

TEN BEST READINGS RELATING TO COLORECTAL CANCER

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Walsh JM, Terdiman JP. Colorectal cancer screening: clinical applications. *JAMA*. 2003;289:1297-1302.

This article outlines guidelines for colorectal cancer screening, reviews the evidence supporting the use of these tests, and evaluates their availability and cost effectiveness. Potential barriers to implementation of colorectal cancer screening and strategies to increase compliance are discussed.

Saltz LB, Cox JV, Blanke C, et al. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. Irinotecan Study Group. *N Engl J Med*. 2000;343:905-914.

Patients receiving irinotecan, fluorouracil and leucovorin in triple combination exhibited longer progression-free survival, a higher response rate, and longer overall survival when compared with patients receiving either combination therapy with fluorouracil and leucovorin or irinotecan alone. Adding irinotecan to a regimen of fluorouracil and leucovorin did not compromise quality of life or add toxicity, making triple-drug therapy a new standard of care.

Benson AB 3rd, Choti MA, Cohen AM, et al. NCCN practice guidelines for colorectal cancer. *Oncology (Huntingt)*. 2000;14:203-212.

The NCCN endorses a multidisciplinary approach in the management of patients with colorectal cancer, with treatment as part of a clinical trial taking precedence over standard therapy. This

article summarizes the findings of a panel convened to recommend treatment standards for colorectal cancer.

Kim CJ, Yeatman TJ, Coppola D, et al. Local excision of T2 and T3 rectal cancers after downstaging chemoradiation. *Ann Surg*. 2001;234:352-359.

This study tested the hypothesis that chemoradiation prior to surgery in patients with T2 and T3 distal rectal cancers could downstage the tumor sufficiently to allow local excision of the tumors, a practice normally associated with high recurrence rates in T2 and T3 lesions. Patients were treated with external-beam radiation and concomitant chemotherapy with fluorouracil. In general, only those patients who exhibited a complete clinical response were considered for local excision. None of the patients with complete pathological response had experienced recurrence.

Kapiteijn EM, Larijnen CA, Nagtegaal ED, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med*. 2001;345:638-646.

This study compared adjunctive preoperative radiation therapy in combination with total mesorectal excision to excision alone. Adjunctive radiation therapy reduced the 2-year local recurrence rate from 8.2% to 2.4%. The 2-year survival rate for both treatment groups, 82%, was the same.

Baron JA, Cole BF, Sandler RS, et al. A randomized trial of aspirin



The 10 best recent articles in the medical literature relating to colorectal cancer are reviewed here.

Ten Best Readings

to prevent colorectal adenomas. *N Engl J Med.* 2003;348:891-899.

This trial examined the efficacy of aspirin as a chemopreventive agent against colorectal adenomas. Although low-dose aspirin seemed to have a moderate chemopreventive effect, it was unclear why the higher dose of aspirin did not significantly reduce the rate of adenoma recurrence. The incidence of stroke and serious bleeding was higher in patients receiving aspirin, but the difference was not statistically significant.

Sandler RS, Halabi S, Baron JA, et al. A randomized trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. *N Engl J Med.* 2003;348:883-890.

In the companion study to the above trial by Baron et al, patients who were cured of colorectal cancer were randomly assigned to receive 325 mg of aspirin or placebo daily. The trial was terminated after a median duration of treatment of 31 months because one or more adenomas were found in 27% of placebo-treated patients but in only 17% of aspirin-treated patients. The size of adenomas formed and the proportion of patients with advanced adenomas were similar in both treatment groups.

Tepper JE, O'Connell M, Niedezwiecki D, et al. Adjuvant therapy in rectal cancer: analysis of stage, sex, and local control. final report of Intergroup 0114. *J Clin Oncol.* 2002;20:1744-1750.

This large study of 1,695 patients compared four different postsurgical fluorouracil (5FU)-

based therapies in patients with T3/4 and N+ rectal cancer: bolus 5FU alone, 5FU plus leucovorin, 5FU plus levamisole, and 5FU plus both leucovorin and levamisole. All patients received two cycles of chemotherapy followed by chemoradiation and two additional cycles of chemotherapy. There was no difference in overall or disease-free survival among the treatment groups.

de Gramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. *J Clin Oncol.* 2000;18:2938-2947.

Patients receiving oxaliplatin had a significantly longer progression-free survival (9.0 vs 6.2 months), but overall survival was not significantly different. Oxaliplatin was associated with a higher incidence of grade 3/4 neutropenia, grade 3/4 diarrhea, and grade 3 neurosensory toxicity, but quality of life was not affected.

Agrawal D, Chen T, Irby R, et al. Osteopontin identified as lead marker of colon cancer progression, using pooled sample expression profiling. *J Natl Cancer Inst.* 2002;94:513-521.

RNA from 60 human colon tumors of multiple stages was pooled according to the stage of tumor. The genetic profiles of these tumors were compared with the genetic profiles of 10 pooled normal mucosal specimens. Gene expression analysis using microarray technology identified more than 300 potential markers of colon cancer progression. Eleven were validated through additional experi-

ments, and the gene for osteopontin, a secreted protein that binds integrin, was the most consistently differentially expressed in relation to the stage of tumor. Osteopontin may be a clinically useful marker of colon cancer progression.