Clinical Utility of Monitoring Serial CA 27.29 in Patients with Different Stage of Breast Cancer

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Abstract: Breast cancer is by far the most frequent cancer in women, worldwide and ranks third overall when both sexes are considered together. For many malignancies, serum tumor markers play an important role in patient management. MUC-1 glycoprotein based serum markers (CA15-3 and CA 27.29) are assays approved by the US Food and Drug Administration for monitoring patients with advanced breast cancer. Potential applications include early detection of recurrent disease and monitoring treatment efficacy in patients with advanced disease. While retrospective data regarding the role of CA27.29 correlates well with progression and treatment of metastatic breast cancer, a multicenter prospective study to further assess the role of CA 27.29 for monitoring of locally advanced disease is warranted.

Keywords: CA27.29, CA15-3, breast cancer.

CA 27.29 (Normal <38 U/mL) is an epitope on the protein core of the MUC-1 mucin glycoprotein (a breast cancer associated antigen). This epitope is molecularly similar to the one recognized by the DF3 monoclonal antibody used in the CA 15-3 assay (Normal <31 U/mL) [1] therefore; both antibodies detect the same antigen. Levels within the normal range do not preclude the presence of cancer, nor are elevated results an absolute indication of breast malignancy as there are false positives in other malignancies and or even benign conditions pregnancy and cirrhosis.

It has yet to be determined that MUC-1 glycoprotein based serum markers (CA15.3 and CA 27.29) are helpful in making treatment decisions in different stages of breast cancer. Although these assay were approved by the US Food and Drug Administration, the FDA does not require tests to show clinical benefit if that is not part of the manufacturer's indication [2].

CA 15-3 and CA 27.29 are well-characterized assays that allow the detection of circulating MUC-1 antigen in peripheral blood. Several studies support the prognostic relevance of this circulating marker in early-stage breast cancer for CA 15-3 [3-6].

Ebeling *et al.* reported CA 15-3 to be a predictor of worse outcome in univariate but not multivariate analysis including tumor size, lymph node status, histologic grade, and estrogen receptor (ER) status [3]. While it is likely that serum tumor markers CA 15-3 and CA 27.29 have prognostic value, their role in the management of early-stage breast cancer is unclear [7, 8].

Several well-designed studies have shown that an increase in CA 15-3 or CA 27.29 after primary and/or adjuvant therapy can predict recurrence in an average of 5 to 6 months before other symptoms or tests [2].

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We wanted to assess the significance of measuring the tumor marker (CA 27.29 levels) to monitor the clinical progress of breast cancer in different stages. After IRB approval, we conducted a retrospective chart review of 394 patients with breast cancer who had regular monitoring of CA 27.29 levels following the diagnosis of breast cancer. A total of 394 patients with different stages who had CA 27.29 monitoring were evaluated from our institution over the past 5 years (2003-2008). Patient CA 27.29 levels were correlated with clinical progression of the disease (diagnostic imaging and history and physical examinations) [9].

A total of 394 patients were reviewed who had adjuvant treatment at our institution and were regularly monitored with CA 27.29 levels. Out of the 330 patients with Stage I, II, and III after treatment with adjuvant therapy, 316 had no evidence of disease (NED) and had normal levels (<38) of CA 27.29. Out of the 14 patients with clinical evidence of disease recurrence, 3 had persistently elevated levels. Of the 62 patients with stage IV breast cancer following chemotherapy, 29 patients had clinical progression of disease with 20 (69%) patients showing increasing levels. Out of the 33 patients with no evidence of progression of disease only 4(12%) had increasing levels [9].

Our trend analysis shows that increasing levels of CA27.29 in metastatic disease correlate well with clinical progression of the disease consistent with ASCO guidelines. A normal CA 27.29 level in patients with Stage I, II, and III, after adjuvant treatment, correlates well with clinically NED status and might be of reassuring benefit to the patients [9].

ASCO 2007 guidelines for monitoring patients with metastatic disease during active therapy suggest that CA 27.29 or CA 15-3 can be used in conjunction with diagnostic imaging, history, and physical examination. Present data are insufficient to recommend use of CA 15-3 or CA 27.29 alone for monitoring response to treatment. However, in the absence of readily measurable disease, an increasing CA 15-3 or CA 27.29 may be used to indicate treatment failure [2].

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The current data is unclear about the role of CA27.29 in early stage breast cancer, but it does correlate well retrospectively with progression of the disease for metastatic disease though one needs to keep watch for the false positives. We need large multicenter prospective study to further assess the role of CA 27.29 for disease monitoring in locally advanced and metastatic breast cancer.

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CONFLICTS OF INTEREST

None declared.

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