



American Society of Clinical Oncology

Making a world of difference in cancer care

**Use of Tumor Markers in
Gastrointestinal Cancer:
2006 Update**

Clinical Practice Guideline

Introduction

- ASCO convened an Update Committee to review and update recommendations for the use of tumor markers in gastrointestinal (GI) cancers.
- These guidelines were originally published in 1996 and previously updated in 2000.
- The 2006 Update expands the scope of the guideline to include a broader range of markers in colorectal cancer and new evidence on pancreatic cancer markers.

Guideline Methodology: Systematic Review

- An ASCO Update Committee completed a review and analysis of data published since 1999 to November 2005 (or from 1966 to November 2005 for new markers):
 - ✓ MEDLINE
 - ✓ Cochrane Collaboration Library

Guideline Methodology (cont'd): Panel Members

- Robert C. Bast, Jr., MD, *Co-Chair*
- Daniel F. Hayes, MD, *Co-Chair*
- Dean F. Bajorin, MD
- Jonathan S. Berek, MD
- Ross S. Berkowitz, MD
- Roy Beveridge, MD
- Herbert Fritsche, Jr., PhD
- Timothy Gilligan, MD
- Stanley Hamilton, MD
- Jules Harris, MD
- Lyndsay Harris, MD
- John M. Jessup, MD

MD Anderson Cancer Center
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Memorial Sloan-Kettering Cancer Center
UCLA School of Medicine
Brigham & Women's Hospital
Fairfax Northern VA Hem/Onc
MD Anderson Cancer Center
Dana Farber Cancer Institute
MD Anderson Cancer Center
Rush-Presbyterian St. Luke's Medical Center
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Guideline Methodology (cont'd): Panel Members

- Philip W. Kantoff, MD
- Nancy E. Kemeny, MD
- Ann Kolker
- Susan Leigh, BSN, RN
- Gershon Y. Locker, MD
- Juanita Lyle
- John S. Macdonald, MD
- Pam McAllister, PhD
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Science Advocate, Colorectal Cancer Coalition

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2006 Updated Recommendations for GI Tumor Markers

- Carcinoembryonic Antigen (CEA) as a Marker for Colorectal Cancer
- CA 19-9 as a Marker for Colon Cancer
- DNA Ploidy or Flow Cytometric Proliferation as a Marker for Colon Cancer
- p53 as a Marker for Colorectal Cancer
- ras as a Marker for Colorectal Cancer
- TS, DPD and TP as Markers in Colorectal Cancer **NEW!**
- MSI as a Marker in Colorectal Cancer **NEW!**
- 18q-LOH/DCC as Markers for Colorectal Cancer **NEW!**
- CA 19-9 as a Marker for Pancreatic Cancer **NEW!**

CEA as a Marker for Colorectal Cancer

Screening	CEA is not recommended to be used as a screening test for colorectal cancer.
Preoperative	May be ordered preoperatively in patients with colorectal carcinoma if it would assist in staging and surgical treatment planning. Elevated preoperative CEA (>5 mg/ml) may correlate with poorer prognosis, but data are insufficient to support its use to determine whether to provide adjuvant therapy.
Postoperative	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. CEA elevations within a week or two of following chemotherapy should be interpreted with caution.
Monitoring Response to Therapy	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 1-3 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 4-6 weeks of a new therapy, since spurious early rises may occur especially after Oxaliplatin.

CA 19-9 as a Marker for Colon Cancer

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

NOT RECOMMENDED				
Screening	Diagnosis	Staging	Surveillance	Monitoring

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

- 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.

NOT RECOMMENDED	
DNA Index	% S-Phase

p53 as a Marker for Colorectal Cancer

- 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.

NOT RECOMMENDED				
Screening	Diagnosis	Staging	Surveillance	Monitoring

ras as a Marker for Colorectal Cancer

- 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.

NOT RECOMMENDED				
Screening	Diagnosis	Staging	Surveillance	Monitoring

TS, DPD & TP as Markers for Colorectal Cancer

Screening	TS, DPD, and TP are tissue markers that have been used to predict response to treatment of established carcinomas and thus are not useful for screening.
Prognosis	None of the three markers—TS, DPD, or TP—is recommended for use in determining the prognosis of colorectal carcinoma
Predicting Response to Therapy	There is insufficient evidence to recommend use of TS, DPD, or TP as predictors of response to therapy
Monitoring Response to Therapy	There is insufficient evidence to recommend use of TS, DPD, or TP for monitoring response to therapy

MSI as a Marker in Colorectal Cancer

- Microsatellite Instability (MSI) ascertained by PCR is not recommended at this time to determine the prognosis of operable colorectal cancer nor to predict the effectiveness of 5-FU adjuvant chemotherapy.

NOT RECOMMENDED	
Determine Operability Prognosis	Predict Response to Therapy

18q-LOH/DCC as Markers for Colorectal Cancer

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

NOT RECOMMENDED	
Determine Operability Prognosis	Predict Response to Therapy

CA 19-9 as a Marker for Pancreatic Cancer

Screening	CA 19-9 is not recommended to be used as a screening test for pancreatic cancer.
Operability	The use of CA19-9 testing alone is not recommended for use in determining operability or the results of operability in pancreatic cancer.
Disease Recurrence	CA19-9 determinations by themselves cannot provide definitive evidence of disease recurrence without seeking confirmation with imaging studies for clinical findings and/or biopsy.
Monitoring Treatment Response	Present data are insufficient to recommend the routine use of serum CA19-9 levels alone for monitoring response to treatment. However, CA19-9 can be measured at the start of treatment for locally advanced metastatic disease and every one to three 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.

Summary

	Not Recommended	Recommended	
CEA Colorectal	Screening test	Preoperative testing, postoperatively in stage II or III patients, and monitoring metastatic cancer during systemic therapy	
CA 19-9 Colon	Screening, diagnosis, staging, surveillance, or monitoring		
DNA Ploidy, Flow Cytometry Colon	Determining prognosis of early stage colorectal cancer		
p53 Colorectal	Screening diagnosis, staging, surveillance or monitoring		
ras Colorectal	Screening diagnosis, staging, surveillance or monitoring		
TS, DPD, TP Colorectal	Screening, prognosis, predicting or monitoring therapeutic response		
MSI Colorectal	Prognosis of operable cancer, prediction of 5-FU effectiveness		
18q-LOH/DCC Colorectal	Prognosis of operable cancer, or predicting therapeutic response		
CA 19-9 Pancreatic	Screening test, solo use for determining operability, operability results, or monitoring response to treatment		Measure at start of treatment for locally advanced metastatic disease and every 1-3 months during treatment.

Additional ASCO Resources

- This slide set, a GI tumor marker matrix, and additional resources can be accessed at: <http://www.asco.org/guidelines/gitm>
- A patient guide can be accessed at the website above or at <http://www.cancer.net>



ASCO Guidelines

It is important to realize that many management questions have not been comprehensively addressed in randomized trials and guidelines cannot always account for individual variation among patients. A guideline is 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 results. Accordingly, ASCO considers adherence to this guideline 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, the guideline describes administration of therapies in clinical practice; it cannot be assumed to apply to interventions performed in the context of clinical trials, given that clinical studies are designed to test innovative and novel therapies in a disease and setting for which better therapy is needed. Because guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions for further research and those settings in which investigational therapy should be considered.