

## 1997 Update of Recommendations for the Use of Tumor Markers in Breast and Colorectal Cancer

Adopted on November 7, 1997 by the American Society of Clinical Oncology\*

**Objective:** The primary objective was to update the 1996 clinical practice guidelines for the use of tumor marker tests in the prevention, screening, treatment, and surveillance of breast and colorectal cancers. These guidelines are intended for use in the care of patients outside of clinical trials.

**Options:** Six tumor markers for colorectal cancer and eight for breast cancer were considered. They could be recommended or not for routine use or for special circumstances. In addition to carcinoembryonic antigen (CEA) and cancer antigen (CA) 15-3, CA 27.29 also was considered in regard to circulatory tumor markers for breast cancer.

**Outcomes:** In general, the significant health outcomes identified for use in making clinical practice guidelines (overall survival, disease-free survival, qual-

ity of life, lesser toxicity, and cost effectiveness) were used.

**Evidence:** A computerized literature search from 1994 to July 1997 was performed.

**Values:** The same values for Use, Utility, and Levels of Evidence were used by the Committee.

**Benefits, Harms, and Costs:** The same benefit, harms, and costs were used.

**Recommendation:** No changes in any guidelines were recommended (see text).

**Validation:** External review by the American Society of Clinical Oncology (ASCO) Health Services Research Committee and by ASCO Board of Directors.

**Sponsor:** American Society of Clinical Oncology. *J Clin Oncol* 16:793-795. © 1998 by American Society of Clinical Oncology.

The following are updated guidelines on the use of tumor markers in breast and colorectal cancer.<sup>1</sup> Each guideline was discussed by the entire Review Committee. All update recommendations were unanimous.

### SUMMARY OF GUIDELINES

#### Colorectal Cancer

- 1a. Carcinoembryonic antigen (CEA) is not recommended to be used as a screening test for colorectal cancer.  
*1997 Update: no change.*
- 1b. CEA may be ordered preoperatively in patients with colorectal carcinoma if it would assist in staging and surgical treatment planning. Although elevated preoperative CEA (> 5 mg/mL) may correlate with poorer prognosis, data are insufficient to support the use of CEA to determine whether to treat a patient with adjuvant therapy.  
*1997 Update: no change.*
- 1c. If resection of liver metastases would be clinically indicated, it is recommended that postoperative serum CEA testing may be performed every 2 to 3 months in patients with stage II or III disease for 2 or more years after diagnosis. An elevated CEA, if confirmed by retesting, warrants further evaluation for metastatic disease, but does not justify the institution of adjuvant therapy or systemic therapy for presumed metastatic disease.  
*1997 Update: no change.*
- 1d. Present data are insufficient to recommend routine use of the serum CEA alone for monitoring response

to treatment. If no other simple test is available to indicate a response, CEA should be measured at the start of treatment for metastatic disease, and every 2 to 3 months during active treatment. Two values above baseline are adequate to document progressive disease, even in the absence of corroborating radiographs. CEA is regarded as the marker of choice for monitoring colorectal cancer.

*1997 Update: no change.*

2. Present data are insufficient to recommend lipid-associated sialic acid (LASA) for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

*1997 Update: no change.*

3. Present data are insufficient to recommend cancer antigen (CA) 19-9 for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

*1997 Update: no change.*

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- 4a. Present data are insufficient to recommend DNA flow cytometrically derived ploidy (DNA index) for the management of colorectal cancer.

*1997 Update: no change.*

- 4b. Present data are insufficient to recommend the use of DNA flow cytometric proliferation analysis (% S-phase and related analyses) for the management of colorectal cancer.

*1997 Update: no change.*

5. Present data are insufficient to recommend the use of p53 expression or mutation for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

*1997 Update: no change.*

6. Present data are insufficient to recommend the use of the *ras* oncogene for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

*1997 Update: no change.*

#### *Breast Cancer*

- 1a. Present data are insufficient to recommend CA 15-3 or CA 27.29 for screening, diagnosis, staging, or surveillance following primary treatment. Although an increasing CA 15-3 or CA 27.29 can detect recurrence following primary treatment, the clinical benefit is not established; therefore, it cannot be recommended.

*1997 Update: One well-designed study has shown that an increase in CA 27.29 can predict recurrence an average of 5.3 months before other symptoms or tests.<sup>2</sup> However, options for therapy remain unchanged, and there has been no demonstrated impact on the most significant outcomes (improved disease-free or overall survival, better quality of life, lesser toxicity, or improved cost effectiveness).<sup>3</sup> The data used by the Food and Drug Administration (FDA) to approve CA 27.29 were available to the panel previously; while the assay was approved by the FDA, the FDA does not require tests to show clinical benefit. Based on the small body of evidence and until there is evidence of clinical benefit, present data are insufficient to recommend routine use of CA 27.29.*

- 1b. Present data are insufficient to recommend routine 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 suggest treatment failure.

*1997 Update: no change.*

- 2a. CEA is not recommended for screening, diagnosis,

staging, or routine surveillance of breast cancer patients following primary therapy.

*1997 Update: no change.*

- 2b. Routine use of CEA for monitoring response of metastatic disease to treatment is not recommended. However, in the absence of readily measurable disease, an increasing CEA may be used to suggest treatment failure.

*1997 Update: no change.*

- 3a. Estrogen and progesterone receptors are recommended to be measured on every primary breast cancer, and may be measured on metastatic lesions if the results would influence treatment planning.

*1997 Update: no change.*

- 3b. In both premenopausal and postmenopausal patients, steroid hormone receptor status may be used to identify patients most likely to benefit from endocrine forms of adjuvant therapy and therapy for recurrent or metastatic disease.

*1997 Update: no change.*

- 3c. Estrogen and progesterone receptors are relatively weak predictors of long-term relapse and breast cancer related mortality rates, and are not recommended to be used alone to assign a patient to prognostic groupings.

*1997 Update: no change.*

- 4a. Present data are insufficient to recommend obtaining DNA flow cytometry derived estimates of DNA content or S-phase in breast tissue.

*1997 Update: no change.*

- 4b. DNA flow cytometry-derived ploidy are not recommended to be used to assign a patient to prognostic groupings. There is insufficient evidence to recommend the use of S-phase determination for assigning patients to prognostic groupings.

*1997 Update: no change.*

- 4c. Present data are insufficient to recommend the use of DNA flow cytometry-derived ploidy (DNA index) or flow cytometric measures of proliferation (% S-phase and related analysis) for selection of the type of adjuvant therapy to be given.

*1997 Update: no change.*

- 4d. Present data are insufficient to recommend the use of DNA flow cytometry-derived information to select among different treatment options of metastatic disease.

*1997 Update: no change.*

5. Present data are insufficient to recommend the use of *c-erbB-2* (HER-2/*neu*) gene amplification or overexpression for management of patients with breast cancer.

*1997 Update: no change.*

6. Present data are insufficient to recommend use of p53 measurements for management of patients with breast cancer.

*1997 Update: no change.*

7. Present data are insufficient to recommend use of cathepsin-D measurements for management of patients with breast cancer.

*1997 Update: no change.*

#### REFERENCES

1. American Society of Clinical Oncology: Clinical practice guidelines for the use of tumor markers in breast and colorectal cancer. *J Clin Oncol* 14:2843-2877, 1996
2. Chan DW, Beveridge RA, Hyman M, et al: Use of truquant BR radioimmunoassay for early detection of breast cancer recurrence in patients with stage II and stage III disease. *J Clin Oncol* 15:2322-2328, 1997
3. American Society of Clinical Oncology: Outcomes of cancer treatment for technology assessment and cancer treatment guidelines. *J Clin Oncol* 14:671-679, 1996