Complete Summary

GUIDELINE TITLE

ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer.

BIBLIOGRAPHIC SOURCE(S)

Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, Somerfield MR, Hayes DF, Bast RC Jr, ASCO. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006 Nov 20;24(33):5313-27. [167 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: 2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001 Mar 15;19(6):1865-1878.

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SCOPE

DISEASE/CONDITION(S)

Gastrointestinal cancer, including colorectal cancer and pancreatic cancer

GUIDELINE CATEGORY

Evaluation
Management

Risk Assessment
Screening
Technology Assessment
Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery
Family Practice
Gastroenterology
Internal Medicine
Oncology
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To update the recommendations for the use of tumor marker tests in the prevention, screening, treatment, and surveillance of gastrointestinal cancers

TARGET POPULATION

Patients with colorectal cancer or pancreatic cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Preoperative carcinoembryonic antigen (CEA) testing for staging and surgical treatment planning
2. Postoperative CEA testing to detect possible metastatic disease
3. CEA testing to monitor metastatic colorectal cancer during systemic therapy
4. CA 19-9 testing for monitoring response to therapy

Note: The following interventions were considered but not recommended.

- CEA as a screening test for colorectal cancer
- CEA testing to determine whether to treat patients with colorectal cancer with adjuvant therapy
- Use of CA 19-9 for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer
- Use of flow-cytometrically derived DNA ploidy (DNA index) or DNA flow cytometric proliferation analysis (%S phase) to determine prognosis of early stage colorectal cancer
- Use of p53 expression or mutation for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer
- Use of the *ras* oncogene for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer

- Use of thymidine synthase (TS), dihydropyrimidine dehydrogenase (DPD), and thymidine phosphorylase (TP) tests for screening, prognosis, predicting response to therapy, or monitoring response to therapy of patients with colorectal cancer
- Microsatellite instability (MSI) ascertained by polymerase chain reaction (PCR) to determine the prognosis of operable colorectal cancer or to predict the effectiveness of fluorouracil (FU) adjuvant chemotherapy
- Assaying for loss of heterozygosity (LOH) on the long arm of chromosome 18 (18q) or deleted in colon cancer (DCC) protein determination by immunohistochemistry to determine the prognosis of operable colorectal cancer, or to predict response to therapy
- Use of CA 19-9 as a screening test for pancreatic cancer
- Use of CA 19-9 testing alone for determining operability or the results of operability in pancreatic cancer and for providing definitive evidence of disease recurrence

MAJOR OUTCOMES CONSIDERED

- Overall survival
- Disease-free survival
- Quality of life
- Toxicity
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

For the 2006 update, methodology was used that was similar to that applied in the original American Society of Clinical Oncology (ASCO) practice guidelines for use of tumor markers. Pertinent information published from 1999 through November 2005 was reviewed for markers that were included in the last update of the guideline; information from 1966 to November 2005 was reviewed for the new markers. The Medline database (National Library of Medicine, Bethesda, MD) was searched to identify relevant information from the published literature for this update. A series of searches was conducted using the medical subject headings or text words for each of the markers with the corresponding disease site (colon, rectal, or pancreatic cancer). Search results were limited to human studies and English-language articles; editorials, letters, and commentaries were excluded from consideration. The Cochrane Library was searched for available systematic reviews and meta-analyses using the phrases, "tumor markers" and "biomarkers." Directed searches based on the bibliographies of primary articles were also performed. Finally, Update Committee members contributed articles from their personal collections. Update Committee members reviewed the resulting abstracts and titles that corresponded to their assigned section. Inclusion criteria were broad. Update Committee members focused attention on systematic reviews and

meta-analyses, and on studies that considered markers in relation to ASCO clinical outcomes for guideline and technology assessment (overall survival, disease-free survival, quality of life, toxicity, and cost-effectiveness).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The American Society of Clinical Oncology (ASCO) first published evidence-based clinical practice guidelines for the use of tumor markers in colorectal cancer in 1996. ASCO guidelines are updated at intervals by an update committee of the original expert panel. The last update of the tumor markers guideline was published in 2000. For the 2006 update, the Panel expanded the scope of the guideline to include a broader range of markers in colorectal cancer and, new to this guideline, pancreatic cancer markers.

The Update Committee had two face-to-face meetings to consider the evidence for each of the 2000 recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Published studies or reviews of cost-effectiveness were considered in the preparation of this guideline:

- Carcinoembryonic antigen (CEA) is considered a valuable component of postoperative follow-up, is the most frequent indicator of recurrence in asymptomatic patients, is more cost-effective than radiology for the detection of potential curable recurrence, and is the most sensitive detector for liver metastases.
- Economic analyses suggest that intensive follow-up that incorporates CEA testing is cost-effective compared with conventional follow-up.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was circulated in draft form to the Update Committee, per the American Society of Clinical Oncology (ASCO) guideline policy. ASCO's Health Services Committee and the ASCO Board of Directors also reviewed the final document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Carcinoembryonic Antigen as a Marker for Colorectal Cancer

2006 recommendation for carcinoembryonic antigen as a screening test. Carcinoembryonic antigen (CEA) is not recommended for use as a screening test for colorectal cancer.

2006 recommendation for preoperative carcinoembryonic antigen (CEA) testing. 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.

2006 recommendation for postoperative CEA testing. Postoperative serum CEA testing should be performed every 3 months in patients with stage II or III disease for at least 3 years after diagnosis if the patient is a candidate for surgery or systemic therapy. 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 (Ueno et. al, 2000). CEA elevations within a week or two following chemotherapy should be interpreted with caution (Sorbye & Dahl, 2003).

2006 recommendation for CEA testing to monitor metastatic colorectal cancer. CEA is the marker of choice for monitoring metastatic colorectal cancer during systemic therapy. CEA should be measured at the start of treatment for

metastatic disease and every 1 to 3 months during active treatment. Persistently rising values above baseline should prompt restaging, but suggest progressive disease even in the absence of corroborating radiographs. Caution should be used when interpreting a rising CEA level during the first 4 to 6 weeks of a new therapy, since spurious early rises may occur especially after oxaliplatin use (Sorbye & Dahl, 2003; Sorbye & Dahl, 2004).

CA 19-9 As a Marker for Colon Cancer

2006 recommendation for use of CA 19-9 in colon cancer. Present data are insufficient to recommend CA 19-9 for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

DNA Ploidy or Flow Cytometric Proliferation Analysis As a Marker for Colon Cancer

2006 recommendation for DNA ploidy or DNA flow cytometric proliferation analysis to determine prognosis. Neither flow-cytometrically derived DNA ploidy (DNA index) nor DNA flow cytometric proliferation analysis (%S phase) should be used to determine prognosis of early-stage colorectal cancer.

p53 As a Marker for Colorectal Cancer

2006 recommendations for p53 testing. 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.

ras As a Marker for Colorectal Cancer

2006 recommendation for ras *testing*. 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.

Thymidine Synthase, Dihydropyrimidine Dehydrogenase, and Thymidine Phosphorylase As Markers in Colorectal Cancer

Note: These topics are new to the guideline.

2006 recommendation for thymidine synthase, dihydropyrimidine dehydrogenase, and thymidine phosphorylase as screening tests. Thymidine synthase (TS), dihydropyrimidine dehydrogenase (DPD), and thymidine phosphorylase (TP) are tissue markers that have been used to predict response to treatment of established carcinomas and thus are not useful for screening.

2006 recommendation for use of TS, DPD, or TP for prognosis. None of the three markers—TS, DPD, or TP—are recommended for use to determine the prognosis of colorectal carcinoma.

2006 recommendation for use of TS, DPD, or TP in predicting response to therapy. There is insufficient evidence to recommend use of TS, DPD, or TP as predictors of response to therapy.

2006 recommendation for use of TS, DPD, or TP in monitoring response to therapy. There is insufficient evidence to recommend use of TS, DPD, or TP for monitoring response to therapy.

Microsatellite Instability/hMSH2 or hMLH1 As Markers in Colorectal Cancer

Note: This topic is new to the guideline.

2006 recommendation for use of microsatellite instability to determine prognosis. Microsatellite instability (MSI) ascertained by polymerase chain reaction (PCR) is not recommended at this time to determine the prognosis of operable colorectal cancer nor to predict the effectiveness of FU adjuvant chemotherapy.

***1* 8q-LOH/DCC As Markers for Colorectal Cancer**

Note: This topic is new to the guideline.

2006 recommendation for use of 18q-LOH/DCC to determine prognosis or to predict response to therapy. Assaying for loss of heterozygosity (LOH) on the long arm of chromosome 18 (18q) or deleted in colon cancer (DCC) protein determination by IHC should not be used to determine the prognosis of operable colorectal cancer, nor to predict response to therapy.

CA 19-9 as a Marker for Pancreatic Cancer

Note: This topic is new to the guideline.

2006 recommendation for use of CA 19-9 as a screening test. CA 19-9 is not recommended for use as a screening test for pancreatic cancer.

2006 recommendation for use of CA 19-9 to determine operability. The use of CA19- 9 testing alone is not recommended for use in determining operability or the results of operability in pancreatic cancer.

2006 recommendation for use of CA 19-9 to provide evidence of recurrence. CA 19-9 determinations by themselves cannot provide definitive evidence of disease recurrence without seeking confirmation with imaging studies for clinical findings and/or biopsy.

2006 recommendation for use of CA19-9 for monitoring response to therapy. Present data are insufficient to recommend the routine use of serum CA 19-9 rules alone for monitoring response to treatment. However, CA19-9 can be measured at the start of treatment for locally advanced metastatic disease and every 1 to 3 months during active treatment. If there is an elevation in serial CA19-9 determinations, this may be an indication of progressive disease, and confirmation with other studies should be sought.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The evidence supporting each recommendation is presented in the original guideline document under "literature update and discussion" following each recommendation. The Update Committee's literature review focused attention on available systematic reviews and meta-analyses of published tumor marker studies. By and large, however, the literature is characterized by studies that included small patient numbers, studies that were retrospective, and studies that commonly performed multiple analyses until one revealed a statistically significant result ($P<.05$). In the scale for grading the clinical utility of tumor markers used by the Update Committee, these studies are designated as Level of Evidence III.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of tumor markers for prevention, screening, treatment, and surveillance of gastrointestinal tumors

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- By and large the literature is characterized by studies that included small patient numbers, studies that were retrospective, and studies that commonly performed multiple analyses until one revealed a statistically significant result ($P<.05$). In the scale for grading the clinical utility of tumor markers used by the Update Committee, these studies are designated as Level of Evidence III. The Level of Evidence in this grading scale defines the quality of the data on a given marker. The Update Committee underscores that the preferred way to assess tumor markers is within Level of Evidence II studies (prospective therapeutic trials in which marker utility is a secondary study objective), or, ideally, within Level of Evidence I studies (single, high-powered, prospective, randomized controlled trials specifically designed to test the marker or a meta-analyses of well-designed studies).
- It is important to emphasize that guidelines and technology assessments cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations, and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at

obtaining the same result. Accordingly, the American Society of Clinical Oncology (ASCO) considers adherence to this guideline assessment to be voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient's individual circumstances. In addition, this guideline describes the use of procedures and therapies in clinical practice; it cannot be assumed to apply to the use of these interventions performed in the context of clinical trials, given that clinical studies are designed to evaluate or validate innovative approaches in a disease for which improved staging and treatment is needed.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources
Quick Reference Guides/Physician Guides
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, Somerfield MR, Hayes DF, Bast RC Jr, ASCO. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol 2006 Nov 20;24(33):5313-27. [167 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2006 Nov 20)

GUIDELINE DEVELOPER(S)

American Society of Clinical Oncology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Clinical Oncology

GUIDELINE COMMITTEE

American Society of Clinical Oncology (ASCO) Expert Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following authors or their immediate family members indicated a financial interest. No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

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Nancy Kemeny					Pfizer; Genetech	Pfizer; Codman; Sanofi		
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Robert C. Bast Jr			Fujirbio; Ciphergen; Tannox			Fujiribio		Fujirbio

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: 2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001 Mar 15;19(6):1865-1878.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Society of Clinical Oncology (ASCO) Web site.

Print copies: Available from American Society of Clinical Oncology, Cancer Policy and Clinical Affairs, 1900 Duke Street, Suite 200, Alexandria, VA 22314; E-mail: guidelines@asco.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- 2006 update of ASCO recommendations for the use of tumor markers in gastrointestinal cancer. J Oncol Prac 2006 Nov; 2(6):314-316. Available in Portable Document Format (PDF) from the American Society of Clinical Oncology (ASCO) Web site.

- 2006 update revisions table. 2006 update of the ASCO guideline for the use of tumor markers in gastrointestinal (GI) cancer. 2006. 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American Society of Clinical Oncology (ASCO) Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- Use of tumor markers in gastrointestinal cancer: 2006 update. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2006. 28 p. Electronic copies: Available in Portable Document Format (PDF) from the American Society of Clinical Oncology (ASCO) Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.

Guidelines are available for Personal Digital Assistant (PDA) download from the ASCO Web site.

PATIENT RESOURCES

The following is available:

- ASCO patient guide: tumor markers for gastrointestinal cancers. 2006 Oct. 4 p. Available from the Cancer.Net Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on November 21, 2006. The information was verified by the guideline developer on December 6, 2006.

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