to decreased sensitivity to trastuzumab [5]. Decreased interaction between trastuzumab and its target receptor HER2, due to steric hindrance of the HER2 receptor by cell surface proteins, such as MUC-4 [6], or by the presence of a truncated HER2 protein [7], may block inhibitory actions of trastuzumab. Novel therapies targeted against these aberrant molecular pathways are being studied in laboratory and clinical settings, and offer hope that the efficacy and duration of response to trastuzumab can be greatly improved.

Lapatinib (Tykerb) is a small molecule tyrosine kinase inhibitor that targets EGFR and HER-2 [8]. Clinical responses were observed in patients with HER2-overexpressing metastatic breast cancer [9]. A recent phase III randomized trial showed that a combination of lapatinib and capecitabine (Xeloda) was superior to capecitabine alone [10], leading to the FDA approval of lapatinib in 2007. Clinical trials are ongoing to determine the role of lapatinib in the frontline setting for metastatic breast cancer in combination with trastuzumab and taxanes, as well as in the neoadjuvant and adjuvant settings.

Other novel strategies being tested in patients with HER2-overexpressing breast cancer include monoclonal antibodies targeting HER-2 on different epitopes than trastuzumab (for example, pertuzumab), attaching toxins to trastuzumab (for example, trastuzumab-DM1), Hsp90 inhibitors that degrade the HER-2 protein (for example, 17-AAG), irreversible small molecule tyrosine kinase inhibitors (for example, HKI-272), agents directed against IGF-IR and multitarget kinase inhibitors. Indirect approaches include immunotherapy and anti-angiogenic therapy. Clinical trials are evaluating the safety and efficacy of targeted biologic therapies, both as single agents and in combination with other biologics and in combination with standard chemotherapy and endocrine therapy. One of the main challenges is to match the right patient with the right drug(s) at the right time.

References


Posters

P1

Prognostic factors for the node-negative breast cancers

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Objective The proportion of node-negative breast cancer patients has been increasing with improvement of diagnostic modalities and early detection. However, there is a 20–30% recurrence in node-negative breast cancer. To identify the prognostic factors for node-negative breast cancers, we studied the impact of many clinico-pathologic parameters on the outcome of the node-negative breast cancer patients.

Methods The data of 1,110 node-negative breast cancer patients who underwent curative surgery at the Severance Hospital, Yonsei University College of Medicine, were reviewed. The impact of many clinico-pathological parameters on the outcome was investigated. Univariate survival curves for disease-free survival and death were estimated using the Kaplan–Meier method: group differences in survival time were tested by the log-rank test. Multivariate Cox regression analysis was performed to compare and identify independent prognostic factors.

Results The mean age was 47.2 years. The median follow-up was 88 months. Recurrence occurred in 161 patients; 64 patients with locoregional recurrences, 129 with systemic recurrences, and 32 with both. The 5-year overall survival rate was 93.3%. The rate of locoregional recurrence for a 10-year period was significantly lower in the mastectomy group compared with those in the breast conservation therapy group (94.7% versus 79.6%, P = 0.000). No other prognostic factors except age affected locoregional recurrence. There was less systemic recurrence in patients with age greater than 35, with histologic grade I, and with intraductal components greater than 20%. Thus, the 10-year distant-relapse-free survival rates were 87.4% versus 79.8% (P = 0.039), 93.5% versus 85.5% (P = 0.024), and 94.4% versus 82.0% (P = 0.007), respectively. There was no statistical significance in the other prognostic factors that influence systemic recurrence.

Conclusion Patient age, histologic grade, and presence of intraductal component were identified as independent prognostic factors in node-negative breast cancer patients.

P2

Retreatment with trastuzumab in Her2-positive metastatic breast cancer patients: a clinical study

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Objective To study the benefit of trastuzumab in monotherapy or combined with different chemotherapeutic agents in the treatment for Her2+ metastatic breast cancer (MBC) patients after progression on prior trastuzumab therapy.
Patients and methods The clinical evolution of patients with Her2+ MBC diagnosed by IHC3+/FISH+, and treated with trastuzumab in several lines for the metastatic disease, has been studied retrospectively.

Results Twenty-four patients with Her2+ MBC were treated with several regimens containing trastuzumab alone or associated with chemotherapy and/or hormonotherapy. In the first line of treatment 12 RR (50%), 11 SD (45%), with a 95% clinical benefit, was observed. The patients received a second line obtaining 8 RR (33%), 15 SD (62%), with a clinical benefit of 95%. Seventeen patients were treated with a third line, 5 RR (29.4%) and 11 SD (64%) being observed, with a clinical benefit of 93%. Seven patients received a fourth line. In these, 2 RR and 4 SD, with a clinical benefit of 85%, were observed. Fifteen of the patients, with RE+, received hormonotherapy plus trastuzumab alone or with chemotherapy in one or more lines of treatment, obtaining 8 RR (53%) and 4 SD (26%), with a clinical benefit of 79%.

Conclusion The association of herceptin with chemotherapy and/or hormonotherapy demonstrates a very active treatment in patients with Her2+ MBC. The benefit seems to continue in patients who already have received treatment with trastuzumab even in more than one regimen.

P3 Do breast cancer tumours downsize as well as downgrade with neoadjuvant chemotherapy?

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Objective Neoadjuvant chemotherapy (NC) is increasingly being used for large primary breast carcinomas with the aim of improving breast-conservation surgery (BCS) rates. This study was conducted to assess the tumour response following NC.

Methods In this retrospective study over a 4-year period, 61 women with large operable invasive breast cancers (T2–4 N0–2 M0), unsuitable for BCS, were consecutively treated with NC (5-FU, epirubicin, cyclophosphamide and Taxotere). Pathological response was monitored, comparing original core biopsy histology with final excisional histology.

Results The mean age of patients was 48.6 years (range 30–70). Of the 61 patients, BCS was achieved in 48 (79%) patients. On the core biopsy, four (6.5%) patients had grade I cancer, 26 (43%) had grade II cancer and 31 (51%) had grade III cancer. Final histology showed no invasive cancer in eight (13%) patients (seven DCIS, and complete pathological response in one patient). In the rest of the patients, four (6.5%) had grade I tumours, 26 (43%) had grade II tumours and 23 (38%) had grade III tumours. Overall, 14 patients (23%) showed a decrease in histological grade (see Table 1). Seven patients (11.5%) had a higher grade than the initial core.

<table>
<thead>
<tr>
<th>Grade</th>
<th>n</th>
<th>No residual invasive cancer</th>
<th>DCIS</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
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<td>4</td>
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<tr>
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Conclusion In our series of patients receiving NC for breast cancer, there is not only a significant downsizeing (permitting BCS) but also a trend of downgrading of the tumour, and this is seen particularly in poorly differentiated tumours. The higher grade on final histology compared with the core could be due to an unrepresentative core biopsy in large tumours prior to NC.