 4.5 d8; P, 175 mg/m^2 d1) every 3 weeks for 4−6 cycles. Median (range) age was 57 (32−76) years and 76% were postmenopausal. Tumor size (median): 80 mm range 7–150 mm; 74% were node positive; 10 had IBC; 85% were hormone receptor positive and 14% were HER2 positive. If there was no sign of response after two cycles of GCP treatment was shifted to CEF (750/60/750 mg/m^2) d1 q3w. After surgery, radiotherapy and adjuvant systemic treatment were given according to standardized guidelines (total of 9 cycles of chemotherapy).

Results: A total of 139 cycles (median 4 cycles (range, 1−6)) were given before surgery; 44 pts was evaluable for toxicity and survival and 39 pts for response. Non-haematological toxicity was mild: no grade 3−4 toxicity was found except that 3% had transient grade 3 increase of transaminases. Most common grade 1−2 toxicities were parestesia (47%) fatigue (36%), myalgia/arthralgia (38%), nausea/vomiting (16%), diarrea (7%) and allergic reactions/hypersensitivity (8%). Grade 1−2 haematological toxicity comprised neutrocytopenia, 21% and thrombocytopenia, 2%; grade 3−4 neutrocytopenia occurred in 12% (one grade 4) and thrombocytopenia in 1%. After two cycles a PR or a minor response (justifying continued GCP) were seen in 64% of the 39 evaluable pts, while NC were observed in 33% of the pts; no complete responses; one patient had progressive disease. A total of 22 pts shifted to CEF before final surgery due to insufficient response (14 pts) or toxicity (8 pts). At surgery 33% obtained a PR and 23% had NC. Radical surgery was possible in all pts. Median follow up time was 48 mos. The 5-year survival was 61% (95CI: 42−80 mos.). In the same period, 47 pts non-eligible to the present protocol or who did not wish to participate in the protocol received CEF (750/60/750 mg/m^2 d, 1q3w x 4−6). The 5-year survival of this (non-randomized) comparable group was 74% (95% CI: 49−89%).

Conclusion: As non-anthracycline drug combinations may be indicated in some clinical settings, we examined the activity of GCP in pts with LABC or IBC. The three drug combination can obtain comparable efficacy and an obvious decreased toxicity compared to traditional anthracyline containing regimens, making this combination an alternative when anthracyclines are not warranted. Updated results in relation to hormone receptor, HER2, P53 and TOP2A status will be presented.

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Locally advanced breast cancer; twelve years results from a single institution

F. Cold[1], O. Svolgaard[1], P. Høger Thygesen[1], S. Cold[1]. *[1]Odense University Hospital, Oncology, Odense, Denmark*

Background: The management of locally advanced breast cancer (LABC) requires a combined modality treatment approach involving surgery, radiation and systemic therapy. The introduction of new modalities in the adjuvant treatment of primary breast cancer treatment, such as taxanes, aromatase inhibitors and targeted treatments has made a major improvement in recurrence-free and overall-survival. These modalities have been passed on to the locally advanced setting. We now report treatment results for LABC patients treated in a single institution in the county of Funen, Denmark.

Material and Methods: Through a cross check from the national database (Danish Breast Cancer Cooperative Group − DBCG) and the treatment files of our department in the period 1.1.97–31.12.08, 111 patients were identified with LABC. LABC includes any **T3,** any **T4,** any **N2, M0**.

The chemotherapy regimens were mainly anthrycyline based whereas taxanes in the second half-part of the study were used either if no response where observed or in the adjuvant setting. Trastuzumab was used from 2005 in patients with HER-2 positive tumors, either preoperatively with a taxane or in the adjuvant setting.

The patients were analyzed according to treatment period (first vs last half-part) and response to treatment (pCR, PR, NC and PD).

Results: Patient characteristics: age median 58 (27−88), primary treatment chemotherapy 101 vs endocrine therapy only 10. Ninety seven

(87%) reached surgery, of these 6 obtained a complete pathologic response (pCR), 42 had a partial response (PR), 48 had no change (NC) and 1 had progressive disease (PD). Thirteen did not go to surgery.

Median survival for the entire study 7.4 years.

The 3-year survival for patients treated in the first half-part of the study was 52% vs 82% for patients treated in the latest half-part. Survival according to response did not show a consistent pattern, 3-year survival for CR, PR and NC was 54%, 73% and 76%, respectively.

Conclusion: Changes in treatment modalities available through the millennium, is reflected in an increase in survival. As surgery mainly was performed as early as possible response at surgery was not reflected in survival.

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Treatment of the axilla in locally advanced breast cancer

M.W. Kolff[1], L. Knijnenberg[1], A.B. Kluit[2], J.W. Wilmink[3], G. van Tienhoven[1]. *[1]Academic Medical Center/University of Amsterdam, Department of Radiotherapy, Amsterdam, The Netherlands; [2]Academic Medical Center/University of Amsterdam, Department of Surgery, Amsterdam, The Netherlands; [3]Academic Medical Center/University of Amsterdam, Department of Medical Oncology, Amsterdam, The Netherlands*

Background: A retrospective analysis of women treated for locally advanced breast cancer (LABC) with local regional radiotherapy with or without neo-adjuvant chemotherapy and/or surgery focusing on axillary control.

Materials and Methods: All consecutive 131 patients diagnosed from January 1990 to December 2005 treated with local regional radiotherapy were reviewed. Treatment consisted of 50 Gy in 25 fractions of 2 Gy to the breast and regional lymph node areas and a boost of 20 Gy in 2 Gy fractions to the primary tumour area in 7 weeks. 80% of the patients had lymph node metastases. 46 patients received an axillary, 4 a supraclavicular and 1 an infraclavicular boost because of gross nodal involvement.

40 patients received irradiation only (**IR**) (1 of whom received breast irradiation only). 34 received neo-adjuvant chemotherapy without surgery (**NC**) and 57 patients received neo-adjuvant chemotherapy with surgery (**NCS**) before irradiation (33 wide local excision, 24 mastectomy) of whom 5 did not receive regional lymph node irradiation.

Of the whole cohort 89 patients (68%) did not receive axillary surgery, all of these patients were irradiated to the axillary lymph node region except for 1 patient. In the **IR** group 2 patients were treated with an axillary lymph node dissection (ALND). In the **NCS**/**NC** groups 36 were treated with an ALND and 4 with a sentinel node (SN) procedure, axillary lymph node irradiation was omitted in 5 of them. Median follow up was 65 months for the entire cohort.

Results: The 5-year local control rate was 76.9% (**IR**), 61.9% (**NC**) and 90.4% (**NCS**) in favour of the neo-adjuvant chemotherapy with surgery group (p-value = 0.004). The 5-year regional control rate was 94% in all groups (p-value 0.919). There were 7 regional recurrences, 4 in the supraclavicular fossa (**IR:** 1, **NC:** 1, **NCS:** 2) and 3 in the axillary region (1 in every group). 5 year axillary control rate was 100% for the 42 patients treated with ALND/SN and 98% for the remaining 89 patients (not significant).

Conclusion: Best outcome is achieved in terms of local control for the trimodality treatment consisting of neo-adjuvant chemotherapy, surgery and loco-regional irradiation in patients with locally advanced breast cancer. The data suggest that in these patients omitting ALND/SN did not influence axillary recurrence rate.

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Trends in advanced breast cancer in a developed Asian society

C.H. Pek[1], E.Y. Tan[1], C. Teo[1], A. Ernest[1], M.Y.P. Chan[1]. *[1]Tan Tock Seng Hospital, General Surgery, Singapore, Singapore*

Introduction: Although the overall incidence of breast cancer in Singapore is about one-third that of Western countries, the incidence of advanced breast cancer, including locally advanced breast cancer and metastatic breast cancer, is more common. It was observed in countries where nationwide mammographic screening was introduced, that breast cancers were being detected at an earlier stage. Singapore introduced nationwide mammographic screening in January 2004; going by previous observations, we would expect the incidence of advanced breast cancer to decrease following this. We therefore examined the trends in advanced breast cancer over a 8-year period, spanning a period before and after the introduction of nationwide breast screening.

Materials and Methods: A retrospective review of the breast cancer database from our institution, a tertiary hospital, from 1st January 2001 to 31st December 2008 was performed. Two thousand two hundred patients were diagnosed with breast cancer during this period. Standard clinicopathological parameters were analysed.

Results: The incidence of advanced breast cancer had not changed significantly over the years, and ranged from 25% to 30% of all cancers (including ductal carcinoma-in-situ) diagnosed. Patient factors that correlated significantly with advanced breast cancer included older age, Malay ethnicity, nulliparity and a positive family history of breast cancer. High tumour grade, the presence of lymphovascular invasion (LVI), hormone receptor negativity and HER2 positivity were also significantly correlated with advanced breast cancer. On multivariate analysis, only Malay ethnicity, older age and the presence of LVI predicted for advanced breast cancer. Interestingly, among Malays, advanced breast cancer was more common among younger women. Tumour grade and LVI, but not hormone receptor or HER2 status, correlated with advanced breast cancer in Malays.

Conclusions: The incidence of advanced breast cancer has not decreased despite the introduction of breast cancer screening. In an earlier publication on breast cancer trends in our institution from January 2001 to December 2004, we had reported that Malays were more likely to present with advanced breast cancer. This has remained unchanged in recent years. Our study suggests that efforts to increase breast cancer awareness and early diagnosis should be directed towards Malay women, who are more likely to present at an advanced stage.

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The use of vertical rectus abdominis myocutaneous flap for post-mastectomy defect cover of large breast tumours

Y.S. Tan[1], E.Y. Tan[1], S. Ho[1], M. Wong[1], M.Y.P. Chan[1]. *[1]Tan Tock Seng Hospital, General Surgery, Singapore, Singapore*

Background: Primary chemotherapy is the mainstay of therapy for advanced breast cancers, but surgery is still needed for local control in selected patients. In such cases, the post-mastectomy defect is often too large to allow for primary skin closure. Split skin grafts were previously used, but in recent years, our institution has moved towards using the vertical rectus abdominis myocutaneous (VRAM) flap. We present our results.

Material and Methods: This is a retrospective review of 13 patients who underwent a VRAM flap from 1st January 2008 to 30th September 2009. We reviewed clinicopathological parameters and various surgical outcomes.

Results: Thirteen patients with T4 tumours underwent VRAM flap following mastectomy. Median age was 61 years (range 33 to 86 years old). Nine were Chinese and 4 were Malays. Median tumour size at the time of presentation was 100 mm (range 30 to 150 mm); all had skin involvement. Nine patients (69.2%) received primary chemotherapy, but either had no clinical response or progressively enlarging tumours. At the time of surgery, 7 patients (53.8%) had fungating tumours and 5 patients had clinical chest wall involvement. All patients underwent mastectomy and axillary clearance. It is our usual practice for the Plastics team to begin raising the VRAM flap concurrent with the mastectomy. The mean total time taken for both procedures was 279 minutes. Two patients developed major post-operative complications. One developed a haematoma, which required emergency haemostasis on the same day. Another developed partial flap loss, which required surgical debridement. There were three minor complications; one of the elderly patients suffered from functional decline post-surgery and received inpatient rehabilitation. Two patients had superficial wound infections which resolved with intravenous antibiotics. None of our patients had an incisional hernia. Median hospital stay was 10 days (range 6 to 40 days). Radial resection margins were clear in all 13 cases, although there was deep margin involvement in 3. Most patients were started on adjuvant therapy within 3 weeks of surgery.

Conclusions: Our review shows that the VRAM flap is a good option for coverage of a large post-mastectomy defect. There are few flap-related and minimal donor-site complications and a shorter hospital stay compared to skin-grafting. The recovery route to adjuvant therapy is short with a robust flap much more able to withstand the rigours of radiotherapy.

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Synchronous and metachronous bilateral breast cancer: one or two entities?

D. Kolarevic[1], Z. Tomasevic[1], S. Jelic[2]. *[1]Institute for Oncology and Radiology of Serbia, Daily Hospital for Chemotherapy, Belgrade, Serbia; [2]Institute for Oncology and Radiology of Serbia, Clinic for Medical Oncology, Belgrade, Serbia*

Background: The aim of this study is to compare histopathological and clinical characteristics of synchronous and metachronous bilateral breast cancer (BBC).

Materials and Methods: We analyzed the data for 64 BBC pts registered during three years in Daily Hospital for Chemotherapy, Institute