time of the primary diagnosis of breast cancer might be caused by a more frequent use of mammography. In line with recent data, this small reduction in tumor size does not necessarily translate into improved prognosis.

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Lack of pharmacokinetic interaction between erlotinib, docetaxel and capecitabine in breast cancer patients.

A. Rakhit[1], S. Fettner[1], S. Davis[2], R. Abbas[1], F. De Rosa[2], U. Brennschneidt[2], C. Twelves[3], J. Baselga[4]. [1] *Hoffman-La Roche Inc., Department of Clinical Pharmacology, Nutley, USA;* [2] *F. Hoffmann-La Roche, Basel, Switzerland;* [3] *Beatson Oncology center, Glasgow, Scotland;* [4] *Universitari Vall d'Hebron, Barcelona, Spain*

Erlotinib (Tarceva™) is an epidermal growth factor receptor (HER1/EGFR) tyrosine kinase inhibitor being developed for the treatment of various solid tumors. This was a multiple ascending-dose safety and tolerability study in metastatic breast cancer patients with additional objective of characterizing the pharmacokinetics (PK) of erlotinib (E), both alone and in combination with docetaxel and capecitabine (D+C). We present here the PK of erlotinib, docetaxel and capecitabine, along with respective active metabolites. Patients were enrolled in three cohorts; Cohort A received 100 mg/day erlotinib for entire 21 day cycle, 825 mg/m^2 b.i.d. capecitabine for first 14 days of cycle and 60 mg/m^2 docetaxel i.v. on first day of cycle; Cohort B received same regimen as in Cohort A, but with an increase to 75 mg/m^2 docetaxel dose level; Cohort C received same regimen as in Cohort B, but with an increase to 1000 mg/m^2 b.i.d. capecitabine dose level. Erlotinib dosing was delayed until day 2 for the first dosing cycle in order allow for characterization of docetaxel and capecitabine PK in absence of erlotinib. PK sampling for erlotinib was performed on Cycle 1, Day 21 (E alone) and on Cycle 2, Day 1 (E + D + C). PK sampling for docetaxel and capecitabine was performed on Cycle 1, Day 1 (D+C) and on Cycle 2, Day 1 (E+D+C). To date, PK data was available from first two cohorts, both of which were comparable. Mean (± SD) Cmax for erlotinib in Cohort B was 1,593 (± 481) ng/mL (E alone) and 1,510 (± 480) ng/mL (E+D+C). Mean (± SD) AUC_{0-24hr} of erlotinib in Cohort B was 25,457 (± 11,251) ng.hr/mL (E alone) and 25,445 (± 10,708) ng.hr/mL (E+D+C). Therefore, mean exposure (Cmax, AUC_{0-24hr}) for erlotinib and its active metabolites (OSI-420 / OSI-413 co-measured) did not appear to change with concomitant adminstration of docetaxel and capecitabine. Mean (± SD) Cmax for docetaxel in Cohort B was 2,850 (± 826) ng/mL (D+C) and 2,197 (± 522) ng/mL (E+D+C). Mean (± SD) AUC_{0-24hr} for docetaxel in Cohort B was 3196 (± 830) ng.hr/mL (D+C) and 2,510 (± 1,020) ng.hr/mL (E+D+C). Mean docetaxel half life was unchanged (9.6 hr versus 10.8hr). Therefore, mean PK parameters for docetaxel indicated somewhat lower exposure in the presence of erlotinib. However, these results should be considered inconclusive considering the large interpatient variability and small number of evaluable patients. Mean (± SD) Cmax for capecitabine in Cohort B was 8,062 (± 6,932) ng/mL (D+C) and 4,975 (± 2,421) ng/mL (E+D+C). Mean (± SD) AUC_{0-24hr} for capecitabine in Cohort B was 5,857 (± 3,401) ng.hr/mL (D+C) and 5,948 (± 2,397) ng.hr/mL (E+D+C). Mean capecitabine half life was also unchanged (0.65hr versus 0.74hr). Mean pharmacokinetic parameters for capecitabine and its metabolites (5-FU and 5'-DFUR) did not appear to change in presence of erlotinib. In conclusion, there was no evidence for any PK interaction between erlotinib, docetaxel and capecitabine (or any metabolites thereof).

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Maximizing internal mammary sentinel lymph node identification

O. Olsha[1], M. Carmon[1], D.B. Odenheimer[1], D. Gimmelreich[1], C. Reinus[2], D. Hain[3]. [1] *Shaare Zedek Medical Center, Surgery, Jerusalem, Israel;* [2] *Shaare Zedek Medical Center, Pathology, Jerusalem, Israel;* [3] *Shaare Zedek Medical Center, Nuclear Medicine, Jerusalem, Israel*

Background: Lymph node mapping has caused renewed interest in the internal mammary nodes in breast cancer. Metastases in these nodes provide important prognostic information both in the presence and in the absence of metastases in axillary lymph nodes. Tracer injection in the dermal lymphatics over the tumor ensures a high rate of identification of the axillary sentinel lymph node (ASLN). Internal mammary sentinel lymph nodes (IMSLNs) are reportedly found in 0% to 35% of patients by conventional mapping methods.

Objective: We carried out a study to test the hypothesis that the addition of a tracer injection into the area of the deep fascia of the breast (near the muscle fascia) would increase the identification rate of IMSLNs.

Methods: Forty-seven consecutive patients with invasive breast cancer, regardless of site, underwent injection of both radioisotope and blue dye in the skin over the tumor and in the deep breast fascia. Pre-operative lymphoscintigraphy and/or intra-operative probe were used to identify the IMSLN. Patients with ductal carcinoma in situ or with known axillary lymph node metastases were excluded.

Results: An IMSLN was identified and biopsied in 24 patients (51%) in 1, 2 or 3 intercostal spaces. For lateral, central and medial lesions the identification rate was 47%, 40% and 75% respectively. A learning curve was evident with an identification rate of 30% for the first 20 patients, and 67% for the next 27 patients. There was 1 instance of metastasis to an IMSLN (2.1%) in a medial lesion. One patient had a small pleural perforation that required no treatment.

Conclusions: The identification rate for IMSLNs with deep fascial injection of tracer was higher than that reported for conventional mapping methods. There is a learning curve, and improvement in the technique of deep fascial injection may maximize identification of the internal mammary sentinel node in the same way that dermal injection ensures maximal ASLN identification. The clinical relevance of this technique in every-day practice has not been established.

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Breast cancer in the elderly - epidemiological characteristics and treatment approach

A. Jovicevic Bekic, Z. Neskovic Konstantinovic, I. Markovic, D. Jovicevic. *Institute for Oncology and Radiology of Serbia, Belgrade, Yugoslavia*

Background. With the aging of the general population, cancer in the elderly has become increasingly common. It is commonly believed that the diagnosis of cancer in the elderly is delayed for a variety of reasons. Ageing also has an impact on cancer's biology and behavior, with some cancers evolving more slowly and the others becoming more rapidly invasive in older patients. There are also differences in the choice of treatment for elderly patients. The aim of the study was to investigate the epidemiological characteristics and the treatment approach in older breast cancer patients in comparison with younger ones.

Results. In our country, about 50% of cancer cases occur in people aged 65 or over. At the Institute for Oncology and Radiology of Serbia, there were about 1,200 newly registered breast cancer patients the year 2001. About 25% were over 65 years of age. The size of the tumor at diagnosis was on average smaller in younger groups than in older ones, both according to the clinical and pathological TNM. However, there was no significant difference either in the lymph node involvement or in the presence of distant metastases at diagnosis. The share of ductal carcinoma in all breast cancers was lower in elder patients than in younger ones (46 vs. 51%) while the situation was the opposite for lobular carcinoma (34 vs. 25%). However, there were no differences in the tumor grades. Hormonal receptors were more frequently positive in older women. About 80% of patients in both groups underwent surgery. However, there were differences in types of surgical procedures performed. Chemotherapy was 2,5-fold less frequently administered in older women; the difference was significant in each stage of the disease. There was also a significant difference in radiotherapy for each stage of breast cancer.

Conclusion. According to our data, there are some differences in the characteristics of breast cancer between patients over 64 and younger ones. There is a significant difference in the treatment approach for each stage of disease. Two questions remain to be further addressed: is breast cancer in elderly a different disease from breast cancer in younger patients, and, is there a rationale to treat elderly breast cancer patients differently from younger ones.

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Primary chemotherapy with gemcitabine (G), myocet (M) and docetaxel (T): results of a phase I/II trial

P. Schmid[1], K. Krocker[2], A. Dieing[1], K. Michniewcz[2], V. Heilmann[3], J.U. Blohmer[4], C. Schulz[1], D. Lueftner[1], D. Elling[2], K. Possinger[1]. [1] *Charité Campus Mitte, Humboldt Universität Berlin, Oncology and Hematology, Berlin, Germany;* [2] *Krankenhaus Lichtenberg, Gynecology and Obstetrics, Berlin, Germany;* [3] *Universitätsklinikum Ulm, Gynecology and Obstetrics, Ulm, Germany;* [4] *Charité Campus Mitte, Humboldt Universität Berlin, Gynecology and Obstetrics, Berlin, Germany*

Introduction: Combinations of anthracyclines, taxanes and gemcitabine are highly effective in breast cancer (BC). Current regimens might be improved by the use of liposomal doxorubicin formulations and by prolonging the