Conclusion: Immediate reconstruction in our experience has resulted in a delay to first adjuvant RT but not chemotherapy. It is unclear whether such a delay is sufficient to reduce the efficacy of RT. However, delays in starting RT that can be anticipated should be avoided. Breast units should ensure that all patients are referred for post-mastectomy RT as early as possible following surgery.

637 POSTER

Late skin reactions after different chemotherapy schemes in irradiated breast cancer patients

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Purpose: Assessment of late changes of irradiated skin after CMF and EC-chemotherapy compared to patients with hormone therapy or no additional therapy.

Patients and methods: In 63 patients, irradiated at University of Ulm for breast cancer, thickness and structure of irradiated and non- irradiated skin was measured by 20 MHZ-ultrasound.

Results: 18/63 patients received either 6xCMF (3 cycles before and 3 cycles after radiotherapy) or 4xEC (before radiotherapy) in addition to breast irradiation. None of these patients received hormone therapy. 29/63 Patients were on tamoxifen during and after radiotherapy. Ultrastructural changes of corium thickness and structure were measured quantitatively by high-frequency 20 MHz-ultrasound. Corium thickness of non-irradiated skin (contralateral breast) showed significant difference in patients treated with chemo- and hormone therapy comparing with those treated without chemotherapy (p=0.03) or hormone therapy (p=0.019). EC showed significant more increase in corium thickness compared to CMF (p=0.0008). No changes in echogenity were observed.

In irradiated skin, reactions (according to corium thickness and echogenity of lower corium) were significant increased in the chemotherapy (p=0.001) and hormone therapy (p=0.003) group. EC showed significant more skin changes compared to CMF (0.0008) and to the hormone therapy group.

Conclusion: Chemotherapy and tamoxifen induce changes of normal (non-irradiated) skin, which increase significant after radiotherapy. Corium thickness and skin structure are more altered by EC-chemotherapy compared to CMF or tamoxifen.

638 POSTER

A pilot study with navelbine (NVB) + fractionated doxorubicin (DX) as neo-adjuvant chemotherapy for locally advanced breast cancer

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A phase II study of i.v. fractioned VNB and DX combination in previously untreated advanced breast carcinoma observed promising results with NVB 25mg/m2 on days 1 and 8, and DX 50 mg/m2 on day 1 (q 21 days); with 74% OR and 21% CR, mainly in visceral sites (JCO, 1994).

Our group observed the same responses with fractionated doses of DX (A. Anelli; et al) for advanced disease. In order to observe potential value of this association for neo-adjuvant chemotherapy (NA chemo) set, a pilot study was done in 25 patients, receiving 4 cycles of NA chemo (NVB 25mg/m2 i.v. + DX 25mg/m2 i.v. -D1 + D8 each drug; in cycles of 21 days), 24 patients were available for response and 25 for toxicity.

Stages IIA=2(8%), IIB=6(25%); IIIA=16(67%); <50 years old=13; >50 years old =12; hystology - ductal infiltrative =17; others not medullary =7.

Clinical responses: CR (1/24-4%); PR (23/24-96%); SD/PD (0/24); OR 100%. Two cycles were the minimal number to observe objective clinical response in 19 patients. Surgery was performed in 23 patients after 4 cycles of NA chemo. Conservative breast surgery was performed in 7/23-30,5%. A pathologic complete response (pCR) was observed in 5/23-22% for primary tumor, with 18/23-78% of pathological partial response (pPR). For nodes pN0, 9/23-39% and pN+, 14/23-61%. At this moment 18 patients went to complimentary radiotherapy, with 01 patient with recurrent disease on radiotherapy.

Grade 3 toxicity was observed in 20 patients with alopecia, 13 patients with neutropenia, 3 patients with nausea and vomiting, 2 patients with phlebitis, 2 patients with mucositis, 1 patient with cutaneous, 1 patient with diarrhoea, no patients with neurotoxicity and no grade 4 toxicity was observed.

Conclusion: neo-adjuvant fractionated is an important neo-adjuvant scheme for breast cancer with low toxicity profile and similar results than schedules with taxanes and/or anthracyclines.

639 POSTER

Significant higher health-related quality of life (HR-QOL) level in women treated with adjuvant hormonal therapy versus chemotherapy: prospective measurement during/after postoperative radiotherapy for breast cancer

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Purpose: To report the results of a prospective HR-QoL asseassment in women with brest cancer during/after postoperative radiotherapy.

Materials and Methods: Hundred-nine consecutivelly treated patients were analysed. For quality of life measurement the EORTC modules QLQ-C30 and BR23 were used. The HR-QoL was asseassed at beginn (T1), at end (T2) and 6 weeks after radiotherapy (T3). We segregated the patients in three prognostic groups: group I, n = 41 (radiotherapy and adjuvant chemotherapy), group II, n = 45 (radiotherapy and adjuvant hormonal therapy) and group III, n = 23 (radiotherapy alone). The reliability was tested. ANOVA analyses were performed.

Ergebnisse: The reliability testing revealed good median Cronbachs Alpha values of 0.77, 0.83, and 0.83 for the measurement points T1, T2 and T3, respectivelly. Twenty-one quality of life dimensions from global health status to arm symptoms were asseassed. The ANOVA statistics revealed significant better HR-QoL for patients in prognostic group II versus I. Patients treated with radiotherapy alone (group III) showed the best results in the quality of life analyses compared with groups I and II.

Conclusions: Measurement of HR-QoL using the EORTC core protocol QLQ-C30 and the breast module BR23 during/after radiotherapy is reliable (median Cronbachs Alpha values >0.7). Adjuvant chemotherapy lowered statistically significant the HR-QoL compared with adjuvant hormonal therapy or radiotherapy alone. The results suggest that the use of adjuvant hormonal therapy is more favorable in terms of quality of life versus chemotherapy.

Breast cancer genetics and biology

640 POSTER

High frequency of mitochondrial DNA mutations in breast cancer: potential application for cancer detection

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The human mitochondrial DNA (mtDNA) has a mutation rate at least 10 times higher than the nuclear DNA. Somatic mutations in the mtDNA have been recently observed in several tumor types and have been used to detect cancer cells in bodily fluids.To determine the frequency and distribution of mitochondrial DNA mutations in breast cancer, 18 primary breast tumors were analyzed by direct sequencing. Twelve somatic mutations were detected in 11 of the tumors screened (61%). Of these mutations, 5 (42%) were deletions or insertions in a homopolymeric C-stretch between nucleotide 303-315 (D310) within the D-loop. The remaining 7 mutations (58%) were single base substitutions in the coding (ND1, ND4, ND5, and Cyt b genes) or non coding regions (D-loop) of the mitochondrial genome. In three cases (25%), the mutations detected in coding regions led to amino acid substitutions in the protein sequence. We then screened an additional 46 primary breast tumors with a rapid PCR-based assay to identify poly C alterations in D310 and found 7 more cancers with alterations. Using D310 mutations as clonal marker, we detected identical changes in 5 of 5 matched fine needle aspirates and in 4 of 4 metastases positive lymph nodes. The high frequency of D310 alterations in primary breast cancer combined with the high sensitivity of the PCR-based assays provide a new powerful molecular tool for cancer detection.