Comparison of CA15-3 and Carcinoembryonic Antigen in Monitoring the Clinical Course of Patients with Metastatic Breast Cancer

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ABSTRACT

Fifty-three women with metastatic breast cancer and serial plasma samples were selected to study the correlation between disease course and variations in circulating CA15-3 and carcinoembryonic antigen (CEA) levels. Forty-nine patients had their first sample drawn at the beginning of therapy, while four patients did not receive any treatment during the period of study. Clinical course was scored as progressive disease (PD), responsive disease (RD), and stable disease on the basis of radiological and physical evaluations. The percentage of variation in antigen level between the initial sample and samples drawn at the time of the clinical evaluation was correlated with clinical course. CA15-3 levels above 22.0 units/ml and CEA levels above 3.0 ng/ml were considered elevated values. Antigen levels that increased ≥25% and decreased ≥25% from the initial value were considered to correlate with PD and RD, respectively. Variations in antigen levels ≥25% from the initial value were considered to correlate with stable disease. Significantly more patients had elevated circulating levels of CA15-3 than CEA (96.2 versus 69.8%; P < 0.01) at some point in the course of disease. Overall, CA15-3 correlated with disease progression, regression, or stability in a higher number of patients than CEA (60.3 versus 39.6%; P = 0.02). CA15-3 increased ≥25% more often than CEA in patients with PD (75.0 versus 58.3%) and decreased ≥25% more often than CEA in patients with RD (38.1 versus 23.8%). In a logistic regression model, changes in CA15-3 levels correlated significantly with both PD (P = 0.004) and RD (P = 0.02), while changes in CEA levels did not (PD, P = 0.34; RD, P = 0.52). Furthermore, correlations obtained when using both antigens together failed to improve the results obtained with CA15-3 alone. The present study thus demonstrates that CA15-3 is more useful than CEA in monitoring the clinical course of patients with metastatic breast cancer.

INTRODUCTION

The murine monoclonal antibody DF3 was generated against a membrane-enriched extract of a human breast cancer metastatic to liver (1). Immunoperoxidase staining has demonstrated the presence of DF3 antigen on the apical borders of secretory mammary epithelial cells and in the cytosol of less differentiated malignant cells (1). Other studies (2) have demonstrated that DF3 antigen is a glycoprotein which circulates as heterogeneous species with molecular weights ranging from 300,000 to 450,000. A double-determinant enzyme immunoassay has been established with MAb2 DF3 to detect circulating DF3 antigen. Using this method, we have demonstrated (2) that DF3 antigen is elevated in 72% of women with metastatic breast cancer when compared with age-matched controls.

MAB 115D8 was prepared against human milk fat globules (3). This MAB also reacts with an antigen expressed on the apical border of mammary glands (3). The MAB 115D8-reactive antigen, designated MAM-6, circulates in human plasma, is elevated in women with metastatic breast cancer, and correlates with the clinical course of these patients (4, 5). Furthermore, immunoperoxidase-staining studies, solid-phase immunoassays, and immunoblotting techniques have demonstrated (1, 4, 6) that MABS DF3 and 115D8 react with distinct epitopes expressed on members of a family of high-molecular-weight glycoproteins. MABS DF3 and 115D8 have been utilized in a bideterminant immunoradiometric assay to detect the circulating breast cancer-associated antigen, designated CA15-3 (7). Approximately 75% of patients with metastatic breast cancer have CA15-3 levels greater than 22 units/ml, while only 10% of normal women have levels above this value (7). Furthermore, changes in serial CA15-3 antigen levels have been shown (7) to correlate with the clinical course of breast cancer patients.

Carcinoembryonic antigen is the most widely used marker in monitoring the clinical course of patients with metastatic breast cancer (8). However, the clinical utility of CEA in these patients is limited by the poor sensitivity of the marker (9). We have previously demonstrated (7) that significantly more patients with metastatic breast cancer have elevated CA15-3 levels than elevated CEA levels. However, the utility of these two markers has not been compared in terms of monitoring the clinical course of patients with metastatic breast cancer. Therefore, we have studied the correlation of changes in CA15-3 and CEA levels with the clinical course of 53 women with this disease.

MATERIALS AND METHODS

Sample Collection and Clinical Information

Plasma samples from patients with breast cancer followed at the Dana-Farber Cancer Institute from October 1982 to July 1986 were serially collected and stored at -70°C. CA15-3 levels are stable for at least 5 years in samples stored at -70°C.4 Samples were collected from each patient at the time of clinical evaluation or administration of therapy. The frequency with which the follow-up samples were taken ranged from 3 weeks to 3 months. One-hundred ten patients with metastatic disease and serial plasma samples were reviewed retrospectively. Fifty-three patients selected for this study had measurable metastatic breast cancer and a minimum of three samples during a period that encompassed at least one evaluable clinical course (progression, stability, or response). Forty-nine patients had the first sample obtained just before initiation of therapy. Four patients had well documented disease progression but did not receive therapy during the period of study. Samples were coded and assayed without knowledge of clinical information.

Criteria of Evaluation

Clinical information was obtained by chart review and evaluation of radiological studies. The radiological studies and the clinical course of 25 patients treated according to DFCI protocols were assessed prospectively by one of the investigators. Radio logical and clinical evaluation.

4 D. F. Hayes and D. W. Kufe, unpublished data.
Antigen levels which varied between ±20% in the absence of clinical change. Therefore, increases or decreases in antigen levels always below 22.0 normal control subjects, CEA levels of 3.0 and 5.0 ng/ml are comparable with CA15-3 reference levels of 22.0 and 30.0 units/ml, respectively (17). Therefore, variations in antigen levels always below 22.0 units/ml for CA15-3 and 3.0 ng/ml for CEA were not considered useful variations in antigen levels, which increased over 25% from the initial level were considered to correlate with clinical evaluation of PD. Decreases in antigen levels ≥25% from the initial level were considered to correlate with clinical evaluation of RD. Variations in between ±25% from the initial value were considered to correlate with SD.

Sensitivity of correlation in patients with PD was defined as

\[
\text{Sensitivity} = \frac{\text{No. of patients with PD}}{\text{No. of patients with RD or SD}}
\]

and with serial Ag levels which increase over 25%

Specificity of correlation for patients with progressive disease was defined as

\[
\text{Specificity} = \frac{\text{No. of patients with RD or SD}}{\text{No. of patients with RD or SD}}
\]

and with serial Ag levels which do not increase over 25%

Specificity of correlation for patients with regressive disease was defined as

\[
\text{Specificity} = \frac{\text{No. of patients with PD or SD}}{\text{No. of patients with PD or SD}}
\]

and with serial Ag levels which do not decrease over 25%

Determination of the “Correlative Value” of a Positive or a Negative Test. Predictive values reflect the clinical relevance of a test and provide an estimate of the probability that a positive or negative test truly predicts the presence or the absence, respectively, of the outcome in consideration. PVs can be determined using Bayes' theorem with the sensitivity and specificity of the test and the prevalence of the predicted outcome (12). In the present study, the changes in antigen levels represent those obtained between the initial antigen level and the level at the time of first evidence of clinical change. Since this is a retrospective analysis and not all patients had blood samples drawn at the same time after the initial sample, we could not calculate the true "predictivity" of early changes in antigen levels. Therefore, in order to have an estimate of the real PVs of changes in CA15-3 and CEA levels in patients with metastatic disease, we calculated theoretical values using Bayes' theorem. The theoretical values were designated correlative values to avoid confusion with true PVs. These correlative values are more likely an overestimation of the real PV. However, if CA15-3 was less useful than CEA or if both markers gave low correlative values, the true predictivity of the test would be very low and further investigation would be discouraged. Correlative values of a positive and of a negative test at the time of the assessment of the clinical course were calculated as

\[
\text{PCV} = \frac{(\text{Sensitivity}) \times P(C)}{[(\text{Sensitivity}) \times P(C) + (1 - \text{Specificity}) \times (1 - P(C))]} \quad | \quad \text{NCV} = \frac{((\text{Specificity}) \times (1 - P(C)) + (1 - \text{Sensitivity}) \times P(C))}{(\text{Specificity}) \times (1 - P(C))}
\]

where P(C) represents the probability of observing the clinical event (PD or RD) in the population of patients concerned. Three different probabilities of progression and regression have been chosen to illustrate the value of a positive or of a negative test in different clinical situations.

Statistical Analysis. Statistical comparisons of the two tests were performed with the McNemar test for paired observations (13). A logistic regression model was used to test the efficacy of combining the two tests (14).

RESULTS

Patient Characteristics

The clinical characteristics of the 53 patients with metastatic breast cancer selected for this study are listed in Table 1. Median age was 51 years (range, 30–78 years). Thirty-four patients relapsed after primary therapy with a median disease-free period of 25.5 months (range, 7–74 months), and 15 of these had previously received adjuvant chemotherapy. Nineteen patients initially presented with metastatic breast cancer. Twenty-five patients had previously received one or more modes of treatment for metastatic disease and the median period since...
patients (66.0%) (Table 2). In 15 cases the CAI5-3 antigen level was above 3.0 ng/ml and CEA levels were above 30.0 units/ml in 50 patients (94.3%) in at least one of the serial samples measured. CEA levels were above 5.0 ng/ml (range, 5.1–589 ng/ml) for CEA. Among the 32 patients with RD or SD, CAI5-3 increased >25% in three patients, while in 26 of 29 patients it increased less than 25% or decreased (specificity for RD, 23.8%) (Table 4). Among these 29 patients with RD or SD, CEA increased less than 25% or decreased in 22 (specificity for PD, 75.8%) (Table 4).

Among the 24 patients with PD, CAI5-3 increased ≥25% from the initial value in 18 patients, while CEA increased ≥25% in 14 patients (sensitivity for PD = 75.0 versus 58.3%) (Table 3). The median absolute increase in antigen levels was 211.3 units/ml (range, 10.5–7722 units/ml) for CAI5-3 and 48.9 ng/ml (range, 5.0–1833 mg/ml) for CEA. Among the 29 patients who had RD or SD, CAI5-3 increased ≥25% in three patients, while in 26 of 29 patients it increased less than 25% or decreased (specificity for PD, 89.6%) (Table 4). Among these 29 patients with RD or SD, CEA increased less than 25% or decreased in 22 (specificity for PD, 75.8%) (Table 4).

Among the 21 patients with RD, CAI5-3 decreased ≥25% from the initial value in 8 cases (sensitivity for RD, 38.1%), while CEA decreased in 5 cases (sensitivity for RD, 23.8%) (Table 3). The median absolute decrease in antigen levels was 147.8 units/ml (range, 12.9–974 units/ml) for CAI5-3 and 14.0 ng/ml (range, 5.1–589 ng/ml) for CEA. Among the 32 patients with PD or SD, CAI5-3 decreased ≥25% in two, while it decreased less than 25% or increased in 30 of 32 patients (specificity for RD, 93.7%) (Table 4). CEA decreased less than 25% or increased in 29 of 32 patients with PD or SD (specificity for RD, 90.6%) (Table 4).

Eight patients had SD according to our evaluation criteria. Six of these 8 patients (75.0%) had variations in CAI5-3 levels less than ±25% from the initial level. In contrast, only 2 of 8 patients (25.0%) had variations in CEA levels less than ±25% from the initial value (Table 3). The limited size of this subset of patients, however, prevented reliable computation of sensitivity, specificity, and correlational values.

Logistic regression models were used to further explore the usefulness of combining changes in both of the two markers as a correlate of PD or RD. In the first model, the outcome (dependent) variable was clinical progression of disease (yes or no). The input (independent) variables were percentage of changes in CAI5-3 and percentage of changes in CEA. When percentage of changes for CAI5-3 and CEA were correlated with clinical progression, only CAI5-3 was significant (P = 0.009 versus P = 0.46 for CEA). The same results were obtained when percentage of changes in CAI5-3 and CEA were only considered as increasing greater or less than 25% from the initial level (CAI5-3, P = 0.0004; CEA, P = 0.34). In the second model, clinical response (yes or no) was the new outcome variable, while the input variables were the same. When percentage of change values for CAI5-3 and CEA were correlated

### Table 1: Clinical characteristics of patients monitored with CAI5-3 and CEA

<table>
<thead>
<tr>
<th>Menopausal status</th>
<th>No. of patients</th>
<th>CEA</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>22</td>
<td>&gt;3.0 ng/ml</td>
<td>51 (96.2%)</td>
</tr>
<tr>
<td>Peri</td>
<td>8</td>
<td>&gt;3.0 ng/ml</td>
<td>37 (69.8%)</td>
</tr>
<tr>
<td>Post</td>
<td>23</td>
<td>&gt;5.0 ng/ml</td>
<td>50 (94.3%)</td>
</tr>
</tbody>
</table>

### Table 2: Comparison of circulating levels of CAI5-3 and CEA in 53 patients with metastatic breast cancer

<table>
<thead>
<tr>
<th>CAI5-3</th>
<th>CEA</th>
<th>CAI5-3</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;22.0 units/ml</td>
<td>&gt;3.0 ng/ml</td>
<td>&gt;30.0 units/ml</td>
<td>&gt;5.0 ng/ml</td>
</tr>
<tr>
<td>51 (96.2%)</td>
<td>37 (69.8%)</td>
<td>50 (94.3%)</td>
<td>35 (66.0%)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses, percentage.
with clinical response, only CA15-3 was significant ($P = 0.009$ versus $P = 0.92$ for CEA). Categorizing the data as a decrease greater or less than 25% from the initial value, the correlation between changes in CA15-3 levels and RD was still significant ($P = 0.022$), while the correlation of changes in CEA levels and RD was not ($P = 0.93$). Thus, the use of both CA15-3 and CEA did not significantly improve the results obtained with CA15-3 alone.

**Correlative Value of a Positive or a Negative Test.** The correlative value of variations in CA15-3 and CEA levels at the time of the assessment of clinical course was calculated for both antigens and for their combined use according to different arbitrary probabilities of progression and regression, respectively. The PCV of an increase in CA15-3 levels was always better than that of CEA for probabilities of progression between 30 and 70% (Table 5). The NCV for a lack of increase in antigen level was also better for CA15-3 than for CEA. Thus, an increase in CA15-3 level of ≥25% would be a better predictor of true progression than an increase in CEA levels for different probabilities of progression. Conversely, a lack of increase in CA15-3 levels of ≥25% would be a better predictor that the patient is not progressing than a lack of increase in CEA.

On the basis of these correlative values, if a patient who starts a new treatment for metastatic disease is believed to have a 30% probability of failing to respond to that treatment and a 70% probability of responding or remaining stable, an increase ≥25% in CA15-3 levels raises the probability that the clinical evaluation will show a true progression from 30 to 75% (Table 5; PCV, hypothetical probability of progression, 0.3). On the other hand, if CA15-3 levels do not increase ≥25%, the probability that the clinical evaluation will show responsive or stable disease rises from 70 to 89% (Table 5; NCV, hypothetical probability of progression, 0.3). Similarly, if a patient is believed to start a therapy with a 70% probability of failing to respond to that treatment and a 30% probability of responding or remaining stable, an increase ≥25% in CA15-3 levels raises the probability that the clinical evaluation will show progressive disease from 70 to 94% (Table 5; PCV, hypothetical probability of progression, 0.7), while a lack of increase ≥25% in CA15-3 levels raises the probability that the clinical evaluation will show responsive or stable disease from 30 to 60%. In contrast, the corresponding probabilities for changes in CEA levels were always lower (Table 5).

The PCV of a decrease in CA15-3 levels was higher for CA15-3 than for CEA, assuming probabilities of response between 30 and 70% (Table 6). The NCV for a lack of decrease in antigen level was better for CA15-3 than for CEA. Therefore, a decrease ≥25% in CA15-3 levels may be a better predictor that the clinical evaluation will demonstrate response than a decrease ≥25% in CEA levels. Conversely, a lack of decrease ≥25% in CA15-3 levels may be a better predictor that clinical evaluation will not show response than a lack of decrease in CEA levels. Finally, the combinations of the two tests did not improve the PCV and NCV of CA15-3 alone.

### Table 3: Sensitivity of changes in CA15-3 and CEA levels to monitor clinical course in patients with metastatic breast cancer

<table>
<thead>
<tr>
<th>Disease course</th>
<th>No. of patients</th>
<th>CA15-3</th>
<th>CEA</th>
<th>CA15-3 and CEA</th>
<th>CA15-3 or CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>24</td>
<td>18 (75.0 ± 8.8)</td>
<td>14 (58.3 ± 10)</td>
<td>12 (50.0 ± 10)</td>
<td>20 (83.3 ± 7.6)</td>
</tr>
<tr>
<td>RD</td>
<td>21</td>
<td>8 (38.1 ± 10)</td>
<td>5 (23.8 ± 9.2)</td>
<td>3 (16.6 ± 8.1)</td>
<td>10 (47.6 ± 11)</td>
</tr>
<tr>
<td>SD</td>
<td>8</td>
<td>6 (75.0 ± 15)</td>
<td>2 (25.0 ± 15)</td>
<td>6 (75.0 ± 15)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>53</td>
<td>32 (60.3 ± 6.7)</td>
<td>21 (39.6 ± 6.7)</td>
<td>17 (32.0 ± 6.4)</td>
<td>36 (67.9 ± 6.4)</td>
</tr>
</tbody>
</table>

* For sensitivity, the correlation of changes in antigen levels with clinical course is defined as an increase ≥25% in patients with PD, as a decrease ≥25% in patients with RD, and as a variation ≥25% in patients with SD.

### Table 4: Specificity of changes in CA15-3 and CEA levels to monitor clinical course in patients with metastatic breast cancer

<table>
<thead>
<tr>
<th>Disease course</th>
<th>No. of patients</th>
<th>CA15-3</th>
<th>CEA</th>
<th>CA15-3 and CEA</th>
<th>CA15-3 or CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD + RD</td>
<td>29</td>
<td>26 (89.6 ± 5.6)</td>
<td>22 (75.8 ± 7.9)</td>
<td>27 (93.1 ± 4.7)</td>
<td>23 (79.3 ± 7.5)</td>
</tr>
<tr>
<td>PD + SD</td>
<td>32</td>
<td>30 (93.7 ± 4.2)</td>
<td>29 (90.6 ± 5.1)</td>
<td>30 (93.7 ± 4.2)</td>
<td>29 (90.6 ± 5.1)</td>
</tr>
<tr>
<td>PD + RD</td>
<td>45</td>
<td>32 (71.1 ± 6.7)</td>
<td>40 (88.8 ± 4.7)</td>
<td>43 (95.5 ± 3.0)</td>
<td>30 (66.6 ± 7.0)</td>
</tr>
</tbody>
</table>

* For specificity, the correlation of changes in antigen levels with clinical course is defined as a lack of increase ≥25% in patients with PD or SD, and as variations greater than ±25% in patients with PD or RD.

* Numbers in parentheses, percentages ± SE.

### Table 5: Correlative values (%) of increases ≥25% in antigen level in patients with metastatic breast cancer

<table>
<thead>
<tr>
<th>Hypothetical probability of progression</th>
<th>CA15-3</th>
<th>CEA</th>
<th>CA15-3 and CEA</th>
<th>CA15-3 or CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV</td>
<td>0.3</td>
<td>75.5</td>
<td>50.8</td>
<td>75.6</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>87.8</td>
<td>70.6</td>
<td>87.8</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>94.3</td>
<td>82.7</td>
<td>94.4</td>
</tr>
<tr>
<td>NCV</td>
<td>0.3</td>
<td>89.3</td>
<td>80.9</td>
<td>81.3</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>78.1</td>
<td>64.5</td>
<td>65.0</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>60.5</td>
<td>43.8</td>
<td>44.4</td>
</tr>
</tbody>
</table>

* PCV, correlative value of a positive test (increase ≥25% in antigen level).

### Table 6: Correlative values (%) of decreases in antigen level in patients with metastatic breast cancer

<table>
<thead>
<tr>
<th>Hypothetical probability of response</th>
<th>CA15-3</th>
<th>CEA</th>
<th>CA15-3 and CEA</th>
<th>CA15-3 or CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV</td>
<td>0.3</td>
<td>72.1</td>
<td>52.0</td>
<td>53.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>85.8</td>
<td>71.7</td>
<td>72.5</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>93.4</td>
<td>85.2</td>
<td>86.0</td>
</tr>
<tr>
<td>NCV</td>
<td>0.3</td>
<td>77.9</td>
<td>73.5</td>
<td>72.4</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>60.2</td>
<td>54.3</td>
<td>52.4</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>39.3</td>
<td>27.4</td>
<td>32.5</td>
</tr>
</tbody>
</table>

* PCV, correlative value of a positive test (decrease ≥25% in antigen level).

* NCV, correlative value of a negative test (lack of decrease ≥25% in antigen level).
DISCUSSION

Several circulating markers have been investigated in patients with breast cancer, including CEA (8, 9, 11, 15–21), tissue polypeptide antigen (22), gross cystic disease fluid protein (23), casein (24), α-lactalbumin (25), ceruloplasmin (26), creatinine kinase (27), sialyltransferase (28), and glycolipids (29). Although both tissue polypeptide antigen and gross cystic disease fluid protein circulate at elevated levels in patients with metastatic disease, the clinical utility of these assays in monitoring metastatic breast cancer has not been superior to that of CEA (30, 31). Thus, CEA is currently the most widely used marker to monitor disease course in women with metastatic breast cancer.

Previous studies have demonstrated that serial CEA levels correlate with clinical course when this antigen circulates at high levels (8, 11, 15–21). Tormey and Waalkes (8) observed a correlation between clinical course and changes in CEA levels when initial values were above 5.0 ng/ml. Lokich et al. (11) demonstrated that CEA levels correlated with clinical course in about one-half of the patients with starting CEA levels between 5 and 20 ng/ml and in all patients with starting values of CEA above 35 ng/ml. Mughal et al. (17) have reported that CEA levels correlate with clinical course in all patients with initial CEA levels above 15 ng/ml but only in 84% of patients responding to treatment who had initial CEA levels below 15 ng/ml. Loprini et al. (21) found a correlation between CEA levels and clinical progression only in five of 13 patients who progressed early after the beginning of induction therapy and in 54% of patients responding to treatment. However, the utility of changes in CEA level for monitoring the course of patients with metastatic breast cancer has been limited by the relatively low percentage of patients who present with elevated values. Indeed, several studies (7–9, 15–21) have demonstrated that only 40–70% of metastatic breast cancer patients present with elevated circulating levels of CEA.

The present study confirms our previous observation (7) that CA15-3 levels are elevated more frequently than CEA levels in women with metastatic breast cancer. Furthermore, CA15-3 levels were more useful than CEA for monitoring clinical course in a retrospectively analyzed population of patients undergoing treatment for metastatic breast cancer. Overall, CA15-3 correlated with the clinical course of disease more often than CEA (60.3 versus 39.6%). In this regard, CA15-3 correlated better than CEA both with PD (75.0 versus 58.3%) and with RD (38.1 versus 23.8%). In addition, CA15-3 was more specific than CEA in PD, while specificity was almost equal for RD. Moreover, logistic regression analysis has demonstrated that the simultaneous use of both markers failed to significantly enhance sensitivity and specificity obtained with CA15-3 alone. Finally, in monitoring patients with metastatic breast cancer, changes in CA15-3 levels provide the clinician with a better predictivity of clinical course than changes in CEA levels, as suggested by comparison of the correlative values of a positive or negative test at the time of clinical evaluation.

A small fraction of patients with breast cancer did not have elevated CA15-3 levels at any time during their clinical course. Our previous studies suggest that CA15-3 elevations are related to bulk of disease (7). However, immunoperoxidase studies with both Mab DF3 (1) and Mab 115D8 (3) demonstrate that a few breast carcinomas do not express the relevant antigen.

The present study thus demonstrates that CA15-3 is more useful than CEA in monitoring the clinical course of patients with metastatic breast cancer. The usefulness of the CA15-3 assay in the therapeutic decision-making process, however, remains an issue of further study. The present results are based upon a retrospective analysis of a limited sample population. In this regard, we have initiated a prospective cooperative group study of the CA15-3 assay to evaluate the following issues: (a) effect of disease progression and response to treatment on early changes in CA15-3 levels; (b) predictive values and lead time of a change in CA15-3 levels following response to therapy and subsequent progression; (c) effect of hormonal receptor level, tumor histology, and stage of disease on CA15-3 correlation with clinical course; and (d) the comparative value of CA15-3 and CEA at different circulating levels in monitoring clinical course. Thus, the results of this prospective trial should provide an opportunity to further compare CA15-3 and CEA in groups of women more homogeneous with respect to site of metastatic disease, hormonal receptor status, and other parameters relevant to the biology of breast cancer.

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REFERENCES

19. Cantwell, B., Duffy, M. J., Fennelly, J. J., and Daly, L. Carcinoembryonic
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