for Oncology and Radiology of Serbia. We defined synchronous bilateral breast cancer (SBBC) as cancer diagnosed in both breasts at the same time or within a 3 months period of diagnosis of the first tumor. In metachronous BBC (MBBC) second cancer is diagnosed more than 3 months after the first one. We had both breast specimens available for 20 SBBC and 23 MBBC pts, for 21 pts there was only one breast specimen.

Results: Out of a total of 64 pts, 48% (31 pts) suffered from synchronous and 52% (33 pts) from MBBC. Median age at diagnosis was 59.3 in SBBC group. In MBBC group median age at first diagnosis was 51.4 and 58.7 for contralateral BC diagnosis, with the median period from first to second BC of 79 months. 84% of SBBC pts were postmenopausal, compared to 55% in the MBBC group. In a group of SBBC, 52% of tumors were found to be lobular and 32% were ductal carcinoma. In a group of MBBC frequency of ductal and lobular carcinoma was similar, 42% of ductal and 40% of lobular. One MBBC patient had both-side tubular carcinoma. Same HP results in both breasts were found in 85% of SBBC and only 48% of MBBC. 70% of SBBC were hormone receptor positive, comparing to only 43% in MBBC group. 16% of SBBC were manifested as inflammatory breast cancer (IBC). In MBBC group, 15% of first and 39% of second malignancy were diagnosed as cancer mastitis. Initial metastases (stage IV) were more frequent in SBBC group, 32%, compared to 12% in MBBC. In SBBC group 8 pts out of 21 (38%) without initial metastasis had a disease progression during follow-up, with a median DFI of 28 months. In MBBC progression was detected in 28% (8/29) pts with a median DFI 34 months after the second BC.

Conclusions: Our study showed that SBBC is more frequent in postmenopausal women, presented more often as hormone receptor positive lobular carcinoma with same HP findings in both breasts. MBBC are usually presented as IBC without distant metastasis. BBC is definitely an unusual clinical entity and because of its atypical and complex presentation patients with bilateral breast cancer require compound and individualized treatment.

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Re-irradiation for recurrent breast cancer − a second curative approach

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Background: Repeat radiation is a rarely used and with caution performed treatment strategy. We investigated the efficacy of a second adjuvant radiotherapy series in case of recurrent and surgically removed breast cancer.

Patients and Methods: Forty-four patients were treated from 1993 to 2003 with modified radical mastectomy or local excision and postoperative re-irradiation for recurrent breast cancer. The median age was 58 years (range 33−76 years). The median exposure due to pre-radiation was 50.4 Gy. Postoperative re-irradiation was conventionally fractionated with single doses of 1.8−2.0 Gy to a median total dose of 60 Gy including regional lymphatics in 17 patients (39%) to a total dose of 50 Gy. In case of close or positive margins, local radiofrequency hyperthermia was offered as additional modality leading to a concurrent application in thirty patients (68%). Further adjuvant treatment consisted of chemotherapy (n = 20, 46%) and/or hormonal therapy (n = 14, 32%).

Results: After a median follow-up of 44 months (range 3−92 months) higher graded late toxicity (⩾G3) according to CTC 2.0 and LENT-SOMA was not observed. The estimated 5-year local control rate reached 62%. Additional hyperthermia for patients at higher risk for local failure resulted in 67% local control. Furthermore, a total dose of ⩾60 Gy given with photons was associated with complete local control (n = 14). The estimated 5-year overall survival and disease-free survival rates were 52% and 48%, respectively. The overall survival improved to 65% when supraclavicular +/− parasternal nodes were also covered by radiation portals.

Conclusions: Up to now, the available data are limited or heterogeneous. Thus, we present a single institution series including only patients with at most microscopic positive margins (R0−1) and sufficient follow-up. Our study reveals that postoperative re-irradiation with a median total dose of 60 Gy can be performed with acceptable toxicity. The local control rate is encouraging and translates into improved long-term survival for almost every other patient. It might be speculated whether additional hyperthermia compensates for positive margin. However, long-term local control depends on manifold and overlapping parameters which can not be isolated evaluated due to sample size. Therefore, the relevance of hyperthermia as well as the impact of irradiation of regional lymph nodes on long-term control need further investigation.

Friday, 26 March 2010 18:15–19:15

POSTER SESSION

Metastatic disease

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Platinum-based chemotherapy in triple-negative metastatic breast cancer: results of the Institut Curie experience with cisplatinum and ifosfamide

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Background: Although recent experimental data strongly suggest that platinum-based chemotherapy (PBCT) could improve triple-negative breast cancer (TNBC) outcome, clinical data are missing in this specific subgroup of patients. In the present study, we reviewed clinical outcome in patients with metastatic TNBC treated with PBCT.

Patients and Methods: We conducted a retrospective analysis of the patients treated between 2000 and 2008 at Institut Curie, Paris, France. 146 female patients, with metastatic breast cancer who received PBCT, were eligible for this study. 93 (63.7%) of them had TNBC. 115 patients (78.8%) received PBCT after more than one line of CT (median 2, from 0 to 6). Mean age was 49 year (range from 29 to 76), median number of delivered CT-cycles was 4.2 (1−9). 123 of 146 patients received cisplatinum (CDDP), the other received carboplatin. The main combination used was CDDP-Ifosfamide N = 118 (80.8%). We analysed overall response rate (OR), OS, PFS, prognosis factors for OS, and safety, for TNBC versus non-TNBC.

Results: Median follow-up was 44 months. For the whole population, median OS and median PFS were 11 months and 5 months respectively. OR was 33.3% in the TNBC group, versus 20.8% for the others, $p = 0.1$. Median response duration was 8 versus 7 months (NS). Median OS and median PFS were statistically improved in the patients responding to CT: 25 months (PR) versus 7 months (PD), $p < 0.001$, and 12 months (PR) versus 3.5 months (PD), $p < 0.001$ respectively. No difference was observed for OS, PFS and response duration between TNBC and others. Other prognostic factor for worse OS was visceral metastasis sites ($p < 0.001$). One patient died from sepsis during aplasia, one other developed CDDP-related grade 3 renal failure. 15 patients had to switch to carboplatin because of unacceptable CDDP-related side effects.

Conclusions: In this series, PBCT tend to increase response rate in metastatic patients with TNBC compared to non-TNBC patients, but did not translate into a significant improvement for PFS and OS. Tolerance was acceptable. Longer observations and further analysis are warranted. Prognosis of metastatic TNBC remains poor and new targeted therapies are needed.

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Individually dose-adjusted treatment with epirubicin and paclitaxel with or without capecitabine as 1st line treatment in metastatic breast cancer. A randomized multicenter trial

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Background: Epirubicin, paclitaxel and capecitabine are effective drugs in the treatment of breast cancer. In the present trial, patients previously untreated with chemotherapy for metastatic disease were randomized to a combination of epirubicin and paclitaxel (ET, epirubicin 75 mg/m^2; paclitaxel 175 mg/m^2, q3w) alone, or with the addition of capecitabine (TEX, epirubicin 75 mg/m^2; paclitaxel 155 mg/m^2; capecitabine 1650 mg/m^{2}x14, q3w). Primary endpoint was time to progression (TTP) with a prolongation from 6 to 8.5 months being a significant clinical improvement.

Material and Methods: 287 patients were randomized to either ET (n = 143) or TEX (n = 144). Doses for each of the drugs were adjusted (escalated/de-escalated) according to predefined levels individually in relation to toxicity. If treatment was discontinued due to side effects

or reasons other than progression, endocrine maintenance therapy was allowed until progression. Patients in the ET group were, upon progression, offered 2nd line treatment with capecitabine monotherapy, 2500 mg/m^2 × 14, q3w.

Results: Median TTP was 12.6 (TEX) *vs.* 10.0 (ET) months (HR 0.84; χ^2 2.70, p = 0.10), time on treatment was 6.1 (TEX) *vs.* 5.2 (ET) months (HR 0.73; χ^2 6.87, p = 0.009). Median overall survival was 29.8 (TEX) *vs.* 27.1 (ET) months (HR 0.87; χ^2 0.92, p = 0.34). Response rates for TEX were CR 4.2%, PR 50%, SD 31.3%, PD 8.3%, for ET CR 3.5%, PR 41.3%, SD 35%, PD 14%. Dose intensity (mg/m^2/week) in relation to the starting dosage for TEX were: epirubicin 93.6%; paclitaxel 90.7%; capecitabine 72%, and for ET: epirubicin 95.6%; paclitaxel 94.3%. Seventy of the patients randomized to ET (49%) received capecitabine as 2nd line therapy upon progression. Incidence of grade 3/4 neutropenic fever was similar in both treatment arms, TEX 17.4%, ET 18.9%. Other frequent grade 3/4 side effects due to the TEX regimen were infection (9.7%) and diarrhea (9.7%), and due to the ET regimen neuropathy (10.5%) and infection (9.1%). Symptomatic CHF was reported in 13 cases (4.5%), all of these with accumulated doses of epirubicin exceeding 800 mg/m^2.

Conclusion: TTP was prolonged by 2.6 months in favour of the TEX regimen, although the improvement was not significant. The results of this study reflect the effect of capecitabine on metastatic breast cancer in a comparison of two equitoxic regimens. Since TTP for both treatment arms was longer than anticipated, it is likely that potential differences in outcome may be more obvious in an extended trial.

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Incidence of selected adverse events (AEs) in phase III studies of bevacizumab (BV) in combination with chemotherapy for the treatment of HER2-negative metastatic breast cancer (mBC)

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Background: Three multicentre, randomised phase III trials have demonstrated significant improvements in progression-free survival (PFS) with BV in combination with chemotherapy for the first-line treatment of mBC. E2100 (n = 722) was an open-label trial evaluating weekly paclitaxel (P) +/− BV 15 mg/kg, AVADO (n = 736) was a placebo (PL)-controlled, double-blind trial evaluating docetaxel (D) +/− BV 7.5 mg/kg or BV 15 mg/kg, q3w and RIBBON-1 (n = 1,237) was a PL-controlled, double-blind trial assessing capecitabine (C), taxane (T) or anthracycline (A) +/− BV 15 mg/kg. BV either as a single agent or in combination with chemotherapy has a characteristic safety profile across a number of different tumour types. Selected AEs from two of these phase III mBC trials are summarised to show how different types of chemotherapy affect AE rates in the first-line setting.

Materials and Methods: The NCI-CTCAE v3 was used to record BV-related AEs (grade 3−5 non-haematological events and grade 4/5 haematological events) in AVADO and RIBBON-1. BV-related AEs included arterial thromboembolism (ATE), gastrointestinal perforation, hypertension (HTN), left ventricular systolic dysfunction, venous thromboembolism, proteinuria, bleeding, and wound-healing complications.

Results: Analysing the incidence of known BV-related AEs in the PL arms and BV-containing arms of AVADO and RIBBON-1 we found that HTN ranged from 0−2% for patients (pts) in the PL arms and from 0.8−10% for pts in the BV-containing arms (AVADO: BV 7.5 mg/kg, 0.8%; BV 15 mg/kg, 4.5%; RIBBON-1: C cohort, 9.4%; T cohort, 8.9%; A cohort, 10.0%). For all other BV-related AEs, differences between the PL arms and the BV-containing arms were of smaller magnitude. Treatment discontinuation rates in the BV-containing arms varied across trials, ranging from 11.9–28.3% compared with 4.0–27.0% for the PL arms. In RIBBON-1, treatment discontinuation rates for pts receiving BV were higher relative to the PL arm for the T cohort (7.8% vs. 24.1%) and the A cohort (4.0% vs. 14.3%). There was no difference in treatment discontinuations for pts in the C cohort (11.9% for both arms).

Conclusions: BV in combination with chemotherapy is associated with an increased frequency of selected AEs. Treatment discontinuation rates for AEs vary across trials and may be a function of the chemotherapy agent, dose, and schedule. With the exception of HTN, BV-related grade 3−5 AEs occurred in <5% of pts.

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Final results of a phase II study of combination with nab-paclitaxel, bevacizumab, and gemcitabine as first-line therapy in patients with HER2-negative metastatic breast cancer

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Rationale: Overall response rates (ORR) for patients with HER2-negative (HER2$^-$) metastatic breast cancer (MBC) treated with single-agent solvent based paclitaxel (P) are ~20%. ORR is improved for P + gemcitabine vs. P alone (41 vs. 22%) or P + bevacizumab vs. P alone (37% vs. 21%). Nanoparticle albumin-bound (*nab*)-P resulted in better ORR (42% vs. 27%) than P alone in a phase 3 clinical trial. Therefore, we examined *nab*-P combined with bevacizumab and gemcitabine for first-line treatment of patients with HER2$^-$ MBC.

Patients and Methods: The primary endpoint was PFS; secondary endpoints were ORR, complete (CR) and partial (PR) response rates, clinical benefit (ORR + stable disease), overall survival (OS), and safety. Patients (⩾18 years; HER2$^-$ MBC) received gemcitabine 1500 mg/m^2, nab-paclitaxel 150 mg/m^2, and bevacizumab 10 mg/kg (each administered intravenously over 30 minutes) on days 1 and 15 of a 28-day cycle. Thirty patients were enrolled. One patient was deemed ineligible and was not included in the analysis. Twenty-nine patients (96.6% female, 34 to 69 years, median 54) were treated. Seventeen (58.6%) patients were Hispanic, 8 (27.6%) were African American, 3 (10.3%) were Caucasian, and 1 (3.4%) was Asian. All patients received ⩾1 cycle (median = 6.5, range 2.5 to 23). Estrogen receptor (ER) was present in 55.2% of all cases and progesterone receptor (PR) in 24.1% of patients; 13 (44.8%) patients had triple negative breast cancer (HER2, ER, and PR negative).

Results: Median PFS was 10.4 months (95% CI: 5.6 to 15.2 mo). The ORR was 75.9%, comprising 8 (27.6%) CRs and 14 (48.3%) PRs; 5 patients had minor responses or stable disease, and 2 patients (6.9%) had progressive disease as their best response. The clinical benefit rate was 92.1% (27/29). Of those 13 patients with triple negative disease, 5 (38.4%) had CR; 4 (30.7%) patients had PR; 2 patients had minor response, and 2 patients had progressive disease as their best response. The clinical benefit rate for triple negative patients was 11 (84.6%) of 13. At 24 months, OS was 61.7% (95% CI: 25.4–84.4). Eight (27.6%) patients had grade 3 or 4 toxicity, comprising 1 episode of grade 4 neutropenic fever and the following grade 3 toxicities: 6 episodes of infection; 1 each of leukopenia, thrombocytopenia, peripheral neuropathy, seizure, shortness of breath, hematuria, and tamponade.

Conclusion: First-line combination therapy with *nab*-P, bevacizumab, and gemcitabine demonstrated a 75.9% ORR and median PFS of 10.4 months in this phase II study of HER2$^-$ MBC.

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Capecitabine in older patients ⩾70 yrs with locally advanced or metastatic breast cancer

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Background: Capecitabine (cap) is effective as single agent therapy in metastatic breast cancer (MBC). Its low toxicity and ease of administration make it a potentially good option for elderly patients (pts) but dose reductions are often required. We have therefore retrospectively analysed efficacy and tolerability of cap in elderly pts with locally advanced (LA) or MBC, treated in our Unit.

Materials and Methods: All pts on our prospectively maintained database aged ⩾70 yrs with LA or MBC who were given cap as 1st, 2nd or 3rd line chemotherapy were assessed for response and toxicity according to RECIST criteria and NCI common toxicity criteria, respectively.

Results: Between 12/2001 and 05/2008, 89 pts ⩾70 yrs were given oral cap, 55 (62%) as 1st line and 34 (38%) as 2nd or 3rd line treatment. Thirty-two (36%) pts had soft tissue and/or bone metastases only and 57 (64%) had visceral disease. Planned starting dose of cap was 1000 mg/m^2 twice daily, days 1−14 every 3 weeks. Thirty-six (41%) pts started on 25% dose reduction because of frailty and 12 (13%) pts reduced dose after the 1st or the 2nd cycle. Median number of administered cycles was 6 (range 2−27) and median duration of treatment was 4 (95% CI: 1−19) months. One (1%) complete response (CR) and 39 (44%) partial responses (PR) were seen, for a 45% overall response rate (ORR) (95% CI: 35−55%). A further 19 (21%) pts achieved stable disease (SD) for ⩾6 months. Therefore, disease control (CR+PR+SD) was achieved in 66% of pts. Median time to progression (TTP) and overall survival (OS) were 30