Re: p27Kip1 and Cyclin E Expression and Breast Cancer Survival After Treatment With Adjuvant Chemotherapy

Porter et al. (1) recently described their evaluation of the association between survival and p27Kip1 and cyclin E immunohistochemical staining on tissue microarrays from 2123 breast cancer patients treated with doxorubicin and cyclophosphamide. Although p27Kip1 was statistically significantly associated with survival, cyclin E was not found to be associated with survival.

This observation is in contrast to previous results from Keyomarsi et al. (2), in which cyclin E, as assessed by western blot analysis, was the most prominent independent prognostic factor associated with breast cancer outcome. However, western blot analysis is a time-consuming technique that requires a large amount of tumor tissue and so is not practical for routine risk assessment of breast cancer patients. This technique does, however, detect the low–molecular-weight form of cyclin E, which is not (specifically) recognized by most cyclin E antibodies that are used in immunohistochemistry. Overall, the results for the association between cyclin E and breast cancer outcome have been diverse. Many authors, including Porter et al. (1), have attributed these disparate results to various forms of cyclin E that might not have been measured with the techniques used in these studies.

We agree that differences in analyses (i.e., reverse transcription–polymerase chain reaction [RT–PCR], immunohistochemistry, or western blot) could have a major impact on the results. However, we have found previously (3) that the association between cyclin E and disease outcome was restricted to patients who were treated with tamoxifen in the adjuvant setting. It has been shown (4) that overexpression of the low–molecular-weight form of cyclin E by breast cancer cells is associated with resistance to antiestrogens in vitro. Furthermore, this association was recently confirmed in additional patient cohorts (4,5). If cyclin E is indeed specifically associated with endocrine therapy resistance, then this explanation is also valid for the lack of an association between cyclin E and survival in the study of Porter et al. (1) because all patients in that cohort received only chemotherapy.

A study of cyclin E expression, as assessed by RT–PCR or immunohistochemistry, preferably directed to the low–molecular-weight form of cyclin E, in a cohort of patients treated with endocrine therapy would resolve the issue of whether cyclin E is associated with breast cancer disease progression.

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References

Notes
Editor’s note: Porter et al. declined an invitation to respond.

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