220 Proffered Paper Oral

Generalizability of survival estimates for patients with breast cancer – a comparison across two population-based series

J. Lundin[1], T. Lehtimäki[1], M. Lundin[1], K. Holli[2], L. Elomaa[3], T. Turpeenniemi-Hujanen[4], V. Kataja[5], J. Isola[6], H. Joensuu[1]. [1]*University of Helsinki, Department of Oncology, Helsinki, Finland;* [2]*Tampere University Hospital, Department of Oncology, Tampere, Finland;* [3]*Turku University Central Hospital, Department of Oncology, Turku, Finland;* [4]*Oulu University Central Hospital, Department of Oncology and Radiotherapy, Oulu, Finland;* [5]*Kuopio University Hospital, Department of Oncology, Kuopio, Finland;* [6]*Tampere University and University Hospital, Institute of Medical Technology, Tampere, Finland*

Background: Recently, attempts have been made to develop tools that generate more individualized and quantitative outcome estimates to aid in decision-making on adjuvant therapy in breast cancer. This is in line with a more general trend in many areas of medicine, where similar approaches for personalized and absolute, instead of relative risk assessments have been proposed.

Objective: The purpose of this study was to analyze the accuracy and transportability of survival estimates for patients with breast cancer by a comparison of outcome data in two population-based series.

Methods: We compared the influence of tumor size, grade, axillary nodal status, estrogen and progesterone receptor contents, and two prognostication schemes (the Nottingham Prognostic Index and St. Gallen's criteria) on outcome between two nationwide cohorts of breast cancer patients diagnosed in 1991–2, the FinProg (n = 2923, Finland) and the SEER series (n = 43,249, the United States).

Results: Eight-year estimates of breast cancer-specific (84% vs. 80%), relative (86% vs. 83%), and overall (70% vs. 69%) survival were slightly better in the SEER than in the FinProg series, respectively. However, after adjustment for the prognostic factors available, no signficant difference between the series remained. Despite differences in demographic variables, adjuvant therapies and mammography screening between the series, the prognostic factors examined produced close to overlapping survival curves with similar shapes between the series, and both prognostication schemes predicted outcome in a roughly similar fashion.

Conclusion: We conclude that quantitative survival estimates based on currently used prognostic factors and prognostication schemes are generalizable and transportable between large, unselected cohorts of breast cancer patients.

221 Proffered Paper Oral

Importance of HER2 and receptor status on the response to adjuvant radiotherapy in high-risk breast cancer – Results from the DBCG82 b&c randomized study

M. Kyndi[1,2], F.B. Sørensen[2], H. Knudsen[3], M. Overgaard[4], H.M. Nielsen[1], J. Overgaard[1]. [1]*Århus University Hospital, Dept. of Experimental Clinical Oncology, Århus C, Denmark;* [2]*Århus University Hospital, Dept. of Pathology, Århus C, Denmark;* [3]*Herlev Hospital, Dept. of Pathology, Herlev, Denmark;* [4]*Århus University Hospital, Dept. of Oncology, Århus C, Denmark*

The study was conducted on behalf of the Danish Breast Cancer Cooperative Group DBCG

Purpose: The DBCG82bc study showed that adjuvant radiotherapy (RT) improved survival in high-risk pts treated with mastectomy and systemic therapy. So far, pts and tumors have been described by classical clinical factors only (e.g. nodal status, tumor size) not by biological markers. However, the disease is heterogeneous and biological markers might describe the response to RT more precisely. The aim of this study was to evaluate the importance of adding information on markers such as estrogen receptor (ER), progesterone receptor (PR), and HER2.

Material: DBCG82bc included 3083 high-risk breast cancer pts, characterized by positive nodes and/or tumor size > 5 cm and/or invasion to skin or fascia. The present analysis included 1241 pts with 8+ lymph nodes removed. Based on paraffin embedded tumor samples, tissue microarrays have been constructed for 918 pts, so far. Successful immunohistochemical staining for ER was obtained in 892 pts, PR in 894 pts and HER2 in 870 pts. Endpoints were loco-regional recurrence as first event (LR), distant metastases (DM) and survival.

Results: Of the 918 pts, 468 pts were randomized to no RT and 450 to RT. LR was found in 134 pts and DM in 516 pts. Overall, RT resulted in a significant reduction in LR (Odds Ratio 0.14 (0.08–0.22, 95% cf.l.)), in DM (OR 0.73 (0.56–0.94)), and death (OR: 0.73 (0.55–0.97)). When combining ER and PR, 658 pts were either ER or PR positive (receptor positive) and 245 pts were both ER and PR negative (receptor negative). HER2 positivity (3+) was observed in 149 pts. Significantly fewer DM were found in pts randomized to RT as compared to no RT, for receptor positive pts (OR: 0.66 (0.49–0.90)) and HER2 negative pts (OR: 0.68 (0.51–0.92)). No difference in DM as a function of RT was seen for the receptor negative pts (OR: 0.97 (0.58–1.63)) and the HER2 positive pts (OR: 1.02 (0.52–2.02)). Cox multivariate analyses of the separate prognostic subgroups showed that RT was not significant for survival in pts with HER2 positive and/or receptor negative tumors, whereas it was important in pts with HER2 negative and receptor positive tumors (P = 0.03).

Conclusion: Postmastectomy RT caused a significant reduction in DM for pts with HER2 negative and receptor positive tumors. This reduction was, however, not found for pts with the poorest prognosis i.e. receptor negative and/or HER2 positive. More exploration in other biologically markers is needed to confine the indication for RT in high-risk breast cancer.

Thursday, 23 March 2006 14:15–16:00

SCIENTIFIC SESSION

Best use of targeted treatment

222 Invited

Overview of biotherapies: standards and new orientations

A. Di Leo, W.M. Claudino. *Hospital of Prato, "Sandro Pitigliani" Medical Oncology Unit, Department of Oncology, Prato, Italy*

In the last decade a new class of compounds targeting critical pathways for breast cancer cell proliferation, migration and survival, has been identified and tested in clinical trials.

Presently, one of these compounds (trastuzumab) has already taken a definite place in the practical management of breast cancer patients, while others have shown promising activity in phase II and phase III (bevacizumab) clinical trials.

This first generation of studies has also been useful to learn some "take home" messages for the development of future biotherapy trials:

1. the identification of molecular predictors of response would certainly help in defining the activity of these compounds. Trastuzumab has so far been the most successful compound because HER-2 gene evaluation allows for the characterization of the molecular profile of responding patients. A similar strategy could lead to the identification of molecular markers predicting the activity of other biotherapies. This would ultimately translate into a more targeted and cost-effective approach to breast cancer treatment;
2. molecular predictors of response to biotherapies are most frequently evaluated on primary tumor samples although biotherapies are first tested in clinical trials for metastatic breast cancer patients. The assumption is that tumor phenotype does not change over time, although tumor clone selection might occur under selective pressures played by systemic therapies administered for metastatic disease. The evaluation of molecular markers in circulating tumor cells collected immediately before starting a new treatment for advanced disease might represent an interesting strategy to be explored in the attempt to properly identify molecular predictors of response to biotherapies;
3. the first proof of clinical activity for biotherapies is still based on the assessment of objective response rates in phase II clinical trials, although tumor shrinkage might not be the most sensitive indicator of clinical activity for this new class of compunds. Additional methods defining the activity of biotherapies might complement the response rate information and might avoid the potential risk of underestimating the worth of new biotherapies. Positron Emission Tomography based on the use of apoptotic markers and Metabolomics might represent new technologies to be introduced in clinical trials in the attempt to improve our current method of tumor response assessment.

The implementation of these concepts into the next generation of clinical trials might lead to new findings in the field of biotherapies and might translate into a more appropriate use of new biotherapies in daily practice.

223 Invited

Searching new active compounds for breast cancer – evolution or revolution?

K.L. Blackwell. *Duke University, Box 3893, Durham, NC, USA*

In the past decade, a number of therapeutic targets in human breast cancer have been identified, and although hundreds of potential therapies have been discovered, metastatic breast cancer remains an incurable problem. The pace at which targeted therapeutic drugs reach the clinical setting is frustratingly slow. The challenge is in matching the appropriate drug to the