The following colorectal cancer research update extends from June 19 – July 17, 2009 inclusive and is intended for informational purposes only.

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**DRUGS / SYSTEMIC THERAPY**

1. Emend Improves Prevention of Chemo-Induced Nausea & Vomiting  
   (Jun. 25/09)

This study showed that Emend (aprepitant) in combination with a standard antiemetic (anti-nausea) regimen of ondansetron and dexamethasone significantly improved the prevention of chemo-induced nausea and vomiting in both men and women with various cancer types – breast, lung, colorectal and ovarian – who received a first cycle of a broad range of moderately emetogenic (vomit-inducing) chemo.

This randomized, double-blind study involved 848 male and female patients. Patients scheduled to receive a single dose of moderately emetogenic chemo with one or more of a broad range of chemo agents were randomized into one of the following:

- Those taking aprepitant who received an antiemetic regimen consisting of 125 mg aprepitant, ondansetron 8 mg twice daily and dexamethasone 12 mg on day 1, and aprepitant 80 mg once daily on days 2 and 3.
- Those in the control group who received the standard regimen consisting of ondansetron 8 mg twice daily and dexamethasone 20 mg on day 1 and ondansetron 8 mg twice daily on days 2 and 3.

More patients taking aprepitant in combination with standard therapy reported no vomiting during the 120 hours following initiation of the first cycle of chemo compared to the control group. (76.2% vs. 62.1%). Significantly more patients achieved a complete response (meaning no vomiting and no use of rescue meds) up to 120 hours post-chemo compared to the control group (68.7% vs. 56.3%).

2. **Avastin + Chemo is Safe & Effective for Older Patients with mCRC** (Jun. 26/09)

This study demonstrated that older patients with metastatic colorectal cancer do not suffer a greater degree of toxicity from treatment with bevacizumab (avastin), according to the results presented at the 11th World Gastrointestinal Cancer Congress of the European Society for Medical Oncology (ESMO-GI). The study compared the clinical benefit of bevacizumab in 3 age-based populations of patients with metastatic colorectal cancer. The study was referred to as the BEAT study and it enrolled 1,914 patients of whom 50% received bevacizumab plus oxaliplatin-based therapy, 35% received bevacizumab plus irinotecan-based therapy, and 15% received bevacizumab plus monotherapy. Of these patients, 1,286 (67%) were aged <65 years, 499 (26%) were aged 65 to 74 years, and 129 (7%) were aged >75 years. Overall, similar median progression-free survival (time before the disease got worse) was seen across all subgroups. The incidence of bevacizumab-related toxicities such as gastrointestinal perforation, postoperative bleeding, wound-healing complications, and hypertension was similar in all groups. Researchers concluded that bevacizumab plus chemotherapy is a safe and effective treatment for older patients with metastatic colorectal cancer and that this patient population can derive similar clinical benefits to younger patients with similar toxicity.

Van Cutsem Eric, et al., Safety and Efficacy of bevacizumab and chemotherapy in elderly patients with metastatic colorectal cancer (mCRC): Results from the BEAT Observational cohort Study. Presented at2009 ESMO-GI. Abstract #5

3. **Adding Erbitux to Standard Chemo Improves Liver Resectability** (Jun. 26/09)

A study presented at the 11th World Gastrointestinal Cancer Congress of the European Society for Medical Oncology (ESMO-GI) showed that tumour response and resectability rates in patients with nonresectable colorectal liver metastases are favourably increased when cetuximab (erbitux) is added to 2 standard chemotherapy regimens. Researchers presented the results of this study (CELIUS) wherein it compared response rates in 111 patients with nonresectable colorectal liver metastases in response to the addition of cetuximab (erbitux) to either folic acid, fluorouracil, and irinotecan (FOLFIRI) or folic acid, fluorouracil, and oxaliplatin (FOLFOX6). Patients were randomized to receive cetuximab weekly plus either FOLFOX6 or FOLFIRI for 8 cycles as preoperative therapy. The response rate was 62% overall: 70% in patients with Kras wild-type tumours and 43% in patients with Kras mutant tumours (68% Folfox 6, 57% Folfiri). Scans from baseline and 4 months were compared and showed that 32% of patients had changed from nonresectable to resectable and 6% from resectable to nonresectable status during this interval. The researchers concluded that the combination of standard chemotherapy plus cetuximab increases response rates, especially in patients with KRAS wild-type tumours, and that resectability was improved.

Kohne, Claus-Henning, et al., Results from the CELIUS Study: Cetuximab plus folfox6 or cetuximab plus folfiri as neoadjuvant treatment for nonresectable colorectal cancer liver metastases. Presented at 2009 ESMO-GI. Abstract #22

4. **Folfoxiri Prolongs Survival in mCRC Patients** (Jun. 29/09)

Prolonged survival is seen in patients with metastatic colorectal cancer (mCRC) treated with irinotecan, oxaliplatin, leucovorin, and fluorouracil (FOLFOXIRI) at ~60 months of follow-up, according to results presented at the 11th World Gastrointestinal Cancer Congress of the European Society for Medical Oncology (ESMO-GI). At 18.4 months, FOLFOXIRI yielded significant improvements in response rate over fluorouracil, leucovorin, and irinotecan (FOLFIRI: 60% vs 34%), secondary radical resection (R0) of metastases (15% vs 6%), progression-free survival – time before disease got worse - (PFS; 9.8 vs 6.9 months), and overall survival (OS; 22.6 vs 16.7 months). Treatment with FOLFOXIRI consisted of irinotecan on day 1, oxaliplatin on day 1, leucovorin on day 1, and fluorouracil 48-hour continuous infusion starting on day 1, every 2 weeks. At 60.6 months, PFS and OS were observed in patients receiving FOLFOXIRI compared with FOLFIRI (PFS, 9.8 vs 6.8 months; OS, 23.4 vs 16.7 months). The 5-year survival rate was 15% in the FOLFOXIRI arm versus 8% in the FOLFIRI arm. According to the researchers, the results demonstrate that the FOLFOXIRI regimen is associated with a better long-term outcome than FOLFIRI.

Falcone, Antonio, et al., Folfoxiri (irinotecan, Oxaliplatin, infusional 5FU/LV) vs. Folfiri as First Line treatment of metastatic colorectal cancer (mCRC): Updated Results after 5 years follow up and risk-stratified analysis. Presented at 2009 ESMO-GI. Abstract #PD-0016

5. **Adding Irinotecan to 5FU After Liver Surgery Adds No Benefit & Increases Side Effects** (Jul. 1/09)

The objective of this randomized, multicenter phase III trial was to investigate whether the addition of irinotecan to infusional fluorouracil (FU)/leucovorin (LV) adjuvant (post surgical) regimen would improve disease free survival (time before disease got worse) in patients with stage III colon cancer. After liver surgery, patients with stage II and III colon cancer were randomly allocated to receive LV/5FU every 2 weeks for 12 cycles with or without irinotecan every 2 weeks. After a followup of 66.3 months, the 5 year disease free survival rate was 56.7% with the irinotecan group and 54.3% in those who did not access...
irinotecan. Combining irinotecan with LV and 5FU did not significantly improve overall survival in this patient group compared with the LV/5FU alone (5 year OS rate was 73.6% vs. 71.3% respectively). And the addition of irinotecan was associated with an increased incidence of grade 3 to 4 gastrointestinal events and neutropenia (diminished white blood cells). The researchers concluded that adding irinotecan to LV/5FU as adjuvant therapy did not confer a statistically significant improvement in disease free survival or overall survival in patients with stage III colon cancer compared with LV/5FU alone.


6. Phase III Sunitinib (Sutent) Trial in mCRC Stopped (Jul. 1/09)

There has been a discontinuation of a phase-3 SUN1122 clinical trial that was evaluating sunitinib plus FOLFIRI vs. FOLFIRI alone in the first-line treatment of metastatic colorectal cancer. An Independent Data Monitoring Committee found that the addition of sunitinib (Sutent) to FOLFIRI did not result in better progression-free survival than FOLFIRI alone among patients with metastatic colorectal cancer. The manufacturer Pfizer has notified clinical trial investigators involved in the study and regulatory agencies. Sutent is a targeted therapy that works by blocking multiple molecular targets implicated in the growth, proliferation, and spread of cancer. The combination of Sutent with chemotherapy for the initial treatment of metastatic colorectal cancer was being evaluated in a Phase III clinical trial known as SUN 1122. The chemotherapy regimen that was used in the trial was FOLFIRI (irinotecan plus infusional 5-fluorouracil and leucovorin). Patients were assigned to receive either FOLFIRI alone or FOLFIRI plus Sutent. The trial was stopped early when the independent Data Monitoring Committee reviewed preliminary data and concluded that the combination of FOLFIRI and Sutent would not result in better progression-free survival than FOLFIRI alone. These results suggest that the addition of Sutent to a standard first-line chemotherapy regimen does not improve outcomes among patients with metastatic colorectal cancer. The study results do not affect the approved indications with sunitinib as monotherapy, where it has played a significant role in advancing the care of patients. Sutent is currently approved by the FDA to treat gastrointestinal stromal tumors (GIST) that have stopped responding to Glivec (Imatinib), as well as for advanced renal cell (kidney) cancers.

www.hemonctoday.com/article.aspx?id=41305

7. Two Avastin-Based Combination Regimens Are Equally Effective in Treating mCRC (Jul. 2/09)

Researchers are reporting that combining bevacizumab (BEV) – also known as avastin - with capecitabine (xeloda) plus irinotecan (XELIRI) is an effective alternative to BEV plus 5-fluorouracil (5-FU), leucovorin, and irinotecan (FOLFIRI) in patients with metastatic colorectal cancer (mCRC). The phase II study was presented at the 11th World Gastrointestinal Cancer Congress of the European Society for Medical Oncology (ESMO-GI). A total of 145 patients, aged 18 to 72 years, were randomized to receive either BEV plus XELIRI or BEV plus FOLFIRI. Patients in the XELIRI arm received irinotecan on day 1, capecitabine twice a day on days 1 to 14 plus bevacizumab on day 1, every 3 weeks for a maximum of 8 cycles. Patients in the FOLFIRI arm received irinotecan on day 1 plus 5-FU plus leucovorin on day 1 followed by 5-FU as a 46-hour infusion plus bevacizumab on day 1, every 2 weeks for a maximum of 12 cycles. The 6-month overall response rate was 54% in the BEV plus XELIRI arm compared with 59% in the BEV plus FOLFIRI arm. Disease progression was seen in 14 (19%) patients in the BEV plus XELIRI arm versus 10 (14%) patients in the BEV plus FOLFIRI arm. Stable disease was achieved by 13 (18%) patients in the BEV plus XELIRI arm and in 15 (21%) patients in the BEV plus FOLFIRI arm. The investigators concluded that both treatment groups demonstrated manageable toxicity and that XELIRI and FOLFIRI plus bevacizumab are both effective in the treatment of patients with mCRC.

Ducreux, Michel, et al., Efficacy and safety of bevacizumab-based combination regimens in patients with metastatic colorectal cancer: Preliminary results from a randomized phase II study of bevacizumab + folfi vs. bevacizumab + Xeliri (FNCLCC Accord 13-0503 Study). Presented at 2009 ESMO-GI. Abstract # O-0006

8. Exiqon Dx Announces BRAF Mutation Analysis for Predicting Anti-EGFR Therapy Response (Jul.6/09)

Exiqon has announced that it can now offer BRAF Mutation Analysis through its CLIA laboratory in California. Cancer treating physicians now have access to this critical test for their advanced stage colorectal cancer patients who are candidates for anti-EGFR targeted therapy. A recent clinical study correlates the presence of BRAF mutations in colorectal cancer tumors with lack of patient response to cetuximab (erbixut) and panitumumab (vectibix) therapy. Confirmed BRAF mutation status is important information for physicians to have when deciding on a treatment regimen. Results of the BRAF Mutation Analysis can help oncologists determine if their colorectal cancer patients are appropriate candidates for cetuximab or panitumumab therapy. BRAF testing is important because it can identify the subset of colorectal cancer patients who do not have a mutated KRAS gene yet still do not respond to anti-EGFR therapy. Non-responsiveness in this group of patients is most likely due to the V600E mutation in the BRAF gene. Testing patients for both KRAS and BRAF provides a more complete analysis of the patient’s tumor when evaluating candidates for anti-EGFR therapy. Both BRAF and KRAS mutation testing is important so that treating physicians may gain a more complete picture of the patient's tumor
before targeted therapy is initiated. Those patients who have the BRAF mutation would most likely not respond and should not be treated with those ineffective and expensive anti-EGFR agents.

www.globenewswire.com/newsroom/news.html?id=168558

SURGICAL INTERVENTIONS

9. Lack of Response to Neoadjuvant Therapy Does Not Preclude Long-Term Survival After Liver Resection  (Jun. 29/09)

Liver resection is the only curative treatment offering a chance of long-term survival in patients with colorectal liver metastases (CRM). Recent data indicated that liver resection in patients with tumor progression while receiving chemotherapy was associated with poor outcome. The aim of this study was to identify risk factors for poor outcome in patients with pre-operative chemotherapy of CRM. Researchers analyzed 160 patients after liver resection for CRM with preoperative systemic chemotherapy. Three groups of patients were identified: 44 patients (27.5%) had a tumor response, 20 (12.5%) showed stable disease, and 96 (60%) patients had tumor progression while on chemotherapy. Patients were followed-up at 2.4 years. Survival was 88%, 53%, and 37% at 1, 3, and 5 years. Noncurative resection, carcinoembryonic antigen levels >200, tumor grading, size of the largest tumor >5 cm, and number of metastases were associated with poor patient outcome. Tumor progression while on chemotherapy had no influence on the long-term survival. Researchers concluded that liver resection offers a long-term survival benefit for patients with CRM, even when tumor growth proceeds during pre-operative chemotherapy.


10. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy to Treat Peritoneal Mets  (Jun. 30/09)

Peritoneal Carcinomatosis is the condition of widespread dissemination of cancer throughout the peritoneal sack that encompasses the organs in the abdomen. The peritoneal carcinomatosis diagnosis is given when the cancer tumors have formed on this peritoneal sack. This only happens after cancer has metastasized from primary cancers such as colorectal. In the past, peritoneal carcinomatosis from colorectal origin carried a poor prognosis. Recent clinical studies show that cytoreductive surgery (CS – surgical removal of the cancer) combined with hyperthermic intraperitoneal chemotherapy (HIPEC – bathing of abdominal organs with heated chemotherapy – see schematic below) improves survival of selected patients with a colorectal carcinoma and isolated peritoneal carcinomatosis in the absence of other metastatic sites. This study reports on the clinical outcomes and survival after cytoreductive surgery and HIPEC of a group of patients treated. Sixty-seven patients underwent surgery. Complete cytoreduction could be performed in 49 patients, who underwent a total of 53 CS-HIPEC procedures. All had peritoneal carcinomatosis originating from primary colorectal, cecal, appendiceal, and gastric tumors. In patients who underwent CS-HIPEC, a resection could be achieved in 88%. The 30-day mortality was 0; one patient died in-hospital after 10 weeks. The average hospital stay was 12 days (range 4-56). Average time to recurrence was 12 months (range 4-22). The 1-year survival was 88% and 2-year survival was 75%. Researchers concluded that in well-selected patients referred to a specialized institution, CS-HIPEC has an acceptable morbidity and high survival rate.
Diagram of the hyperthermic intraoperative intraperitoneal chemotherapy apparatus


11. Treatment of Rectal Adenomas by Transanal Endoscopic Microsurgery (TEM) (Jul. 6/09)

This study presented results concerning the management of rectal adenomas through the use of transanal endoscopic microsurgery (TEM). The goals of the study were to examine the institution's experience by evaluating surgical morbidity, mortality, and local recurrence rate associated with the removal of rectal adenomas through TEM. This retrospective study investigated 402 patients who underwent TEM for a preoperative diagnosis of adenoma from January 1993 to October 2008. The average age of patients was 65 years (range = 22–92 years). All patients were regularly followed up to determine treatment efficacy in terms of local recurrence rate. No 30-day mortality occurred. There was no conversion to laparoscopic or open procedures. Minor complications occurred in 28 (7%) patients, whereas major complications were found only in 2 (0.5%) patients. Confirmed adenomas were found in 366 cases (91%). At an average follow-up of 84 months (range = 1–190 months), 16 (4%) adenomas recurred and were successfully retreated by TEM [14 cases (87.5%)] and by conventional surgery [2 patients (12.5%)]. No further recurrences were observed at subsequent follow-up. Researchers concluded that TEM is a safe, effective treatment for rectal adenomas where endoscopic removal is not applicable and has low morbidity and no mortality.

Fine instrumentation is used to remove tumors during transanal endoscopic microsurgery, sparing patients from major abdominal surgery. TEMS is not appropriate for patients with advanced rectal cancers unless they are ineligible for abdominal surgery, but for patients with benign or precancerous lesions.

CREDIT: Richardwolf Medical Instruments Corporation

12. Endoscopic Submucosal Dissection for Rectal Carcinoid Tumours (Jul. 15/09)

Endoscopic submucosal dissection (ESD) has an advantage over endoscopic mucosa resection (EMR) by enabling removal of gastrointestinal tumors en bloc (in one piece). The ESD procedure is the treatment of choice for rectal carcinoids (neuroendocrine tumors that originate in the rectum) that fulfill certain criteria. This Japanese study assessed the use of endoscopic submucosal dissection (ESD) for rectal carcinoids that fulfilled the following criteria:

- a diameter of 10mm or less,
- no muscular layer invasion and
- no metastases to the lymph nodes or nearby organs.

The study enrolled 20 rectal carcinoid tumours from 20 patients. The average size of the rectal tumor was 7.6mm. En bloc removal (removal of the tumor in one piece) was achieved for all the tumors, and complete resection (en bloc with tumor free margins) rate was 90% (18/20). There were 2 cases in which the margins were not evaluable due to burn effects, but these are still free of recurrence and metastasis when the researchers wrote the paper. One patient experienced perforation which was managed nonsurgically. Researchers concluded that en block resection through ESD of small rectal carcinoid tumors may reduce tumor recurrence and metastasis and that ESD is associated with nominal risks of metastatic disease.


13. Preoperative Use of MR Colonography To Evaluate Synchronous Colorectal Cancer (Jun. 27/09)

Synchronous cancers (cancers occurring at the same time - incidence, 2%-11%) and polyps (incidence, 12%-58%) can occur in patients with colorectal cancer. Magnetic resonance colonography (MRC) might become the choice as a diagnostic tool in the preoperative evaluation, because it is noninvasive, and most of the colon can be evaluated. Furthermore, it has higher patient acceptance, and no sedation or radiation is used. The purpose of this study was to determine the feasibility of performing MRC preoperatively in an everyday clinical situation in a group of patients who were not offered a full conventional colonoscopy or in whom full conventional colonoscopy was not possible. In a 13-month period, 47 patients diagnosed with rectal or sigmoid colon cancer scheduled for operation were included in the study. MRC was performed with bowel preparation either the night before surgery or the week before surgery as an outpatient. Full MRC was performed in 98% of the patients. In four patients, 12 synchronous lesions (one cancer, two plaques of carcinosis, and nine adenomas) were found. One flat adenoma and five small polyps were missed by MRC but found later (post surgical) with colonoscopy. The findings resulted in a changed surgical strategy in three patients. Researchers concluded that this study shows the feasibility and potential gain of preoperative MRC in patients with sigmoid colon cancer or rectal cancer who have not had a complete colonoscopy.


14. Radiofrequency Ablation With Chemo Improves Outcomes in Unresectable Colorectal Cancer Liver Mets (Jul 1/09)

The combination treatment of radiofrequency ablation (RFA) and standard chemotherapy prolongs progression-free survival (PFS) and decreases local disease recurrence, according to a study presented at the 11th World Gastrointestinal Cancer Congress of the European Society for Medical Oncology (ESMO-GI). A team of researchers sought to demonstrate the benefit of adding RFA of the tumor to chemotherapy in patients with unresectable colorectal cancer liver metastases. RFA is a minimally invasive method that uses thermal energy to destroy tumor cells. Initially computed tomography or ultrasound is performed to locate the tumor. A special needle is introduced into the tumor using direct image guidance. This is equivalent to a standard needle biopsy. The needle is attached to a radiofrequency generator. The generator sends radiofrequency through the needle, which generates heat from frictional movement of ions. The heat destroys the tumor cells. (See diagram below)

Unresectable tumours were defined as those having no surrounding disease-free margin in the liver. The primary endpoint (or objective) was overall survival (OS) at 30 months, and secondary endpoints included safety and PFS. Patients with a maximum of 9 lesions and without extrahepatic disease (disease outside the liver) were randomized to receive 6 months of chemotherapy consisting of oxaliplatin and LV5FU2 plus, since October 2005, bevacizumab (avastin) or RFA plus the same chemotherapy regimen. In the
RFA/chemotherapy arm, 30 patients (52.6%) received only RFA, and RFA was combined with resection in 27 patients (47.4%). The chemotherapy toxicity experienced by patients in both groups was comparable. At 1 year, the PFS in the chemotherapy group was 39.35%, versus 60.06% in the RFA/chemotherapy group. Five patients had local recurrence at the RFA site, and 10% of the tumours converted to being resectable. The investigators concluded that this study demonstrates that a regimen of RFA combined with chemotherapy is safe, improves progression free survival and has a superior clinical benefit over folfox treatment in patients with unresectable colorectal cancer liver metastases.

[With RFA, the interventional radiologist guides a small needle through the skin into the tumor. From the tip of the needle, radiofrequency energy (similar to microwaves) is transmitted to the tip of the needle, where it produces heat in the tissues. The dead tumor tissue shrinks and slowly forms a scar. It is ideal for nonsurgical candidates and those with smaller tumors. See schematic below for progression of treatment with RFA:]

Source:
www.sirweb.org/images/patients/radiofrequency_ablation_2.jpg
15. **Age and Illness Increase Colonoscopy Risks** (Jun. 18/09)

Researchers from the National Cancer Institute and the University of North Carolina have reported that the risk of complications from colonoscopy screening is increased in the very elderly and in those with certain chronic health conditions. Screening for colorectal cancer is recommended starting at the age of 50 for individuals at average risk of developing the disease and earlier for those at higher risk. Several screening tests are available, including the fecal occult blood test, sigmoidoscopy, double-contrast barium enema, optical colonoscopy, and CT colonography. To explore the safety of colonoscopy and whether safety varies by the age and health of the patient, researchers evaluated information from 53,220 Medicare beneficiaries aged 66 to 95 who underwent colonoscopy between 2001 and 2005. These researchers found that a serious gastrointestinal event (perforation or bleeding within 30 days of colonoscopy) occurred in 6.9 per 1,000 colonoscopies. Although this risk was low, it varied by age. The risk of a serious gastrointestinal event was more than twice as high among persons aged 85 and older than among persons between the ages of 66 and 69. These results are consistent with recommendations from the U.S. Preventive Services Task Force (USPSTF). The USPSTF recommends against colorectal cancer screening among adults over the age of 85 because the risks are likely to outweigh the benefits. In addition to varying by age, the risk of serious gastrointestinal events also varied by the health of the person being screened. People with a history of stroke, chronic obstructive pulmonary disease, atrial fibrillation, or congestive heart failure were more likely than people without these conditions to experience a serious gastrointestinal event following colonoscopy. This study suggests that the overall risk of colonoscopy complications among Medicare beneficiaries is low. Nevertheless, risk increases with age and with certain chronic health problems. These observations suggest that some elderly or debilitated patients might have fewer complications from a CT colonoscopy when the risks of perforation and bleeding are nonexistent.


16. **CT Colonography (Virtual Colonoscopy) May Benefit Some High Risk Patients** (Jun. 22/09)

Among people at increased risk for colorectal cancer, computed tomographic (CT) colonography, or virtual colonoscopy, correctly classified 85% of the people with advanced adenomas or cancer and 88% of the people without advanced adenomas or cancer. For individuals at increased risk of colon cancer as a result of personal or family history, colonoscopy is the recommended screening test. During the procedure, a lighted tube with an attached camera is inserted into the rectum and through the colon. The physician views the colon on a screen and is able to remove abnormal-looking areas or growths. Although colonoscopy is a highly effective screening tool, some patients are reluctant to undergo the procedure. CT colonography is another screening test for colorectal cancer. The procedure requires the same bowel preparation as colonoscopy, but uses a computed tomography (CT) scanner to visualize the large intestine. The procedure is less invasive than colonoscopy (which may make people more willing to be screened), but individuals who are found to have colorectal growths will still require a traditional colonoscopy in order to have those growths removed. There is also some debate about the accuracy of CT colonography. To evaluate the accuracy of CT colonography among individuals at increased risk of colorectal cancer, researchers in Europe conducted a study among 937 people. The study participants were considered to be at increased risk of colorectal cancer as a result of advanced adenoma or colorectal cancer in a first-degree relative (parent, sibling, or child), a personal history of colorectal adenoma, or a positive result from a fecal occult blood test (FOBT). Study participants underwent both CT colonography and colonoscopy on the same day. Colonoscopy is considered to be the gold standard, and was the test to which CT colonography was compared. The study assessed the ability of CT colonography to detect colorectal growths (advanced adenomas or cancer) that measured 6 mm or larger. The results are as follows:

- CT colonography detected 151 of the 177 people with advanced adenomas or colorectal cancer (the sensitivity of the test was 85%).
- Of the 760 people without advanced adenomas or colorectal cancer, CT colonography correctly classified 667 (the specificity of the test was 88%).

The researchers note that CT colonography may not be the best initial test for the group of patients with positive FOBT. These patients have a relatively high rate of advanced adenomas, which means that many will require traditional colonoscopy. In addition, some measures of CT colonography performance were worse in this group of patients. Nevertheless, the researchers note that CT colonography may be an option for FOBT-positive patients who refuse colonoscopy. The results of this study suggest that CT colonography may be an acceptable alternative to colonoscopy among people at increased risk of colorectal cancer as a result of personal or family history. CT colonography misses some colorectal growths, but may increase adherence to colorectal cancer screening guidelines.
17. Deep Sedation May Improve Cancer Detection in Colonoscopies (Jun. 22/09)

More pre-cancerous polyps were found in colonoscopies performed with deep sedation primarily using Propofol than with milder sedation in which patients remained conscious, according to a recent study conducted at the Oregon Health and Science University. This improvement in cancer detection may save lives and reduce the number of patients requiring surgery and chemotherapy. The retrospective review of nearly 105,000 procedures shows doctors found polyps larger than 9mm or suspected colorectal tumors at a 25% higher rate in patients under deep sedation. This research bolsters the findings of studies completed by the University of Pennsylvania and State University of New York. Those studies tracked facilities that switched from having the GI doctor perform the colonoscopy and also deliver the sedatives, to having an Anesthesiologist administer Propofol. The findings revealed the number and percentage of patients who had a polyp detected improved up to 43%. 25% and 43% improvements in cancer detection can't be ignored according to study researchers. Propofol can help improve outcomes, but only if it is administered correctly. For safety reasons, and now for clinical outcome reasons, a sleep this deep must be administered and supervised by an Anesthesiologist. Propofol's label states it should be administered by a person trained in general anesthesia and who is not performing the surgical procedure.

www.ddw.org/wmspage.cfm?parm1=882

18. More Accurate and Less Invasive Colorectal Cancer Screening - iFOBT (Jul. 1/09)

The Immunochemical Fecal Occult Blood Test (iFOBT) has been found to be more accurate than the traditional fecal occult tests. The benefits of the new iFOBT screening are that it requires no dietary restrictions prior to the test, and has been FDA approved for a single fecal specimen collected at home, instead of up to three with the traditional fecal occult test. The iFOBT is also more sensitive to occult blood and is more specific in what it tests. The ease of use with this new test also encourages more people to complete it. Parrish Medical Center offers this new screening through its Direct Access Testing service, which requires no doctor's order and costs just $20. The iFOBT detects occult (hidden) blood in the stool. This test reacts to part of the human hemoglobin protein, which is found on red blood cells. When doing the iFOBT, fecal samples are taken at home using a kit that is supplied to the patient. When the required sample has been taken the test kit is returned to the lab as soon as possible. If the results are positive for hidden blood, a colonoscopy is required to investigate further, which is the definitive test for colorectal cancer. With Parrish Medical Center's Direct Access Testing, you can order your own tests and results will be given to you and your physician (if you choose). The cost is minimal and tests can be done without an appointment. Parrish Direct Access Testing offers many other laboratory tests for a minimal cost without your doctor's orders. If you wish to access the test, go online to www.parrishmed.com/programs_services/clinicallab_direct.cfm and learn more about them.

www.wftv.com/health/19916948/detail.html

19. TheraScreen Kras Mutation Kit Approved For Use in Canada (Jul. 13/09)

DxS, a personalised medicine company, has had its TheraScreen: K-RAS Mutation Kit granted a licence by Health Canada for use as a diagnostic for anti-EGFR therapies and as the companion diagnostic for Amgen's colorectal cancer therapy, Vectibix (panitumumab). The availability of the TheraScreen: K-RAS Mutation Kit will allow colorectal cancer patients in Canada to be screened using the DxS diagnostic to assess their candidacy for treatment with Vectibix. Studies have shown that patients with the non-mutated K-RAS gene may respond to treatment with Vectibix. Approximately 60% of metastatic colorectal cancer patients have a non-mutated K-RAS gene. Canada now has a registered method for K-RAS testing. The DxS K-RAS test is simple to use, highly sensitive and is the companion diagnostic test of choice for assessing a patient's response to Vectibix. The approval of the TheraScreen: K-RAS Mutation Kit is a step forward in making personalised medicine more readily available to physicians and patients in Canada. The future of cancer treatment will be guided by the use of technological advances such as these, which enable physicians to better manage a patient's disease or predisposition towards a disease. Now physicians can choose a treatment approach that is likely to work best in the context of a patient's genetic and environmental makeup. Following the global distribution agreement signed in 2008, Roche Diagnostics will be distributing and supporting sales of the TheraScreen: K-RAS Mutation Kit in Canada beginning in August of this year.
20. Capsule Endoscopy vs. Colonoscopy for the Detection of Polyps/Cancer  (Jul. 16/09)

An ingestible capsule (PillCam Colon) consisting of an endoscope equipped with a video camera at both ends was designed to explore the colon. This study compared capsule endoscopy with the gold standard – optical colonoscopy – for the detection of colorectal polyps and cancer. The multi-center study enrolled 328 patients between January 2006 and July 2007 with known or suspected colonic disease. The primary endpoint (objective) of the study was detection of colorectal polyps and cancer. Patients underwent colon preparation and the capsule was excreted within 10 hours after ingestion and before the end of the lifetime of the battery in the majority of patients. Researchers calculated the sensitivity and specificity of capsule endoscopy for detecting polyps that were 6 mm in size or bigger to be 64% and 84% respectively; and for detecting advanced adenoma, the sensitivity and specificity were 73% and 79%. Out of the 19 cancers that were detected by colonoscopy, 14 were detected by capsule endoscopy. Based on the results, researchers concluded that the use of capsule endoscopy of the colon allows visualization of the colonic mucosa in most patients, but its sensitivity for detecting colonic lesions is low as compared with the use of optical colonoscopy.

Given Imaging is the manufacturer of PillCam Colon which is available commercially in Europe, Asia, Latin America, Canada and Australia. PillCam Colon is not approved for use in the US.

As illustrated above, the PillCam Colon is no bigger than a U.S. quarter and is swallowed for the purpose of taking pictures of the colon.


NUTRITION & HEALTHY LIFESTYLE

21. Vitamin B3 May Increase Neutrophil Count  (Jun. 29/09)

Many cancer patients know that when the immune system bounces back after each treatment cycle, treatment need not be interrupted. And while some decrease in immune function during chemotherapy is expected, in certain cases, immunity is so seriously affected that patients must take a break from treatments. Also unfortunate is that severe declines in immune function put patients at high risk for infections. This complicates treatment, decreases quality of life, sometimes requires hospitalization, and generally is something doctors wish to prevent in their patients. Medications that increase immune cell counts are an option, but some people cannot take these medications and others react poorly to them. For all of these reasons, cancer researchers continue to seek safe ways to help patients maintain good immune function throughout treatment. This study offers new hope that a safe way to improve immunity in cancer patients may be available soon. It details, for the first time, how vitamin B3, also called niacin, can improve the ability of the body to make new immune cells known as neutrophils. In addition to this finding, the researchers discovered that giving high doses of vitamin B3 significantly increases neutrophil count in healthy people. The vitamin B3 doses used in the study ranged from 10 to 20 milligrams per kilogram of body weight per day (mg/kg/day). To put this into perspective, this means a 175 pound person would take between approximately 800 and 1,600 mg of vitamin B3 per day. The safe upper limit for niacin is set at 35 mg per day, so these doses are quite high. On a positive note, high doses of niacin, up to several thousand mg per day, are given as a cholesterol treatment medication; hence it can be used safely in that setting. If you have had to take frequent breaks from your treatment due to poor immunity or your immune system isn't recovering the way it should, consult your doctor as to what can be done. Medications may be prescribed that improve immune function. As well, under proper medical supervision, it may be appropriate to try niacin as a way to improve neutrophil count.


22. Vitamin B6 May Reduce Colorectal Cancer Risk By Over 50%  (Jul.2/09)

Increased intake of vitamin B6 from dietary and supplements may reduce the risk of colorectal cancer by over 50%, according to a Harvard study. According to the results, almost 15,000 people took part in the
study, which reported that increased blood levels of the vitamin’s active form, pyridoxal 5'-phosphate (PLP), were significantly associated with a reduced risk of colorectal cancer. The study follows similar findings from Scotland-based researchers published in the same journal last year. Researchers from the University of Edinburgh, Western General Hospital (Edinburgh) and the University of Aberdeen, reported that increased intakes of vitamin B6 from dietary and supplements may reduce the risk of colorectal cancer by over 20% (Cancer Epidemiol Biomarkers Prev., Vol. 17, pp. 171-182). The researchers evaluated the link between blood PLP levels and risk of colorectal cancer amongst 14,916 men. During the course of the study, 197 incident cases of colorectal cancer were documented, and these cases were subsequently compared to 371 healthy cases. Researchers report that PLP levels were positively correlated with blood levels of folate and vitamin B12. PLP levels were also slightly inversely correlated with blood levels of homocysteine, and the inflammatory markers C-reactive protein (CRP), tumour necrosis factor-alpha receptor 2, and interleukin-6 (IL-6). Regarding the incidence of colorectal cancer, plasma PLP levels were inversely linked with risk of colorectal cancer, according to researchers. The protection of vitamin B6 may work through reducing oxidative stress. Vitamin B6 is known to be vital for DNA production, so lack of it might lead to the kind of DNA damage that is associated with cancer. The researchers concluded that vitamin B6 may protect against colorectal cancer independent of other one-carbon metabolites and inflammatory biomarkers.

Good food sources of vitamin B6 include fortified cereals, fish, nuts, legumes, meat, bell peppers, bananas, avocados, potatoes and greens such as spinach, turnip, collard, mustard, kale and chard.


23. Low Folate Diets Increase Risk of Colorectal Cancer (Jul.6/09)

Increased intakes of folate from the diet may reduce a woman’s risk of colorectal cancer by about 50 per cent, according to new findings from Korea. The highest intakes of folate, a B-vitamin found in green leafy vegetables, chick peas and lentils, were associated with a 66, and 70% reduction in a woman’s risk of cancers of the colon and rectum, respectively, report researchers. However, men did not benefit from the vitamin, said the researchers. The study adds to an ever-growing body of evidence which has reported that increased intakes of folate may reduce the risk of colorectal cancer by 40 to 60%. The Korean researchers analysed data obtained from 596 men and women with colorectal cancer, and compared this to data from 509 people free of the disease. All the participants were aged between 30 and 79. According to the report, the overall data showed that the highest levels of folate intake were linked to a 53, 58 and 52% reduced risk of colorectal, colon, and rectal cancer, respectively for all the people studied. However, when the researchers focussed on the sex of the participants, only women were found to benefit, where the highest levels of folate intake were linked to a 64, 66, and 70% reduced risk of colorectal, colon, and rectal cancer, respectively. Researchers found a statistically significant relationship between higher dietary folate intake and reduced risk of CRC, colon cancer and rectal cancer in women. Of worthy importance is the fact that some studies have linked folic acid intakes to an increased risk of the disease. A possible explanation for the contradictory results of studies with the vitamin and colorectal cancer may be the difference between the synthetic and natural forms of the vitamin. The fact that folic acid, which is not a naturally occurring form of the vitamin, is used by food and pharmaceutical industries for fortification and supplementation is potentially of importance. On passage through the intestinal wall, folic acid is converted to 5-methyltetrahydrofolate, the naturally circulating form of folate. However, some studies have suggested that oral doses of folic acid in high doses may overwhelm this conversion pathway, leading to measurable levels of folic acid in the blood. There has been some concern that this oxidized, non-substituted form of folate might feasibly be detrimental because it is not a naturally occurring co-enzymatic form of the vitamin.


24. Understanding How Vitamin D Can Prevent & Treat Colon Cancer (Jul.7/09)

A new Spanish study offers an understanding of vitamin D’s apparent anti-cancer properties. The findings advocate on behalf of the need for further clinical trials to examine the potential of the active form of vitamin D3 to prevent and treat colon cancer. In the past, a number of studies have indicated that the active form of vitamin D3 may have significant anti-cancer properties. Earlier studies on human colon cancer cell lines have shown that activity levels of a gene called CST5 may be affected by the active form of vitamin D3. CST5 is responsible for making a protein called cystatin D. In this latest study, Spanish researchers studied this protein in greater detail. Their investigations reveal that cystatin D has important tumour-suppressing properties, and that it is the mechanism through which vitamin D3 affects cancer cells. These results account for the higher susceptibility to colon cancer caused by vitamin D deficiency in animal models and the results of studies that indicate antitumoural action of vitamin D in humans. Firstly, the researchers established that the active form of vitamin D3 directly activates the CST5 gene in human colon cancer cell lines. This increases the levels of the cystatin D protein in the cells. It turns out that the cystatin D protein blocks the growth of human colon cancer cell lines both in the test tube and in mice. Artificially reducing the activity of the CST5 gene renders cells unresponsive to the anti-cancer effects of vitamin D. The exact mechanisms by which cystatin D exerts control over cancer cells remain...
25. Colon Cancer Risk: Meat & How it's Cooked

Past research has shown that eating too much red and processed meat increases risk of colorectal cancer. Now, a large population study suggests that how meat is cooked – white and red meat – is also important. The European study linked increased risk of pre-cancerous growths in the colon to cancer-causing compounds that form when meat is grilled or fried at high temperatures. This study questioned more than 25,000 adults about details of their diets, including what and how much red meat and poultry they ate and how it was cooked. Based on this, researchers estimated levels of three major heterocyclic amine (HCA) compounds typically consumed. HCAs form when long or intense heat reacts with animal muscle, both red and white meat, as well as fish. These compounds can damage DNA and begin the development of cancer. As in past studies, people who ate more red and processed meat were more likely to develop colorectal adenomas (benign tumors that can transform into cancerous ones and are the source of most colorectal cancer). Consumption of all three of the major HCAs was also higher among those who developed adenomas. Looking only at the left section of the colon that seems most vulnerable to meat-associated risks, those with greatest consumption of the most abundant HCA were 59% more likely to develop adenomas than those who consumed the least. Previously, a major U.S. study examined more than 14,000 men to see how HCA consumption was linked to adenoma in that left section of the colon most sensitive to meat’s impact. The U.S. researchers suggested that looking at total HCA consumption may provide an unclear picture because that total figure could include varied proportions of HCAs that are more or less damaging. Besides, colon cancer and adenoma risk may relate not only to HCAs, but also to other damaging compounds formed in cooking (ie. PAHs – which form when fat drips off the meat into the flame or heating element and smoke is generated). The PAHs rise in the smoke and can deposit on the food). Consumption of processed meat presented the strongest association. Yet consumption of total cell-damaging compounds seemed to be a separate influence, even after accounting for processed meat intake. Together, these and other studies tell us that although a primary step to lower risk of colon cancer is limiting red and processed meat, the issue of how our meat, poultry and fish is cooked is also important. The HCAs and other cell-damaging compounds that form when meats are cooked with high temperature grilling and frying, especially when well-done or extremely browned, are not carcinogenic on their own. Proteins in the body must activate them and activation depends upon both diet and genetics. The effect seen in studies is likely an average of individuals who are strongly and not strongly affected. The bottom line for consumers is to watch what they eat and how it’s cooked. Avoid frying and if grilling, reduce the temperature and don’t char food. A mostly plant-based diet plays an important protective role: less meat automatically means less of meat’s cell-damaging compounds and more plant foods mean more of the protective compounds that inactivate activation depends upon both diet and genetics. The effect seen in studies is likely an average of individuals who are strongly and not strongly affected. The bottom line for consumers is to watch what they eat and how it was cooked. Based on this, researchers estimated levels of three major heterocyclic amine (HCA) compounds typically consumed. HCAs form when long or intense heat reacts with animal muscle, both red and white meat, as well as fish. These compounds can damage DNA and begin the development of cancer. 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- Grill fish and skinless chicken breasts rather than red or processed meat
- If meat is grilled, select lean cuts. Cuts with “loin” in the name, such as tenderloin or loin chops are the leanest along with round steaks
- Keep meat portions small by cutting them into chunks, such as kabobs
- Serve any meat as an accent to a meal of plant-based foods, not as the main attraction
- Precook or marinate meat and grill at low temperatures
- Flip meats often during cooking to reduce the chemicals produced by high heat that cause cancer

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26. Diet & Lifestyle Choices Can Prevent Colorectal Cancer

Exercise, diet, and lifestyle choices are key factors in preventing colon cancer, according to the results of this study. Evidence continues to mount indicating that a patient’s lifestyle habits and diet may significantly decrease the risk of certain types of cancers. Researchers from Australia conducted an analysis of 103 studies that evaluated colorectal cancer risk factors and were conducted between 1966 and 2008. The purpose of the review was to evaluate the strength of the associations for risk factors for colorectal cancer. The results of the analysis indicated that although several lifestyle factors increase the risk of colorectal cancer, alcohol poses the most significant risk. Individuals who consume one or more alcoholic beverage per day have a 60% higher risk of developing colon cancer than individuals who are light or non-drinkers. In addition, the researchers found that smoking, obesity, diabetes, and high intake of red and processed meats were each associated with a 20% higher risk of colorectal cancer. Exercise provided a protective benefit against colorectal cancer. The researchers concluded that colorectal cancer is largely a disease of lifestyle. Individuals can protect themselves from developing the colon.
disease by modifying lifestyle habits such as alcohol consumption and smoking. By staying active, avoiding obesity, and choosing more healthful foods, individuals can decrease their risk of developing colorectal cancer.


27. Diet & Exercise Produce Positive Results in Long Term Survivors (Jul.14/09)

According to the results of this study, long-term survivors of breast, colorectal, and prostate cancer who participated in a year-long home-based diet and exercise intervention reported a smaller decline in physical function compared with their counterparts who did not participate in the program. Research has consistently indicated that proper nutrition, physical activity, and healthy body weight are critical for maintaining optimal health and preventing cancer. Cancer survivors are at an increased risk of developing subsequent cancers. Furthermore, cancer and its treatment have been associated with accelerated functional decline. As cancer treatments continue to improve, more cancer survivors are surviving beyond the five-year mark, making it imperative that these survivors maintain healthy lifestyle habits in order to maintain optimal health. The study (RENEW) included 641 overweight, long-term survivors of colorectal, breast, and prostate cancer between the ages of 65 and 91 who were randomly assigned to the intervention group (319) or the control group (322). The patients were recruited from Canada, the United Kingdom and 21 U.S. states between 2005 and 2007. The intervention group received a 12-month, home-based program of telephone counseling and mailed materials that promoted exercise, improved nutrition, and modest weight loss. The control group was wait-listed for 12 months before undergoing the program. All subjects in the study responded to several questionnaires, before beginning and at 12 months, in order to measure physical function, lower extremity function, and general health and quality of life. These questionnaires assessed the impact of health on the performance of various activities ranging from basic self-care to more vigorous activity. The results indicated that the control group experienced more than twice the decline of the intervention group in overall physical function. Furthermore, the lower extremity function in the control group declined significantly more than that of the intervention group. The intervention group reported an increase in targeted behaviors such as strength exercise, endurance exercise, and intake of fruits and vegetables. In addition, the intervention group reported a better overall quality of life. The researchers concluded that a diet and exercise intervention among older, long-term survivors of breast, prostate, and colorectal cancer reduced the rate of functional decline in this population.