Inter-person correlation coefficient (Spearmans correlation)

	oncologist 1 - radiologist	oncologist 2 - radiologist
Axial plane	r=0.23, n=19, p=0.337	r=0.15, n=12, p=0.636
Coronal plane	n=8	n=5
Sagittal plane	r=0.47, n=16, p=0.065	r=0.44, n=13, p=0.131

Conclusions: MRI of the postoperative breast with the patient in the conventional treatment position demonstrated a quantifiable tumour cavity in all three planes with generally good agreement for measurements made. Scar was more difficult to visualise; it was best seen in the sagittal plane, almost certainly because skin incisions were perpendicular with this plane. Application of oil-filled markers to the scar would facilitate its measurement. MRI can be used to visualise the target volume when planning three-dimensional adjuvant breast radiotherapy.

References

[1] UKCCCR Breast Cancer Subcommittee START protocol: a randomised comparison of fractionation regimens after local excision or mastectomy in women with early stage breast cancer; 1998.

433 POSTER

Breast morbidity after breast conserving treatment and sentinel node biopsy

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Background: Sentinel node biopsy (SNB) is associated with less arm morbidity compared to axillary clearance. Little is known if also the risk of breast morbidity is diminished after breast conserving therapy with more limited axillary surgery. Therefore we aimed to evaluate breast morbidity after breast conserving therapy and SNB or axillary clearance (AC).

Patients and methods: Altogether 161 consecutive breast cancer patient who underwent breast conserving surgery and SNB only (57), AC node negative (57) and AC node positive (46) were enrolled to the study. The clinical status and the breast ultrasonography were examined a year after the surgical treatment.

Results: In the clinical examination breast oedema was most common (48%) in patient in AC node positive group compared to 36% in AC node negative group and to 25% in SNB group ($p < 0.05$ between SNB and AC node positive). Accordingly, the operated breast was smaller than the contralateral breast most often, in 46% of patients in the SNB group compared to 20% in the AC node positive group ($p < 0.01$). In the breast ultrasonography subcutaneous oedema in the operated breast was more common (68-70%) in the AC groups compared to 25% in the SNB group ($p=0.0001$ between SNB vs AC node negative, $p=0.001$ between SNB vs AC node positive). Also the skin in the operated breast was the thickest, a median of 3,05 mm in the AC node positive group and thinnest in the SNB group, a median 1,8 mm, measured by ultrasonography. There were no statistical significant differences in the pigmentation of the skin and in the tenderness of the breast between the groups.

Conclusions: Breast lymphoedema was more common one year after the breast conserving surgery in patients who underwent axillary clearance than in those who underwent SNB only.

434 POSTER

Change of cosmetic results in time, evaluation of parameters influencing cosmetic results after breast conserving therapy (BCT) in patiens with breast cancer.

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Purpose: Cosmetic results of breast conserving therapy in patients with breast cancer are influenced by effects of surgical treatment, radiotherapy (RT) and chemotherapy. Surgery may cause breast asymmetry, disturbing scar or nipple displacement. RT, due to fibrosis, may cause intensification of breast and nipple asymmetry, changes in breast skin pigmentation as well as intensify edema of treated breast and ipsilateral upper limb.

The aim of the paper is to define to which extent radiotherapy may influence the change of cosmetic result after BCT and how the result changes in time.

Material and method: Clinical material included 43 patients with breast cancer stage I and II. Mean observation time was 4,7 years(3-7 years).37% of patients were treated with tumorectomy, 63% with quadrantectomy. Later, all patients received external radiotherapy. Measurements of breast asymmetry, and photographs were made before radiotherapy and during follow up every 6 months. The evaluated effects were nipple displacement in medio-lateral sense, upward nipple retraction, upward retraction of the interior breast contour, difference in oblique distances between the ingular fossa and nipple. Cosmetic result was evaluated annually using Four Point Scoring System defining the result as excellent, good, fair or poor. The amount and extent of teleangiectasia were analysed and also intensification of late radiation skin damage according to EORTC. Circumference of upper limbs was measured too.

Results: Qualitative and quantitative evaluation of cosmesis before radiotherapy and 3 years after was compared. Before RT, in 88% of patients cosmetic result was excellent and good. In 12% of patients it was fair and poor.3 years after radiotherapy the results were assessed respectively in 70% and 30%. Moderate edema of arm was observed in 18% of patients. Breast edema remained until 2 years after treatment causing pain assessed according to Visual Analogue Scale of Pain. 3 years after radiotherapy, in 32% of patients late radiation damage to the skin stage I was observed {according to EORTC} and in 7% the damage was in stage II. Teleangiectasia in areas bigger than 4 square cm was observed in 18% of patients.

Conclusions: Essential intensification of breast asymmetry caused by RT after 3 years of observation was not observed irrespective of received cosmetic result of surgery. Fibrotic retraction of breast, nipple and breast contour displacement in lateral sense slightly lower the cosmetic effect. Late radiation skin damage, changes in pigmentation of breast skin, teleangiestasia, breast and arm edema slightly influence the decrease of cosmetic result. The main factor responsible for low cosmetic effect was the kind of surgery and the amount of removed breast tissue.

435 POSTER

Prognostic factors of breast-conserving treatment for early –stage breast cancer

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Background: The incidence of breast cancer in Spain range between 40 and 55/100.000 habitants and it is the 20% of total dying, by cancer, in female population. It is one of the most frequent causes of dying for women in the developed countries.

Material and Methods: We analysed 603 patients diagnosed of breast cancer and treated with breast conserving therapy consisting of wide excision of the primary tumor, and axillary dissection in all cases except on 14 (caused for medical reasons). All the patients were treated with radiotherapy in University Hospital "12 de Octubre" in Madrid.

Results: The median follow-up period was 63 months (range 5-242) A total of 109 patients (18.08%) were diagnosed were included in a screening program. Histopathologic examination revealed a diagnosis of infiltrating ductal carcinoma in 510 patients (84,6%). A total of 82.9% (490 patients) presented negative margins. The incidence of local recurrence was 6,8% (41 patients) at the moment that we closed the study. Five-year disease-free survival for stage I stage II were 88%, and 80% respectively. Five year overall survival rates for stage I was 95%. The overall survival at 5, 10 and 15 years for stage II were 90%, 82% and 69% respectively. We analysed also the disease free survival and the overall survival in function of age, and regional nodal involvement. Radiation therapy was administered to the breast through two opposing tangential fields giving a dose of 45 Gy in 36,6% of patients and 50 Gy in 62,5% of patients respectively. In the analysis of multiple logistic multitomic regression, the patients with histologically positive margins, younger than 50 years or with undifferentiated histological grade developed statistically significantly more local recurrences. The administration of adjuvant endocrine therapy was essential in the reduction of the possibility of local recurrences. The presence of positive margins, the nodal involvement, the size of the tumor, and the undifferentiated histological grade were factors statistically significant in the risk of develop distant metastases. In the analysis of multiple logistic dicotomic regression demonstrated that the presence of affected margins, the presence of carcinoma in situ, the age younger than 50 years, to avoid the administration of adjuvant endocrine therapy, and if the patients had been diagnosed outside a screening program, they had more risk of develop a local recurrence.

Conclusion: Breast conserving therapy is an effective treatment for a selection group of patients diagnosed of breast cancer in stage I or II. The presence of positive margins, carcinoma in situ, and age younger that 50 years are adverse prognostic factor with an increased of risk of local

recurrence. For distant metastases, the presence of positive margins, the nodal involvement, the size of the tumor, the undifferentiated histological grade were factors statistically significant.

Metastatic breast cancer

436 POSTER

Renal safety of intravenous ibandronate with short infusion times

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Background: Reducing treatment toxicity is an important consideration in MBD management, not least because of the unpleasant adverse effects associated with primary cancer therapy. Existing intravenous (i.v.) bisphosphonates for metastatic bone disease (MBD) are associated with renal toxicity, such that continual monitoring of creatinine clearance levels, hydration of the patient and lengthy infusion times (up to 2 hours) may be required. There is a clinical need for an i.v. bisphosphonate that can be infused over relatively short time periods without renal adverse effects. The pharmacokinetic and renal safety profile of i.v. ibandronate, a third-generation bisphosphonate, has been investigated over infusion periods of 1560 minutes.

Patients and methods: The pharmacokinetic and renal safety parameters of i.v. ibandronate were assessed in a parallel-group study of healthy male (n=27) and female (n=30) volunteers. Subjects received a single infusion of i.v. ibandronate 6mg administered over 60 (n=19), 30 (n=20) or 15 (n=18) minutes. Pharmacokinetic parameters included maximum plasma concentrations (C max), volume of distribution(Vz), half life (t1/2), renal clearance (CLr) and fraction of dose excreted (f e). Renal function was assessed by measures of urinary creatinine clearance, serum creatinine levels, and urinary excretion of microalbumin, a1 -microglobulin or N-acetyl-b-D-glucosaminidase (b-NAG) prior to, and up to 72 hours following, infusion. In a sub-analysis of a placebo-controlled, double blind, phase III clinical trial, patients with MBD from breast cancer were randomized to receive i.v. ibandronate 6mg (n=28) or placebo (n=23) infused over a 1hour period every 34 weeks, for a 3-month period. Proteinuria, albuminuria, a1 -microglobulin or b-NAG were assessed prior to drug infusion and 1, 2, 5, 10 and 28 days following each administration, as markers of renal function.

Results: In healthy volunteers, reducing the infusion time of a single dose of i.v. ibandronate 6mg from 60 to 15 minutes was associated with an increase in C max(mean ± SD: 308 ± 44.8 ng/mL vs 397 ± 94.5 ng/mL), but had little impact on Vz (118 ± 17.7L vs 141 ± 32.1L), t (10.6 ± 1.1 hours vs 10.3 ± 2 hours), CLr (70.6 ± 14.4 mL/min vs 88.2 ±24.0 mL/min) or f (percentage dose excreted: 51.6 ± 7.30% vs 52.3 ± 10.3%). S hortening the infusion time of i.v. ibandronate 6mg from 60 to 15 minutes had no adverse effects on any of the renal function parameters assessed (creatinine clearance, serum creatinine levels, urinary microalbumin, a1 -microglobulin or b-NAG).

In patients with MBD from breast cancer, infusion of ibandronate 6mg i.v. over a 1-hour period produced no significant changes in proteinuria, albumin, a1 -microglobulin or b1-NAG levels. Transient rises in proteinuria in both the ibandronate and placebo groups were considered to be related to previously existing renal dysfunction and individual biological variability.

Conclusions: In healthy volunteers, the pharmacokinetics of i.v. ibandronate 6mg are comparable when infused over 60 or 15 minutes. Shortening the infusion time to 15 minutes had no effect on renal function parameters. In patients with MBD, 1-hour infusion of i.v. ibandronate every 3-4 weeks was well-tolerated, with no significant renal toxicity. This contrasts with renal adverse event profile of other i.v. bisphosphonates (zoledronate and pamidronate). As the pharmacokinetics of ibandronate are clinically equivalent between healthy volunteers and MBD patients, i.v. ibandronate 6mg infused over 15 minutes may also have a favourable renal safety profile in this indication. Further investigation of renal functioning following 15-minute infusion of i.v. ibandronate 6mg in patients with MBD is warranted in future clinical trials.

437 POSTER

A multicenter Phase II trial to evaluate gefitinib ('Iressa', ZD1839) (500 mg/day) in patients with metastatic breast cancer after previous chemotherapy treatment

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Background Epidermal growth factor receptor (EGFR) is a key modulator of tumor cell function and is considered to be a viable drug target in a variety of solid tumors. The clinical benefit and safety of gefitinib ('Iressa', ZD1839), an orally active EGFR tyrosine kinase inhibitor (EGFR-TKI), was evaluated in this non-randomized, open-label, Phase II, multicenter study of patients (pts) with heavily pre-treated, metastatic breast cancer.

Methods Eligible pts had received anthracyclines and taxanes and 1 or more chemotherapy regimen for advanced breast cancer. Pts took gefitinib (500 mg/day), the majority as 3rd- or 4th-line treatment, until disease progression. A dose delay of up to 14 days or a dose reduction to 250 mg was permitted if toxicity was observed. The primary endpoint was the clinical benefit rate (CR + PR [RECIST criteria] + SD) at 6 months.

Results Data for 46 pts, median age 54 years (range 31-70), are available as the basis for this abstract. The metastatic sites of disease were liver (51 lesions), lymph nodes (24), lung (19), skin/soft tissue (11), bone (19), and others (19). After 12 weeks, 1 pt (2.2%) had a PR, 3 pts (6.5%) had SD (2 patients >3 months) and 42 pts (91.3%) had PD. The PR was seen in a pt with 4 liver lesions at study start. After 3 months, 1 of the 4 lesions was no longer detected and pleural metastases had diminished significantly. Currently, at 168 days of therapy the pt is still receiving gefitinib. Two pts reported a significant improvement in pain at metastatic sites (1 liver, 1 bone). Adverse events (AEs) were: facial rash, 7 pts (15%); nausea, vomiting, and bowel disturbance, 26 pts (57%). CTC grade 3 AEs considered gefitinib-related were seen in 3 pts (exanthema, diarrhea, and non-infectious wound). No grade 4 drug-related AEs were reported. One pt (2.2%) withdrew due to gefitinib-related AEs (grade 2 pruritus, peripheral edema and weakness). Dose interruptions occurred in 16 pts (35%) and 6 pts (13%) had a dose reduction due to persistent grade 1/2 skin or gastrointestinal AEs. Further details of efficacy, safety, and quality of life analyses will be presented. In addition, tumor samples are being collected and will be analyzed to try to identify which patients benefit from this innovative treatment.

Conclusion These preliminary data provide evidence that gefitinib may be effective as monotherapy in recurrent breast cancer. 'Iressa' is a trademark of the AstraZeneca group of companies

438 POSTER

Increased pretreatment serum lactate dehydrogenase (LDH) is the most important determinant of central nervous system (CNS) metastases in patients with metastatic breast cancer.

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Purpose: To identify predictive factors and estimate the risk of development of CNS metastases in patients with metastatic breast cancer.

Patients and methods: Data from 579 stage III-IV breast cancer pts treated between Nov. 1983- May 1995 with an epirubicin based chemotherapy were retrieved. Statistical analysis included Kaplan-Meyers survival plots, Cox proportional hazard analysis and competing risk analysis using the cumulative incidence (CI). The endpoints of interest: occurrence of CNS metastases. Meanwhile, two other event could preclude (were competitive)