347 Poster

The Impact of Chemotherapeutic Regimens On the Cost-utility Analysis of Oncotype DX Assay

B. Madaras[1], P. Rózsa[2], Z. Gerencsér[2], T. Radovics[3], I. Láng[1], Z. Nagy[4], Z. Horváth[1]. *[1]National Institute of Oncology, Chemotherapy B and Clinical Pharmacology, Budapest, Hungary; [2]MediConcept Kft., Budapest, Hungary; [3]Semmelweis Medical University, Faculty of Medicine, Budapest, Hungary; [4]Med Gen-Sol Kft, Budapest, Hungary*

Background: The Oncotype DX® breast cancer (BC) multigene expression assay can predict the likelihood of chemotherapy (CT) benefit for patients (Pts) treated with different CT regimens as well as the risk of recurrence in early-stage BC. The assay is intended for women with stage I or II, node-negative (N−), estrogen receptor-positive (ER+), HER-2-negative and for post-menopausal Pts with 1−3 node-positive (N+), HR-positive invasive BC who will be treated with endocrine therapy.

We analysed the clinical and pathological data of these Pt groups at National Institute of Oncology (NIO) in order to study the cost-effectiveness of the use of Oncotype DX®.

The outcome is sensitive to the treatment modalities and CT regimens. We estimated the impact of the choice of CT on the cost-utility of ODX.

Methods: Between 01.10.2009. and 01. 10.2010. our multidisciplinary institutional breast oncoteam has consulted 410 Pts who had Stage I−II, ER-positive and HER-2 negative disease. We entered these Pts into two subgroups: Group I: N− (pT1−3pN0M0, N = 306) and Group II: 1−3 N+ (pT1−2pN1M0; N = 104). Based on these epidemiological data we made a cost-utility model. The model's main assumption is the following: if a Pt has low Recurrence Score® she can avoid CT which raises the quality of life while the chemotherapy associated costs are decreasing. We calculated the outcomes both with use of the actual and with the current most effective CT regimens. A systematic literature review suggests that the total net change in CT use because of Oncotype DX is −34.4% (in the pN0 group) and −10% for pN1a-c Pts. The increase in quality adjusted life years (QALYs) by avoiding chemo equales 0.5 (Simes et al, 2001). In addition we assume utility of 0.9 for women without recurrence or other tumor and utility of 0.7 for women recurrence or another tumor.

The costs are based on the official database (National Health Insurance Fund. Hungary. 2010). The time horison was 30 years, the costs over 1 year are discounted at rate of 5%.

Results: According to the recent Hungarian practice the incremental cost-effectiveness ratio (ICER) is 6 871 €/QALY respectively. If the treatment would be more 'agressive' the ICER would be 6,649 €/QALY. The total net costs per Pt is 1,137€, while the QALY gain is 0.171 (exchange rate 1 € = 310 HUF).

Conclusion: The more "aggressive" chemoterapy we use, the more cost-effective the Oncotype DX is. Recent ICERs are favourable among the oncology related health technologies.

348 Poster

What Have We Learned From Recursive Partitioning Analyses in Breast Cancer Patients? a Single Institution Report On More Than 2000 Patients

J. Hammer[1], C. Track[1], K.J. Spiegl[1], H.D. Thames[2], D.H. Seewald[3], A.L. Petzer[4], D. Heck[5], J. Feichtinger[1], E. Rechberger[4], E. Bräutigam[1]. *[1]Barmherzige Schwestern Hospital, Radiation Oncology, Linz, Austria; [2]M.D.Anderson Cancer Center, Biostatistics, Houston TX, USA; [3]General Hospital, Radiotherapy, Vöcklabruck, Austria; [4]Barmherzige Schwestern Hospital, Internal Medicine I − Hematology and Oncology, Linz, Austria; [5]Barmherzige Schwestern Hospital, Surgery, Linz, Austria*

Background: The aim of this RPA-study is to evaluate which risk factors gain in importance after breast conserving surgery (BCS), systemic treatment (ST) and radiation therapy (RT).

Materials and Methods: From 1984 to 1999, 2207 patients with breast cancer were referred to our institution. Lost to FU: 56 pat. Mean FU period is 119 months. After BCS, all patients underwent whole breast RT ± a boost to the tumour bed. Co-variates included were age, T-size, number of excised nodes, number of involved nodes (N pos), and their ratio (NR), grading, ER/PR status, menopausal status, type of systemic therapy and tu-location (loc). The relative hazard ratio (RHR, HR relative to median patient) and the 10 yr results of LR and DFS were calculated in subgroups. For each endpoint RPA was used to estimate prognostic cut points. The software finds the cut point, the point of the highest significance. The relative hazard ratio (RHR) was estimated for each prognostic group. p-values: $\leqslant 0.05$.

In addition we separated loc (med, lat) according to N neg and N pos stages.

Results: For LR age is of prime importance followed by NR and hormonal medication; and thirdly loc is relevant. For DFS, NR is the most important prognostic factor followed by T-size, age, PR and loc.

The 10-yr-rate of LR was 5.9%, and DFS was 80.8%; for med 8.37% and 76.3%; and for lat 5.23% and 81.5%, respectively. In particular, for N0-patients loc is more relevant! DFS is significantly worse in med compared to lat, e.g. DFS for med & N0 pat is 80.16%, for lat & N0 87.87%, p = 0.0004.

In premenopausal pat the 10 yr LRR was 8.9% (post-menopausal 4.1%), DFR was 76.0% (post-meno 83.0%). For LR the most relevant parameter is T-size with a cut point at 25.5 mm (10-yr LRR 7.6% vs. 20.6%), followed by age and loc. For DFS there is a cut point in NR at 16% (10-yr: <16%: 80.4%; >16%: 45.5%!), followed by T-size and PR. The worst 10-yr DFS rate is found in patients with NR >16% and PR neg: 26.7%!

The number of positive axillary nodes was insignificant whenever the node ratio was included in the statistical analysis.

Conclusion: In this update we could verify the hypothesis that after BCS±ST and RT, subgroups of patients with medial tumour location, with high node ratio and with negative progesteron receptors are at higher risk. Proper diagnostic examination (e.g. PET-CT) and more aggressive treatment are to be considered in individual subgroups, in particular in patients with medial tumour location and axillary N0-status.

Medial tumour location, PR negativity and a high node ratio may be considered as negative prognostic factors in future therapy decisions and in trials.

349 Poster

High Ki67 Values Are Significantly Correlated with Oncotype DX Scores

C. Uras[1], N. Cabioglu[1], F. Tokat[2], G. Basaran[3], D. Boler[1], B. Atalar[4], O. Er[3], N. Bese[5], U. Ince[6]. *[1]Acibadem University Faculty of Medicine, Surgery, Istanbul, Turkey; [2]Acibadem Maslak Hospital, Pathology, Istanbul, Turkey; [3]Acibadem University Faculty of Medicine, Medical Oncology, Istanbul, Turkey; [4]Acibadem University Faculty of Medicine, Radiation Oncology, Istanbul, Turkey; [5]Acibadem Maslak Hospital, Radiation Oncology, Istanbul, Turkey; [6]Acibadem University Faculty of Medicine, Pathology, Istanbul, Turkey*

Background: Oncotype-DX breast cancer assay has been used as an emerging genetic assay by estimating the recurrence risk from the expression of a panel of 21 genes in patients with early stages to determine any clinical benefit from chemotherapy in addition to hormonal therapy. Ki67 as measured on treatment has recently emerged as an effective predictive marker of treatment for both endocrine treatment and chemotherapy in neoadjuant studies. In this single institutional study, any associations of traditional biomarkers and histopathologic factors with Oncotype DX assay were investigated.

Material and Methods: Paraffine sections of patients with early stage hormone receptor positive breast cancer were studied by Genomic Health (Redwood City, CA, USA) to assess the Oncotype DX recurrence score as determined by the 21-gene RT-PCR expression analyses. Results were correlated with histopathologic factors including tumor size, nuclear grade (NG), histologic grade (HG), tumor histology, lymphovascular invasion and different cut-off values of Ki67 (>10%, $\geqslant$15%, $\geqslant$20%, $\geqslant$25%), and c-erbB2 positivity as determined by immunohistochemistry and FISH findings.

Results: Between July 2010 to May 2011, 24 patients with stage I-II breast cancer (stage I, n = 17; stage II, n = 7) were included into the study. The median age was 51 (36−67). Nine-teen patients (79%) underwent breast conserving surgery with SLNB, while mastectomy was performed in 5 patients (21%). Of 24 patients, 3 (12.5%) had isolated tumor cells or micrometastasis in sentinel lymph nodes. Ten patients (42%) were found to have an Oncotype DX score $\geqslant$18 for intermediate or high recurrence risk. No significant correlations could be found between intermediate/high Oncotype DX scores ($\geqslant$18) and tumor size 2 cm, intermediate/high NG, a histology of invasive ductal type, presence of lymphovascular invasion, c-erbB2 positivity, and different cut-off values of Ki67 (>10%, $\geqslant$15%, $\geqslant$20%). However, patients with intermediate/high HG (53% vs 0%, p = 0.05), or with Ki67 $\geqslant$25% (100% vs 32%, p = 0.05) were more likely to have intermediate/high Oncotype DX scores. Even though expressions of ER and PR by immunohistochemistry strongly correlated with the RT-PCR expressions in Oncotype DX assays, the c-erbB2 expression as determined by immunohistochemistry and/or FISH did not correlate with c-erbB2 expression in Oncotype DX assay. Finally, based on the Oncotype DX results, only 7 patients (29%) received chemotherapy.

Conclusions: These results suggest that Oncotpe DX assay may be of little value in certain patients with low histologic grade or high Ki67 scores ($\geqslant$25%) as treatment selection criteria to determine any benefit from chemotherapy. Therefore, considering the cost of these gene assays, careful selection of patients is needed to determine whether they offer significant benefit to justify their use.