Annals of Oncology 22 (Supplement 2): ii48–ii50, 2011
doi:10.1093/annonc/mdr087

loco-regional therapy

96P INFLUENCE OF MOLECULAR SUBTYPES OF BREAST CANCER ON THE RISK OF LOCOREGIONAL RECURRENCE

R.V. Liubota[1], I. Liubota[2], A. Zotov[3], V. Zaychuk[3]
[1]*Oncology, National Medical University named After A.A. Bogomolets, Kiev/UKRAINE,* [2]*Kiev Oncology Municipal Centre, Kiev/UKRAINE,* [3]*National Medical University named After A.A. Bogomolets, Kiev/UKRAINE*

Background: The aim of the study was to evaluate the incidence of breast cancer locoregional recurrence and duration of recurrence-free period, depending on molecular biological characteristics of the primary tumor.

Patients and methods: Among the 96 patients with breast cancer, 48 patients had breast-conserving surgery (BCS), and 48 underwent radical mastectomy (RME), all patients had regional lymph node dissection. Molecular subtypes of primary tumor (luminal A, luminal B, HER2 + and triple negative type) were evaluated as a prognostic factor of locoregional recurrence.

Results: It was defined that the locoregional recurrence frequency in patients with BCS worked out 13%, and in patients after RME – 9%; the recurrence-free period was 53±8 months and 56±10 months, respectively. Influence of molecular subtypes of primary tumor on the incidence of locoregional recurrence and duration of recurrence-free period are showed in the Table 1.

96P Table 1. Influence of molecular subtypes of primary tumor on the incidence of locoregional recurrence and duration of recurrence-free period.

Molecular subtypes	Locoregional recurrence frequency		Recurrence-free period (months)	
	No. (rec.+)	%	Average value	Median
Luminal A	50 (11)	22	57±16	29
Luminal B	9 (8)	89	56±20	28.5
Her2+	1 (4)	40	27±8*	25
Triple negative	27 (9)	33	30±4*	30

* p< 0,05 compared with luminal A and B molecular subtypes

Conclusions: The type of the surgical intervention doesn't essentially affect the recurrence appearance frequency and the recurrence-free period duration. The incidence of locoregional recurrence of breast cancer highest among women with luminal B molecular subtype, and the lowest in patients with luminal A. Duration of recurrence-free period, the lowest in patients with Her2+ type of breast cancer.

Disclosure: All authors have declared no conflicts of interest.

97P EVALUATING TIMP-1, KI67 AND HER2 AS MARKERS FOR NON-SENTINEL LYMPH NODE METASTASES IN BREAST CANCER PATIENTS WITH MICROMETASTASES IN THE SENTINEL LYMPH NODES: A CASE-CONTROL STUDY

T.F. Tvedskov[1], A. Bartels[2], M. Jensen[3], B. Paaschburg[4], N. Kroman[1], E. Balslev[5], N. Brünner[2]
[1]*Department of Breast Surgery, Copenhagen University Hospital, Copenhagen/DENMARK,* [2]*Section of Patobiology, Faculty of Life Sciences, Frederiksberg C/DENMARK,* [3]*Danish Breast Cancer Cooperative Group, Copenhagen/DENMARK,* [4]*Department of Breast Surgery, Herlev Hospital, Herlev/DENMARK,* [5]*Department of Pathology, Herlev Hospital, Herlev/DENMARK*

Background: Only about 15 % of breast cancer patients with micrometastases in the sentinel lymph nodes (SN) have additional metastatic spread to non-sentinel lymph nodes (NSN) and only these patients may benefit from an axillary lymph node dissection (ALND). It has not yet been possible to identify this subgroup of the patients by using traditional prognostic markers alone. We investigated if the biochemical prognostic markers TIMP-1, Ki67 and HER2 could be used in predicting metastatic spread to NSN in breast cancer patients with micrometastases in the SN.

Methods: We consecutively included all breast cancer patients with micrometastases in the SN operated at the Department of Breast Surgery, Herlev Hospital, between 2001 and 2007. The study was designed as a matched case-control study with 25 cases with micrometastases in the SN and, in addition, metastatic spread to NSN and 50 matched controls with micrometastases in the SN but without NSN metastases. Information on age at diagnosis, tumor size, hormone receptor status, histological type, malignancy grade and number of removed lymph nodes were retrieved from the Danish Breast Cancer Cooperative Group database. Immunohistochemical analyses of TIMP-1 and Ki67 and measurements of HER2 on formalin fixed paraffin embedded tumor tissue were performed.

Results: No significant differences in the immunoreactivity of TIMP-1 and Ki67 were found between patients with and without NSN metastases. Six out of seven HER2 positive patients did not have NSN metastases, but the results did not reach statistical significance.

Conclusion: Despite being prognostic markers in breast cancer, TIMP-1 and Ki67 were not found useful in predicting NSN metastases in women with micrometastatic disease in the SN. Larger studies are needed to further validate HER2 as a marker for NSN metastases in these patients.

Disclosure: All authors have declared no conflicts of interest.

98P HYPERTHERMIA TRIGGERS SUPPRESSION OF ALTERNATIVELY SPLICED CD44 ISOFORMS IN BREAST CANCER CELLS

M. Jaeger[1], M. Hirschfeld[2], G. Gitsch[2], E. Stickeler[2]
[1]*Gynecological Hospital, University Medical Center, Freiburg/GERMANY,* [2]*Gynecological Hospital, Molecular Oncology, University Medical Center, Freiburg/GERMANY*

The clinical application of hyperthermal therapy is recently getting more attention and is applied in addition to chemotherapy or radiotherapy in malignant diseases. This approach might improve the effect of these classical anti-cancer treatment strategies. The CD44 cell-surface glycoprotein is involved in various cellular biological processes like cell adhesion and signal transduction. In breast cancer, variable alternatively spliced isoforms are induced and their expression is positively correlated to tumor progression and formation of distant metastasis. We investigated potential regulatory effects of hyperthermia on the expression of alternative spliced CD44 isoforms. Various breast cancer cell lines (MCF-7, T47D, MDA-MB-231, Jimt-1) were cultured under hyperthermia (42°C, 2 hrs) followed by maintenance under regular culture conditions (37°C, 4 hrs). As a negative control the same cell lines were permanently cultivated under regular temperature conditions. Transcript and protein expression levels of selected CD44 isoforms were analyzed by RT-PCR, Western blot and immunocytochemistry, respectively. The analyses presented a decreased mRNA and protein level of alternative spliced CD44 isoforms. Our results show a regulatory effect of hyperthermal treatment on tumor relevant alternative spliced CD44 isoforms triggered by hyperthermia. We hypothesize that hyperthermia can regulate the expression of tumor relevant alternative spliced CD44 isoforms, thus probably leading to a suppression of tumor progression. According to our findings, hyperthermal treatment seems to represent a method that may improve classical anti-cancer therapies by adirect influence on the regulation of gene expression of important factors in breast cancer biology.

Disclosure: All authors have declared no conflicts of interest.

99P DOSE FRACTIONATION IN COMBINED TREATMENT BY PARTIAL BREAST IRRADIATION AND TRASTUZUMAB

P. Pedicini, G. Califano, R. Caivano, A. Fiorentino, V. Barbieri, P. Sanpaolo, G. Castaldo, V. Fusco
Radioterapia, IRCCS CROB, Rionero in Vulture, Potenza/ITALY

Aim: To identify the optimal dose fractionation in patients treated by partial breast irradiation and trastuzumab.

Materials and methods: To investigate the effects of increased radiosensitivity, because of the presence of molecular targeting agent, cell lines of human breast adenoma (MDA-MB-231) were cultivated on culture slides and incubated with different concentration of trastuzumab (from 10 nM to 100 nM with steps of 10 nM) in a preclinical study. Afterwards each colony formation was irradiated by increasing levels of dose radiation (between 2 Gy and 6 Gy, dose-rate of 3 Gy/min at 37°). We measured the corresponding expression of HER-2 by FISH, and curves of Surviving Fraction (SF) to obtain modulated α/β values. In clinical study these values were introduced in software, created by our group, to obtain optimal dose fractionation for 10 eligible patients that had measurable disease, normal cardiac function, and biopsy-confirmed residual HER-2-positive disease. All patients received weekly trastuzumab (2 mg/kg intravenously), concurrent with partial breast irradiation.

Results: We found a strong correlation between increased expression of HER-2 and corresponding values α/β derived by SF. This relationship is reflected in a dose fractionation modulated on the pharmacokinetic decay of trastuzumab in vivo: 3,4; 2,9; 2,4; 1,9; 1,5 Gy from Monday to Friday, 1 fraction/day for 4 weeks. This schedule is equivalent of Standard Fractionation (2 Gy/day for 5 weeks) in terms of local control