p53 expression and disease outcome of breast cancer patients undergoing primary chemotherapy with anthracycline-containing regimens

Primary chemotherapy administered to breast cancer patients is the best model to identify baseline features able to predict which patients may be most likely to benefit or not from a cytotoxic regimen. In the March issue of *Annals of Oncology* two papers evaluated the predictive role of immunohistochemical p53 expression on disease outcome of locally advanced breast cancer patients undergoing primary chemotherapy with anthracycline-containing schemes. The study by Bonnefoi et al. [1] analyzed 187 of 448 patients prospectively enrolled in a multicenter phase III trial comparing FEC versus EC, while the paper by Anelli et al. [2] evaluated 73 patients prospectively enrolled in a phase II trial testing the activity of a paclitaxel and doxorubicin combination regimen. Both papers showed a negative relationship between p53 expression and overall survival; p53 was a negative predictor of clinical response in the paper by Anelli et al. but not in that of Bonnefoi et al. This latter study, however, demonstrated a negative correlation between p53 expression and disease-free survival. The major pitfall of the Bonnefoi et al. study is that only a minority of the patients potentially available had baseline histology specimens and could be included in the analysis. This limits the generalization of the results and underlines the importance of planning an adequate tumor sample at baseline condition (by means of incision biopsy or thru-cut biopsy) when designing a study on primary chemotherapy.

The assessment of response of breast cancer by clinical palpation needs experienced clinicians and the results cannot be checked a posteriori by extramural reviewers. The absence of correlation between p53 expression and clinical complete response in the Bonnefoi et al. study may be at least in part attributable to the heterogeneity of response evaluation of a multicenter study.

In the Breast Unit of Cremona, Italy, two consecutive phase II studies of primary chemotherapy were conducted involving 157 consecutive breast cancer patients with T2–4 N0 M0 disease. The first 76 patients received the CMF regimen plus tamoxifen, and the subsequent 81 were treated with single-agent epirubicin [3]. An incision biopsy was performed in all patients before starting chemotherapy. We observed that p53 expression negatively correlated with clinical complete response in overall series, but this relationship was mainly evident in the subset of cases treated with epirubicin. As expected, in our epirubicin-treated series there was a tendency of lower response rate in tumors expressing gp-170. Interestingly, p53 and gp-170 expression were reciprocally correlated. The putative role of mutated p53 in preventing response to chemotherapy is usually attributed to its inhibitory role of the apoptotic pathway. Our data suggest that p53 could upregulate gp-170 expression, providing an additional mechanism of resistance to anthracycline-containing regimens. The authors of both articles should assess gp-170 expression in their patients and correlate gp-170 status to either tumor response or p53 expression.

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