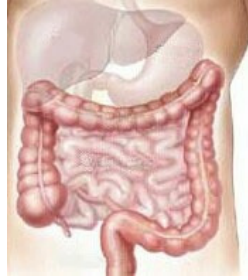


COLORECTAL CANCER RESEARCH Month Ending February 19, 2010



The following colorectal cancer research update extends from January 16 – February 19, 2010 inclusive and is intended for informational purposes only.

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DRUGS / SYSTEMIC THERAPIES

1. Avastin Plus Chemo Confirmed to be Effective in Advanced Colorectal Cancer (Jan. 15/10)

This study confirmed that among patients with advanced colorectal cancer, the addition of Avastin (bevacizumab) to chemotherapy improves overall and progression-free survival but also increases side effects. Avastin is a targeted therapy that blocks a protein known as VEGF. VEGF plays a key role in the development of new blood vessels. By blocking VEGF, Avastin deprives the cancer of nutrients and oxygen and inhibits its growth. Avastin's effects on blood vessels may also improve the delivery of chemotherapy to the tumor. To summarize available information about Avastin in advanced colorectal cancer, researchers evaluated information from five clinical trials. The studies compared chemotherapy plus Avastin to chemotherapy alone for first- or second-line treatment. The results are as follows:

- The addition of Avastin to chemotherapy improved overall survival by 21% and improved progression-free survival by 37%.
- The most common side effects related to Avastin included high blood pressure, protein in the urine, bleeding, and blood clots.

The results of this review confirm that the addition of Avastin to chemotherapy improves overall survival and delays cancer progression among patients with advanced colorectal cancer. Avastin also, however, increases the occurrence of side effects. The researchers note that the benefit of Avastin may vary depending on the specific chemotherapy regimen that is used.

Welch S, et al. Bevacizumab combined with chemotherapy for patients with advanced colorectal cancer: a systematic review. Annals of Oncology [early online publication]. November 25, 2009.

2. How Long Should Adjuvant (Post surgical) Chemo Last? (Jan. 22/10)

Surgery of primary tumour is the backbone of colorectal cancer treatment. But in stage III cancer, metastatic or local relapse is often observed in approximately 50% of the population. Hence, adjuvant treatment (post surgical treatment) is always considered in this setting. Adjuvant chemotherapy for CRC actually lasts 6 months. The choice of optimal duration is based upon old studies using 5-fluorouracil (5FU). During the last ten years, results of major randomized controlled studies comparing different durations of treatments and different schedules in adjuvant setting were published. Several studies compared a 6-month chemotherapy with a longer treatment. Conversely, a single study compared a 6 month chemotherapy with continuous treatment lasting 3 months. But the optimal duration of these chemotherapies could be challenged. Even though the optimal duration of chemotherapy in CRC is a major issue, it has never been answered adequately. This study confirmed that adjuvant chemotherapy of CRC should not last for more than 6 months. Prolonged duration would result in lower benefit to risk ratio. However, the results do not make it possible to favor either 3 or 6 month durations. They should help design a future Randomized Controlled Study comparing different durations of continuous treatment.

3. **Peripheral Neuropathy Associated with CAPOX** (Jan. 25/10)

There is speculation that peripheral neuropathy (PN) with capecitabine and oxaliplatin may be more common than with FOLFOX4. The investigators sought to determine PN incidence and associations during CapOx, and 6 and 12 months after CapOx. This was a retrospective study of 188 oxaliplatin-naive colorectal cancer patients (87 adjuvant, 101 palliative) who received at least one cycle of CapOx. Overall, 94% experienced acute PN. Incidence of acute PN during CapOx appeared similar to FOLFOX4 but chronic PN in adjuvant patients may be more common with CapOx.

Storey, DJ, et al., Capecitabine combined with oxaliplatin (CapOx) in clinical practice: how significant is peripheral neuropathy? Annals of Oncology. Published online on January 20, 2010.

4. **1-Keryx Cancer Drug Improves Survival in Mid-Stage Trial** (Jan. 25/10)

A new drug KRX-0401 is in clinical trials and has recently demonstrated an improvement in overall survival in heavily pre-treated patients with advanced metastatic colon cancer, as compared with a dummy drug. The drug is manufactured by Keryx and the study enrolled a total of 38 patients, who were either given the drug KRX-0401, or perifosine, in combination with a chemotherapy drug capecitabine – better known as xeloda-, or just capecitabine in combination with a dummy drug. Patients receiving KRX-0401 showed a greater than 60% improvement in overall survival and also demonstrated statistically significant advantage for time to progression during the mid-stage trial. However, the patients on the drug showed a higher incidence of adverse events like anemia and hand-foot syndrome as compared with those on the dummy drug. The company is eager to finalize the design of a phase III protocol in metastatic colorectal cancer within the next 3 months, in consultation with the federal US agency FDA and to commence the [phase III study as soon as practicable thereafter.

<http://www.reuters.com/article/idUSSGE60O0KT20100125>

5. **Xeloda Is Just As Effective as 5FU in Colorectal Cancer** (Jan. 25/10)

This study presented at this year's Gastrointestinal Cancers Symposium in Orlando demonstrated that patients assigned to oral capecitabine (or xeloda) do as well and perhaps even better than patients who are assigned to receive intravenous 5FU. The study was a meta-analysis which means investigators pooled results from 6 studies and compared outcomes among 3,074 patients who received 5FU containing therapies with 3,097 patients who received therapies containing capecitabine. The overall survival analysis found a 5% reduction in the risk of mortality for patients who were receiving capecitabine. Capecitabine can be considered a suitable alternative to 5-fluorouracil. The studies included in the meta-analysis compared the 2 drugs in first line treatment of metastatic colorectal cancer, in resected stage III colon cancer, as second-line therapy in metastatic colorectal cancer, and in first-line gastric cancer. The most important prognostic factor for overall survival in the meta-analysis was a performance status greater than 0. The median time to events in the patients receiving 5-fluorouracil was 22.5 months compared with 23.1 months for patients receiving capecitabine

2010 Gastrointestinal Cancers Symposium, Presentation title: Efficacy of Capecitabine vs. 5FU in Colorectal and Gastric Cancer: Meta-Analysis of Survival in 6 Clinical Trials. Abstract 340.

6. **Kras Status Affects Metastatic Colorectal Cancer Treatment Vectibix** (Jan.25/10)

Among patients with metastatic colorectal cancer that do not have a mutation in the *KRAS* gene, initial treatment with a combination of chemotherapy and Vectibix (panitumumab) delays cancer progression by 1.6 months compared with chemotherapy alone. These results were presented at the 2010 ASCO Gastrointestinal Cancers Symposium. Targeted therapies are anticancer drugs that interfere with specific pathways involved in cancer cell growth or survival. Some targeted therapies block growth signals from reaching cancer cells; others reduce the blood supply to cancer cells; and still others stimulate the immune system to recognize and attack the cancer cell. Depending on the specific "target," targeted therapies may slow cancer cell growth or increase cancer cell death. Vectibix inhibits cancer cell growth and survival by targeting a protein known as the epidermal growth factor receptor (EGFR). Vectibix has been approved for the treatment of EGFR-expressing, metastatic colorectal cancer that has progressed on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens. Vectibix appears to benefit only those patients whose cancers do not contain a mutation in a gene known as *KRAS*. *KRAS* mutations occur in an estimated 40-50% of metastatic colorectal cancers and can be identified by testing a sample of tumor tissue. To evaluate the effectiveness of Vectibix in the initial (first-line) treatment of metastatic colorectal cancer, researchers conducted a Phase III clinical trial known as PRIME (Panitumumab Randomized trial In combination with chemotherapy for Metastatic

colorectal cancer to determine Efficacy). The study enrolled 1,183 patients. Study participants were assigned to receive treatment with FOLFOX4 chemotherapy alone or FOLFOX4 plus Vectibix.

- Among patients without *KRAS* mutations, the addition of Vectibix delayed cancer progression. Progression-free survival was 9.6 months among patients treated with chemotherapy plus Vectibix compared with 8.0 months among patients treated with chemotherapy alone.
- Among patients with *KRAS* mutations, the addition of Vectibix worsened outcomes. Progression-free survival was 7.3 months among patients treated with chemotherapy plus Vectibix compared with 8.8 months among patients treated with chemotherapy alone.
- Side effects of Vectibix included skin rash, low magnesium levels, and diarrhea.

The results of this study suggest that the addition of the targeted therapy Vectibix to first-line chemotherapy modestly improves progression-free survival among patients with metastatic colorectal cancer. The benefit of Vectibix only applies to patients whose tumors do not contain *KRAS* mutations.

GI Cancers Symposium 2010, Presentation title: Randomized Phase III Study of Panitumumab with folfox4 compared to folfox 4 alone as first line treatment for metastatic colorectal cancer: PRIME trial. Abstract 283.

7. **Xelox After Surgery Can Benefit the Elderly** (Jan. 25/10)

This study reported at the GI Cancers Symposium that colon cancer patients over 70 actually had a greater reduction in disease-free survival than did younger ones with a new regimen of Xeloda and oxaliplatin compared to older IV 5-FU treatments. With the bolus IV 5-FU and leucovorin regimens, stage III colon cancer patients over 70 had about a 60% chance of being alive and free from cancer three years after surgery. With a combination of Xeloda (capecitabine) and oxaliplatin in a treatment called XELOX, their three-year disease-free survival was 66%. Younger patients had about a 3% absolute improvement between the two treatments from 69-72%. The Xeloxa clinical trial compared the oral drug Xeloda plus intravenous oxaliplatin to then standard IV 5-FU and leucovorin regimens after surgery for stage III colon cancer. After three years, there was a six percentage point increase in disease-free survival in the older patients. The spread remained true when the cut-off age was dropped to 65. Patients 65 and older had a 62% chance of disease-free survival at three years on the older 5-FU treatments compared to 68% on the XELOX regimen. Investigators concluded that XELOX is a new standard of care for patients with early colon cancer, regardless of age. Patients receiving XELOX immediately after surgery live disease-free for longer, and there is a trend towards superior overall survival with XELOX.

GI Cancers Symposium 2010. Presentation Title: Efficacy findings from a randomized phase III trial of capecitabine plus oxaliplatin vs bolus 5FU for stage III colon cancer (NO16968): No impact of age on disease free survival (DFS), Abstract #284

8. **Neoadjuvant Xeloda + Oxaliplatin Well Tolerated in Poor-Risk Rectal Cancer** (Jan. 26/10)

Neoadjuvant (pre-surgical) chemotherapy consisting of capecitabine (xeloda) and oxaliplatin in potentially operable patients with poor-risk rectal cancer was well-tolerated and showed “promising” anti-tumor activity, according to the results of this phase-2 study. Most patients who had locally advanced rectal cancer at presentation were able to proceed to total mesorectal excision with microscopically complete resection. The phase-2 study enrolled 105 patients with poor-risk rectal cancer without metastatic disease as supported by high-resolution MRI. Patients were given neoadjuvant capecitabine plus oxaliplatin followed by six weeks of 54 Gy of chemoradiotherapy. Patients then underwent total mesorectal excision followed by an additional 12 weeks of postoperative adjuvant capecitabine. The primary endpoint was complete response. Patients were followed for an average of 55 months. Patient objective response rate was high: 74% after neoadjuvant treatment, 89% after chemoradiotherapy. 95 patients were able to proceed with total mesorectal excision; 93 of these patients had microscopically clear resection margins and 21 had complete response. Progression free survival (time before disease got worse) at three years was 68%; overall survival was 83%. The safety profile of this chemotherapy combination seems to be consistent with findings of randomized trials of capecitabine and oxaliplatin in advanced colorectal cancer, for which it is a well-established treatment option.

Chua, YJ, et al., Neoadjuvant capecitabine and oxaliplatin before chemoradiotherapy and total mesorectal excision in MRI-defined poor-risk rectal cancer: a phase 2 trial. Lancet Oncology; Early Online Publication, 26 January 2010, doi:10.1016/S1470-2045(09)70381-X

9. **Erbix Improves Overall Survival in Patients with Kras Wild Type** (Jan. 25/10)

According to the results of this study, erbitux (cetuximab) provided an improvement in overall survival (OS) when added to the standard 1st-line FOLFIRI chemotherapy regimen for metastatic colorectal cancer (mCRC) patients with *KRAS* wild-type tumors in the CRYSTAL study. In addition, the final results from this study included an analysis of the predictive value of BRAF status on Erbitux efficacy – one of the first to be based on a large subgroup of a prospective, randomized study in the 1st-line setting. The analysis indicates that patients with *KRAS* wild-type tumors bearing a BRAF mutation also benefit from Erbitux treatment; therefore, *KRAS* remains the only validated, clinically predictive marker of responsiveness to this drug. These study results were presented at the American Society of Clinical Oncology’s 2010 Gastrointestinal Cancers Symposium in Orlando. It is clear that overall survival is a critically important outcome in metastatic colorectal cancer, so it is extremely rewarding to achieve this

result in patients with KRAS wild-type tumors. The analysis indicating that BRAF is not predictive for Erbitux efficacy is also of interest, as it confirms the current role of KRAS as the only clinically predictive biomarker for Erbitux.

ASCO-GI, Van Cutsem E, et al., Abstract #281

10. Using Systemic Therapy and Hepatic Artery Infusion for Resected Liver Mets (Jan. 27/10)

In this phase II study of patients with colorectal cancer metastasized to the liver, surgery followed by **alternating** hepatic artery infusion of floxuridine and systemic capecitabine/oxaliplatin yielded some positive results. Surgery can provide a long-term survival benefit in certain patients who have resectable metastases from colorectal cancer (CRC). In addition, the introduction of oxaliplatin-based chemotherapy for metastatic CRC has further improved response rates and overall survival in these patients. Unfortunately, a large percentage of patients will develop recurrence in the liver after metastasectomy (surgical removal of distant metastases). Thus, use of regionally-delivered adjuvant chemotherapy is of interest. Fluorouracil therapy delivered by hepatic artery infusion (HAI), as compared with systemic delivery, has improved survival and decreased the likelihood of hepatic recurrence in patients with CRC-related liver metastases. Based on promising results from preliminary studies, investigators conducted a nonrandomized phase II trial to determine the benefit of combining systemic capecitabine plus oxaliplatin with HAI of floxuridine (FUHR) in CRC patients with resectable liver metastases. The study enrolled 123 patients who had undergone resection for CRC. All of the patients subsequently developed potentially resectable metastasis to the liver. The primary endpoint was 2-year survival. Of the enrolled patients, 76 achieved complete resection of their metastases. Of these, 71 patients underwent resection and 4 had cryoablation (obliteration of liver mets through a freezing technique); 12 patients underwent adjunctive radiofrequency ablation. The patients received alternating courses of HAI and systemic therapy. The results of this study showed that a postsurgical regimen consisting of alternating treatment with HAI FUHR and systemic capecitabine/oxaliplatin was safe in patients who had CRC with resectable liver metastasis. However, the overall benefit of the alternating regimen is unclear, given that this was a phase II trial.

O'Connell, MJ, et al., *Alternating Systemic and hepatic artery infusion therapy for resected liver metastases from colorectal cancer. J Clinical Oncology*; 2010 Jan. 4; Epub ahead of print.

11. Erbitux + Chemo Effective Against Liver Metastases (Jan. 27/10)

According to this study, among patients with liver metastases from colorectal cancer, the combination of Erbitux (cetuximab) and chemotherapy may improve treatment response rates and increase the number of patients who become candidates for surgery. Surgical removal of liver metastases can improve patient outcomes. Many patients with liver metastases, however, are not candidates for surgery as a result of the extent or location of the cancer. Initial treatment with chemotherapy may reduce the extent of the liver metastases and allow more patients to be treated surgically. Erbitux is a targeted therapy that inhibits growth of the cancer by binding to a portion of the epidermal growth factor receptor (EGFR), a protein located on the surface of many cancer cells. Response to Erbitux among patients with colorectal cancer appears to vary by whether or not the tumor contains a mutation in a gene known as KRAS. Tumors with KRAS mutations may not respond to treatment with Erbitux. The combination of chemotherapy and erbitux was evaluated among 114 patients with liver metastases from colorectal cancer. At the start of the study, the patients were believed to have liver tumors that could not be surgically removed. Study participants were assigned to receive Erbitux in combination with one of two chemotherapy regimens (FOLFOX6 or FOLFIRI).

- A response to treatment (a reduction in detectable cancer) was observed in 68% of patients treated with Erbitux and FOLFOX6 and 57% of patients treated with Erbitux and FOLFIRI.
- Response rates were higher among patients whose tumors did not contain a KRAS mutation (70% among patients without a KRAS mutation, compared with 41% among patients with a KRAS mutation).
- Complete surgical removal of all tumors was possible in 38% of patients treated with Erbitux and FOLFOX6 and 30% of patients treated with Erbitux and FOLFIRI.

These outcomes are better than what has been observed in the past and suggest that the combination of Erbitux and chemotherapy may be effective for patients with unresectable liver metastases from colorectal cancer.

Folprecht G, Gruenberger T, Bechstein WO et al. *Tumour response and secondary respectability of colorectal liver metastases following neoadjuvant chemotherapy with cetuximab: the CELIM randomized phase 2 trial. Lancet Oncology [early online publication]*.

12. Erbitux + Chemo Not Beneficial in Stage III Colon Cancer (Jan. 27/10)

According to the results of this Phase III clinical trial, the addition of Erbitux (cetuximab) to chemotherapy with FOLFOX did not improve outcomes among patients with Stage III colon cancer. Erbitux is a targeted therapy that inhibits growth of the cancer by binding to a portion of the epidermal growth factor receptor (EGFR), a protein located on the surface of many cancer cells. Response to Erbitux among

patients with colorectal cancer appears to vary by whether or not the tumor contains a mutation in a gene known as KRAS. Tumors with KRAS mutations generally don't respond to treatment with Erbitux. The benefit of Erbitux among selected patients with metastatic colorectal cancer prompted interest in the role of Erbitux among patients with earlier-stage disease. The addition of Erbitux to FOLFOX chemotherapy was evaluated in a Phase III clinical trial among approximately 1,760 patients with Stage III colon cancer. All patients underwent complete surgical removal of their cancer before chemotherapy. A review concluded that no group of patients benefited from the addition of Erbitux to chemotherapy.

National Cancer Institute News Note: Addition of Cetuximab to Standard Chemotherapy in Early-Stage Colon Cancer Shows No Benefit in Phase 3 Clinical Trial. Available at: <http://www.cancer.gov/newscenter/pressreleases/CetuximabClosure>.

13. Vectibix Improves Outcome of Previously Treated CRC (Jan. 27/10)

Among patients with previously treated, metastatic colorectal cancer, the addition of the targeted therapy Vectibix (panitumumab) to chemotherapy delayed cancer progression. This benefit was only observed in patients whose tumors did not contain a mutation in the KRAS gene. These results were presented at the 2010 ASCO Gastrointestinal Cancers Symposium. Targeted therapies are anticancer drugs that interfere with specific pathways involved in cancer cell growth or survival. Some targeted therapies block growth signals from reaching cancer cells; others reduce the blood supply to cancer cells; and still others stimulate the immune system to recognize and attack the cancer cell. Depending on the specific "target," targeted therapies may slow cancer cell growth or increase cancer cell death. Vectibix inhibits cancer cell growth and survival by targeting a protein known as the epidermal growth factor receptor (EGFR). Vectibix, however, appears to benefit only those patients whose cancers do not contain a mutation in a gene known as KRAS. KRAS mutations occur in an estimated 40% of metastatic colorectal cancers and can be identified by testing a sample of tumor tissue. To evaluate the effectiveness of Vectibix in the second-line treatment of metastatic colorectal cancer, researchers conducted a Phase III clinical trial among 1,186 patients. Study participants were assigned to receive treatment with FOLFIRI chemotherapy alone or FOLFIRI plus Vectibix.

- Among patients without KRAS mutations, the addition of Vectibix improved progression-free survival (time before disease got worse). Progression-free survival was 5.9 months among patients treated with chemotherapy plus Vectibix compared with 3.9 months among patients treated with chemotherapy alone. The addition of Vectibix did not significantly improve overall survival.
- Among patients with KRAS mutations, the addition of Vectibix did not improve progression-free or overall survival.
- Side effects of Vectibix included skin rash, low magnesium levels, and diarrhea.

The results of this study suggest that the addition of the targeted therapy Vectibix to second-line chemotherapy improves progression-free survival among patients with metastatic colorectal cancer. The benefit only applies to patients whose tumors do not contain KRAS mutations.

Peeters M, Price T, Hotko Y et al. Randomized phase III study of panitumumab (pmab) with FOLFIRI versus FOLFIRI alone as second-line treatment (tx) in patients (pts) with metastatic colorectal cancer (mCRC): Patient-reported outcomes (PRO). Presented at 2010 ASCO Gastrointestinal Cancers Symposium. Orlando, FL, January 22-24, 2010. Abstract 282.

14. Folfox Before Surgery for Lymph Node Mets With Synchronous Liver Mets (Jan. 28/10)

The combination of chemotherapy and surgery holds promise for improving CRC patient prognosis. This retrospective study evaluated the impact of chemotherapy on primary lesions and lymph node (LN) metastases. 16 CRC patients with synchronous (discovered at the same time) liver metastasis underwent a radical operation between March 2005 and August 2007. 8 of the 16 cases (surgery group) were operated on for the primary lesion without chemotherapy and another 8 cases (chemotherapy group) were operated on after chemotherapy with FOLFOX. 5 of the 8 patients in the surgery group were found to have LN metastasis. However, only 2 of the 8 patients in the chemotherapy group were found to have LN metastasis. The ratio of LN metastasis (number of metastatic LNs/resected LNs in total) was 11.1% in the surgery group, but it was 4.8% in the chemotherapy group. Necrotic areas (areas of dead tumour cells) were widely detected in the LN specimens of the chemotherapy group. The percentage of lymphatic (ly) and vascular (v) invasion in the primary lesions was smaller in the chemotherapy group (ly 12.5% vs. 25.0%) than in the surgery group (ly 62.5% vs. 50.0%). The patients in the chemotherapy group had no significant adverse effects and did not show a worse survival rate overall than the surgery group. Investigators concluded that there was a promising effect of chemotherapy on the status of LN metastasis and vessel invasions at the primary site as observed in the patients who responded to FOLFOX.

Sawayama, Hiroshi, et al., Treatment results of folfox chemotherapy before surgery for lymph node metastasis of advanced colorectal cancer with synchronous liver metastasis: the status of LN metastasis and vessel invasions at the primary site in patients who responded to folfox. International J of Clinical Oncology: Vol. 15, No. 1, February, 2010. Pp. 7076.

15. New Drug AZD6244 (ARRY-142886) Tested Against Xeloda (Feb. 4/10)

This study sought to assess the efficacy and safety of the MEK1/2 inhibitor AZD6244 (ARRY-142886) in patients with metastatic colorectal cancer who had failed one or two previous chemotherapeutic regimens that included oxaliplatin and/or irinotecan. This was a Phase II, multicentre, open-label, randomized, two-arm, parallel-group study comparing AZD6244 with capecitabine (xeloda) monotherapy. Patients received either 100 mg twice daily oral AZD6244 every day or 1,250 mg/m² twice daily oral capecitabine, for 2 weeks, followed by a 1-week rest period, in 3-weekly cycles. The primary endpoint was the number of patients experiencing disease progression events. Sixty-nine patients were randomized in the study (34 and 35 patients in the AZD6244 and capecitabine groups, respectively). Disease progression events were experienced by 28 patients (~80%) in both the AZD6244 and capecitabine treatment groups. Median progression-free survival was 81 days and 88 days in the AZD6244 and capecitabine groups, respectively. Ten patients in the AZD6244 treatment arm had a best response of stable disease. For capecitabine, best response was a partial response in one patient, with stable disease in a further 15 patients. Investigators concluded AZD6244 showed similar efficacy to capecitabine in terms of the number of patients with a disease progression event and of progression-free survival. AZD6244 is currently undergoing evaluation in Phase II trials in combination with other chemotherapeutic agents.

Bennouna, Jaafar, et al., A phase II, open label, randomized study to assess the efficacy and safety of the MEK1/2 inhibitor AZD6244 (ARRY-142886) versus capecitabine monotherapy in patients with colorectal cancer who have failed one or two prior chemotherapeutic regimens. Investigational New Drugs. DOI: 10.1007/s10637-010-9392-8. Feb. 1/10

16. **Hormone Replacement Therapy Shown To Reduce Colon Cancer** (Feb. 9/10)

Women in this study of California teachers who were taking hormone replacement therapy (HRT) after menopause had a 36% reduced risk of colon cancer over ten years than women who weren't on HRT at the beginning of the study. Risk reduction was even greater for women with a first-degree relative who had colon cancer. Their risk fell 55%. Over 57,000 women were part of the study, about 60% of them on HRT at the study start. Over the next ten years, 444 got colon cancer. Despite the reduction in colon cancer in the study, doctors caution women about using HRT because of raised risks for breast cancer, heart attack, stroke, and blood clots. Advice is to use the lowest dose for the shortest time to offset severe menopausal symptoms.

DeLellis Henderson, Katherine, et al., Menopausal Hormone Therapy Use and Risk of Invasive Colon Cancer. American J of Epidemiology. Advance Access published online on Jan. 11, 2010. 171(4): pp. 415-425.

17. **Pre-emptive Skin Treatment With Vectibix** (Feb. 11/10)

Panitumumab is a fully human monoclonal antibody targeting the epidermal growth factor receptor (EGFR). Skin toxicities are the most common adverse events with EGFR inhibitors such as panitumumab or better known as vectibix. This is the first study designed to examine differences between pre-emptive and reactive skin treatment for specific skin toxicities in patients with mCRC (metastatic colorectal cancer) for any EGFR inhibitor. Patients receiving panitumumab-containing therapy were randomly assigned 1:1 to pre-emptive or reactive treatment (after skin toxicity developed). Pre-emptive treatment included use of skin moisturizers, sunscreen, topical steroid, and the antibiotic doxycycline. Of 95 enrolled patients, 48 received pre-emptive treatment, and 47 received reactive treatment. The incidence of grade 2 skin toxicities during the 6-week skin treatment period was 29% and 62% for the pre-emptive and reactive groups, respectively. Investigators concluded that the pre-emptive skin treatment regimen was well tolerated. The incidence of specific grade 2 or greater skin toxicities during the 6-week skin treatment period was reduced by more than 50% in the pre-emptive group compared with the reactive group. Patients in the pre-emptive group reported less quality of life (QOL) impairment than patients in the reactive group.

Lacouture, Mario, et al., Skin Toxicity Evaluation protocol with panitumumab (STEPP), a phase II, open label, randomized trial evaluating the impact of a pre-emptive skin treatment regimen on skin toxicities and quality of life in patients with metastatic colorectal cancer. J of Clin Oncology. Published online ahead of print Feb. 8, 2010. DOI: 10.1200/JCO.2008.21.7828

18. **Administering Erbitux Weekly vs. Biweekly in Combination with Irinotecan** (Feb. 15/10)

The aim of this study was to compare the efficacy and safety of weekly versus an every 2-week administration of cetuximab (erbitux) in association with irinotecan in patients with metastatic colorectal cancer (MCRC). Investigators reviewed the clinical records of 50 patients with MCRC who began treatment with cetuximab from February 2004 to January 2007. Two different treatment schedules were used. In the first group of 32 patients, cetuximab was given at an initial dose of 400 mg/m², followed by weekly infusions of 250 mg/m². In the second group of 18 patients, cetuximab was administered every 2 weeks at a dose of 500 mg/m². The two groups were compared for tumor response, time to progression (TTP), overall survival (OS), and toxicity. : All patients had received irinotecan and 5-fluorouracil; a majority had previously received oxaliplatin. Disease control (partial response + stable disease) was achieved in 56.3% of patients receiving weekly cetuximab versus **77.8%** in the other group. The median follow-up for all patients was 34.2 months. TTP (Group 1: 28% vs. Group 2: **18%**) and OS (Group 1: 75% vs. Group 2: 72%) rates at 7 months were similar in the two groups. Skin toxicity was the most relevant adverse event: 78.1% of the patients had acne-like rash in the first group and 61% in the second group. However, only one patient in each group had a grade 3 toxic reaction. Investigators concluded that there is no major difference of efficacy and safety between cetuximab given every 2 weeks and a weekly dosing regimen, in association with irinotecan.

19. Should Chemotherapy Be Administered to Stage II CRC Patients (Feb. 15/10)

While most patients with stage II colon cancer are at low risk of recurrence, there are patients in this group who are at increased risk and who may need chemotherapy to reduce their risk or recurrence. The average stage II patient has an absolute benefit of only 1 or 2% from chemotherapy. In other words, the average Stage II patient will decrease risk of recurrence by only 1 or 2% if they have chemotherapy. And since chemotherapy has its own risks, it is important to identify those at increased risk whose potential benefit would be greater than average. Currently a variety of factors are used to try to identify which stage II patients are at increased risk of recurrence.

- The first is the **number of lymph nodes** examined. Not only is examination of at least 8 to 12 nodes essential to accurate staging but the number of nodes removed is a strong prognostic indicator. In other words, people with more nodes removed do better than people with fewer. At the 2010 Gastrointestinal Cancer Symposium it was again confirmed that patients with 12 or more lymph nodes examined had a recurrence risk at 3 years about 5% lower than those with examined fewer nodes. It was further noted that the prognostic value of lymph node number was independent of the 12 gene recurrence score.
- The 12 gene recurrence score (Oncotype DX Colon recently released by Genomic Health) reports patients as at high, medium or low risk of recurrence at 3 years. The recurrence scores range from an average risk of 12 % for low risk, 18% for medium risk to 22% for high risk.
- Also frequently used to evaluate stage II tumors is lymphovascular invasion (the visualization of cancer cells in small vessels within the tumor), T stage (T3 versus T4), and the markers **18qLOH** and **MSI** (microsatellite instability).
- **Microsatellite status** has been shown to be a prognostic indicator in stage II colon cancer. Patients with pMMR (proficient mismatched repair) have worse outcomes than those who are deficient in mismatch repair (dMMR or MSI-H). The 5 year survival for patients who have pMMR is less than 75% in comparison with those who have dMMR (MSI-H) whose 5 year survival is greater than 90%. About 15% of patients have deficient mismatch repair (are MSI) and are at reduced risk of recurrence. A presentation at the ASCO Gastrointestinal Symposium indicated a need for physician **education on the value of mismatch repair testing** and use in treatment planning.
- Those who have **loss of heterozygosity at 18q**, a place on a chromosome, (18qLOH) are at increased risk of recurrence.

Examination of these factors and others can assist patients and their physicians to decide whether or not to have chemotherapy. At this point, no single factor is adequate to guide treatment decisions. When many factors available are used together, though, sufficient information is available to assist physicians and their patients to decide whether or not chemotherapy is warranted. Since patients vary widely in the amount of decreased risk necessary to justify the toxicity and expense of chemotherapy, the decision must be made on an individual basis. This will require better education of physicians so they can better inform their patients.

C3 Research Update. Feb. 16, 2010. www.c3colorectalcancer.com

20. Irinotecan in The Elderly Who Have Metastatic Colorectal Cancer (Feb. 16/10)

Several studies have confirmed the benefits of adjuvant (post surgical) chemotherapy with 5-fluorouracil/leucovorin for treatment of colorectal cancer. Few studies have evaluated other chemotherapies that are now available for colorectal cancer management. This study primarily sought to evaluate the survival benefit of first-line irinotecan use in a group of elderly patients with stage IV (metastatic) colorectal cancer. Data on chemotherapy users with a diagnosis of colorectal cancer reported between 1998 and 2002 were obtained from the Surveillance Epidemiology and End Results (SEER)–Medicare database. Irinotecan was one of the newer chemotherapy agents in the available data. Chemotherapy episodes, defined as periods of continuous chemotherapy treatment with no gaps >90 days between successive claims, were identified. The first chemotherapy episode after diagnosis was used to identify lines of treatment: patients may have initiated irinotecan therapy within 2 months (first-line), used irinotecan later in the first episode (second-line), or not used irinotecan at all. Of 3327 chemotherapy users (mean/median age, 75 years), 842 (25.3%) initiated chemotherapy using irinotecan. No overall survival benefit for irinotecan was observed in the primary analysis comparing irinotecan initiators with all other chemotherapy users (including those who used irinotecan subsequently). Factors that were negatively associated with survival included older age, presence of >1 comorbidity, a high tumor grade, lymph node involvement, and a primary tumor site in the colon. Surgery was positively associated with a lower hazard of death. Irinotecan users had higher rates of hospitalizations possibly due to chemotherapy-related adverse effects. This retrospective claims study had limitations such as a lack of information on patient performance status, dosing, and the types of regimens used; hence, certain assumptions had to be made and selection bias may have been involved. The definitive survival advantage of irinotecan observed in clinical trials was not reproducible in this population of elderly

Medicare patients. The results emphasize the need for expansion of trials to include a more diverse patient group as well as continued evaluation of more recent chemotherapies in real-world settings.

Obeidat, NA, et al., Outcomes of irinotecan based chemotherapy regimens in elderly medicare patients with metastatic colorectal cancer. American J Geriatric Pharmacother, 2009. Dec. 1; 7(6): pp. 343-354

21. New Monoclonal Antibody Being Tested in Colorectal Cancer Patients (Feb. 17/10)

Johns Hopkins Hospital has initiated a Phase I trial with a new therapeutic antibody, NPC-1C, in patients with late stage pancreatic or colorectal cancer. NPC-1C is a novel, chimeric (composed of genetically different tissues) monoclonal antibody intended for the treatment of advanced pancreatic and colorectal cancer, and is the company's first antibody to target specific cancers. Pre-clinical studies have demonstrated that NPC-1 specifically targets pancreatic and colorectal cancer sparing healthy tissue. Having a treatment that would target the cancer specifically and spare healthy organs would represent a significant advancement in the treatment of this disease. Neogenix Oncology is a cancer therapeutics and diagnostic company focused on developing innovative new products targeting a broad range of cancers. The company's portfolio includes monoclonal antibodies that have been shown to target tumor-specific immunogenic proteins derived from specific tumor subtypes. Neogenix Oncology monoclonal antibodies are unique in that they define the immunogenic tumor protein as both a diagnostic marker and as a therapeutic target for tumor destruction. This revolutionary approach could offer patients a new range of therapeutic alternatives in the future.

www.medicalnewstoday.com

SURGICAL THERAPIES

22. Specialization Can Improve Outcomes After Surgery (Jan. 17/10)

According to this study, patients who undergo emergency colorectal surgery have better outcomes if the surgeon is specialized in colorectal surgery. Investigators compared outcomes in 1,046 patients who underwent emergency colorectal resection by either a colorectal surgeon (368 patients) or a general surgeon (678 patients). The researchers found that patients operated on by a colorectal surgeon had significantly lower postoperative morbidity (52.2 versus 60.5%), significantly less anastomotic dehiscence (the opening of the joined end of the large intestine) (6.2 versus 12.1%), and significantly lower postoperative mortality (17.9 versus 28.3%). According to the investigators, being operated on by a colorectal surgeon was predictive of all three outcomes. They concluded, this study shows that specialization in colorectal surgery improves mortality, morbidity, and anastomotic dehiscence rates after colorectal emergencies as well as raising the percentage of single-stage procedures."

Biondo, Sebastiano, et al., Impact of surgical specialization on emergency colorectal surgery outcomes. Archives of Surgery. Vol.145, No. 1, January 2010: pp. 79-86

23. Acupuncture Does Not Help Prevent Ileus After CRC Surgery (Jan. 20/10)

This study found that daily acupuncture did not reduce the number of patients who did not have bowel function return by the fourth day after their operation, a condition known as *prolonged post-operative ileus (PPOI)*. Bowel function included passing gas (*flatus*) or a bowel movement. Patients were randomly assigned to a daily acupuncture treatment by an experienced physician acupuncturist. By the fourth day, there was no difference in patients who had acupuncture and those who didn't in either return of bowel function or quality of life. The study team concluded that acupuncture did not prevent prolonged post-operative ileus (PPOI) and was not useful for treating PPOI once it had developed in this population.

Meng, Zhi-Qiang, et al., Electro-acupuncture to prevent prolonged postoperative ileus: a randomized clinical trial. World J of Gastroenterology. January 7, 2010. 16(1): pp. 104-111

24. Stage I and II Colon Cancer Retrieved Lymph Nodes Connected to Microsatellite Instability (Jan. 20/10)

According to this study, many retrieved lymph nodes are strongly connected with microsatellite instability (MSI) in stage I and II colon cancer. Among 82 patients with stage I or II cancer, the average number of negative nodes found was 13.7 in a group of 71 with microsatellite stable tumors. However, the average number for MSI tumors was 23.6. The average number of examined nodes for all stage I and II cancers in the hospital where the study was completed was 15, and 9 of the 11 MSI tumors (82%) had more than this number of nodes retrieved and tested. Investigators concluded that good prognosis that is usually associated with tumors having a high number of uninvolved lymph nodes might reflect the high prevalence of MSI among these tumors. The number of examined lymph nodes as a quality criterion should be used with caution. For stage I or stage II colorectal carcinomas, restricting MSI phenotyping to tumors with more than the mean number of lymph nodes identifies almost all MSI tumors.

25. Positive Results Dependent on Liver Resectability (Jan. 28/10)

Patients with stage IV colorectal cancer live longer when tumors in their liver can be removed surgically, but not all patients have cancer that can be operated on. Separating patients with liver tumors from colorectal cancer into three groups according to possible liver resectability, British doctors found a wide variation in both overall survival and progression-free survival three years later. A team of surgeons, medical oncologists, and radiologists divided patients in a clinical trial studying CAPOX (xeloda plus oxaliplatin) chemotherapy into three groups:

- A : those whose treatment was considered to be *palliative* and not treatable with surgery.
- B : those where chemotherapy might *convert* initially unresectable metastases and make surgery possible.
- C : patients with resectable liver mets receiving *neoadjuvant* chemotherapy before surgery.

Among 128 patients who were part of the study, 74 were in the palliative group, 22 in the conversion, and 32 in the neoadjuvant groups. Patients had scans every four cycles of chemotherapy, and when it was possible liver surgery was attempted after four or eight cycles. Ten patients (45%) of the conversion group and 19 (59%) of the neoadjuvant group eventually had surgery.

- Three years later, 10% of the conversion and 37% of the neoadjuvant group were alive and their cancer had not gotten worse (*progression-free survival*).

Median overall survival for all three groups:

- Palliative treatment — 14.6 months
- Conversion chemotherapy — 24.5 months
- Neoadjuvant chemo — 52.9 months

Patients in the study received CAPOX chemotherapy in three week cycles. The CAPOX regimen was oral Xeloda (capecitabine) daily for 14 days after an initial infusion of oxaliplatin on day one. The team concluded that this prospective study shows the wide variation in outcome according to baseline resectability status and highlights the potential clinical value of a modified staging system to distinguish between these patient subgroups.

Watkins, DJ, et al., Defining patient outcomes in stage IV colorectal cancer: a prospective study with baseline stratification according to disease resectability status. British J of Cancer (2010); 102: pp. 255-261

26. Endoscopic Mucosal Resection for Colorectal Cancer Tumours Exceeding 4cm (Feb. 5/10)

This study sought to evaluate the feasibility and the outcome of endoscopic mucosal resection (EMR) for large colorectal tumours exceeding 4 cm (LCRT) undergoing piecemeal resection. From January 2005 – April 2008, 146 digestive tumours larger than 2 cm were removed with the EMR technique. Of these, 34 tumours were larger than 4 cm and piecemeal resection was carried out on 26 colorectal tumours. The average age of the patients was 71 years. The average follow up duration was 12 months. Investigators report that LCRTs were located in the rectum, left colon, transverse colon and right colon in 58%, 15%, 4% and 23% of cases, respectively. All were sessile tumours larger than 4 cm with an average size of 4.9 cm. During follow-up, recurrence of the tumour occurred in 3 patients (12%), three of whom received endoscopic treatment. Researchers concluded that EMR for tumours larger than 4 cm is a safe and effective procedure that could compete with endoscopic sub mucosal dissection, despite providing incomplete histological assessment.

Soune, Ah, et al, Large endoscopic musocal resection for colorectal tumours exceeding 4 cm. World J of Gastroenterology. February 2010. 16(5): pp. 588-595

27. Lynch Syndrome and the Best Colon Surgery (Feb. 5/10)

Removing the entire colon (*subtotal colectomy*) is sometimes recommended for patients with Lynch syndrome when colon cancer is diagnosed. In addition, some people who have an inherited Lynch mutation have their colons removed to prevent the onset of colon cancer. While subtotal colectomy didn't reduce deaths from Lynch-related colon cancer, it did cut down on additional colorectal cancer diagnoses and the need for other abdominal surgery. Five years after surgery, 93% of patients who had subtotal colectomy were alive compared to 88% of those who had more limited operations or no surgery. This wasn't a significant difference. However, 84% survived the five years without needing additional abdominal surgery compared to 63% of the group who had limited or no surgery. Researchers analyzed people with Lynch syndrome. Cases included those who had *subtotal colectomy*, either at the time of colon cancer diagnosis or as preventive surgery. They were compared to controls who had limited operations to remove only part of the colon (*segmental colectomy*). In subtotal colectomy the colon is removed and the small intestine is attached to the rectum, which remains in place. Five years after surgery, comparing those who had subtotal colectomy to those with limited resection:

- 94% were alive without another colorectal cancer compared to 74% of the controls alive and without subsequent colorectal cancer.
- 84% survived without needing abdominal surgery compared to 63% of controls.
- 93% lived five years compared to 88% of controls.
- Time to another colorectal cancer or the need for abdominal surgery was shorter for those who had a limited resection.

Investigators concluded that even though no survival benefit was identified between the cases and controls, the increased incidence of metachronous colorectal cancer and increased abdominal surgeries among controls warrant the recommendation of subtotal colectomy in patients with Lynch syndrome. Lynch syndrome is a highly increased risk for colorectal and other related cancers caused by an inherited mutation in one of the mismatch repair genes. People with a Lynch syndrome genetic mutation have a lifetime risk for colorectal cancer as high as 80%.

Natarajan, Nagendra, et al., Comparison of extended colectomy and limited resection in patients with lynch syndrome. Diseases of the Colon & Rectum: January 2010; Vol. 53, Issue 1: pp. 77-82

28. CEA Levels Important Before Surgery For Stage II Patient Prognosis (Feb. 9/10)

According to the results of this study, patients whose CEA (carcinoembryonic antigen) blood levels before surgery were low — below 5 ng/ml — had significantly better overall and disease free survival than those whose CEA's were 5 or higher. For those with low CEA, overall survival at five years was 81.7% compared to 69.9% for high CEA. Disease-free survival was 82.4% for low CEA and 70.6% for CEA that was 5 ng/ml or higher. However, CEA levels only made a difference in stage II patients. There was no significance for stage I or III. Investigators concluded that preoperative serum CEA is a reliable predictor of recurrence and survival after curative surgery in patients with colon cancer, particularly in those classified as having stage II disease.

Huh, Jung Wook, et al., Preoperative carcinoembryonic antigen level as an independent prognostic factor in potentially curative colon cancer. J of Surgical Oncology. Published online 29 Jan. 2010.

RADIATION / INTERVENTIONAL RADIOLOGY

29. The Use of PET in Oncology (Jan. 17/10)

This study speaks to the utility of PET; that it is a crucial technique in molecular imaging, allowing live assessment and localization of pathological processes, thanks to its ability to detect very small amounts of radioactive molecules. This is of particular interest in oncology where abnormal metabolism or synthesis in tumor cells but also various tumor characteristics can be studied using this nuclear medicine technique. FDG is currently the most widely used tracer, nowadays essential in the management of various malignancies, with large applications in **diagnosis, initial assessment, therapy monitoring, and recurrence detection**. The combination of anatomical information provided by PET/CT further increased its interest. Beyond its spread use in daily practice, future applications of PET will involve other tracers than FDG and develop research applications in humans as well as in small animals.

Papathanassiou, D, et al., Positron emission tomography in oncology: present and future of pet and pet/ct. Crit Rev Oncol hematol. 2009 Dec 15; Epub ahead of print.

30. SBRT For Liver Mets (Jan. 22/10)

Stereotactic body radiation therapy (SBRT) is a treatment option for colorectal liver metastases. Local control patient survival and toxicity were assessed in an experience of SBRT for colorectal liver metastases. SBRT was delivered with curative intent to 20 consecutively treated patients with colorectal hepatic metastases who were candidates for neither resection nor radiofrequency ablation (RFA). The median number of mets was 1 and median size of mets was 2.3 cm. The median follow up was 26 months. The two year local control and survival rates were 74 and 83% respectively. The investigators reported that SBRT is a treatment option for patients with colorectal liver metastases who are not candidates for resection or RFA.

Van der Pool, AEM, Stereotactic body radiation therapy for colorectal liver metastases. British J of Surgery. Vol. 97, Issue 3: pp. 377-382

31. Brachytherapy Treatment: Cesium-131 Implanted into Colon Cancer Patient (Jan. 24/10)

Physicians in the U.S. have performed the world's first Cesium-131 (Cs-131) implant for the treatment of colorectal cancer. This implant was performed on a 38-year-old patient with locally recurrent colon cancer who underwent surgical resection of the tumor as a part of the treatment. The patient has a history of multiple prior surgeries and chemotherapy for colorectal cancer. The patient tolerated the procedure well and had no evidence of cancer recurrence or any side effects that can be attributed to the Cesium-131 seed implant at the last follow-up visit. Cesium-131 was chosen for its short half-life and higher dose rate. In addition, the Cs-131 seed brachytherapy procedure has the advantage of relative safety to the medical staff (because of faster radioactive dose fall-off) if the patient requires additional medical care soon after the implant. Cesium-131 is now being used successfully to treat lung, head and

neck, ocular melanoma, and prostate cancers in other patients. In doing so, Cs-131 is expanding brachytherapy options for patients beyond the prostate to locally recurrent cancers in many areas of the body.

<http://www.medicalnewstoday.com/articles/176870.php>

32. CT Colonography Use in the Elderly

(Jan. 28/10)

CT colonography (*virtual colonoscopy*) found more than twice the rate of large polyps or cancer in patients 65 and older compared to everyone being screened for colorectal cancer using the radiology-based test. About one in six older patients was referred for an optical colonoscopy (conventional colonoscopy) based on findings from the scans. There were no major complications including colon perforations or bleeding, from either the CT procedure or the follow-up colonoscopy. Researchers reviewed results of 577 people from 65 to 79 tested with CT colonography screening program and found either an advanced adenoma or cancer in 44 (7.6%). There were 5 cancers detected. The rate of *advanced neoplasia* (advanced adenoma or cancer) for all the patients screened in the program, young and old, was 3.2%. The percentage of older patients who were referred for an optical colonoscopy was about twice that of those under 65 — 15.3% of patients 65 and older, 7.6% of younger people. Optical colonoscopy confirmed the positive CT findings in all but 4% of cases, not verifying 3.6% of smaller polyps measuring 6 to 10 mm and 2.1% of those larger than 10 mm. The scans also found potential problems outside the colon in 89%, 45 of whom needed additional medical studies. Workups discovered 21 previously undetected abnormalities including a lung cancer and 18 aneurysms. The authors point out that the study was retrospective, looking back at experience in their program, and that negative findings were not verified by an optical colonoscopy. In the past, there has been a lack of evidence for its effectiveness in people 65 and older. And there was also concern that CT colonography identifies issues outside the colon which require additional medical follow-up and may not be serious medical problems. Researchers from this study concluded that CT colonography is a safe and effective screening modality for the older population.

Kim, David H, et al., CT Colonography: Performance and program outcome measures in an older screening population. Radiology; Vol. 254, pp. 493-500, February 2010.

33. RFA For Liver Metastases (Feb. 16/10)

An expert panel consisting of ASCO scientists sifted through published RFA research so they could answer “How useful is radiofrequency ablation (RFA) in treating liver metastases from colorectal cancer”? While the panel could not find sufficient evidence to establish an evidence-based practice guideline for RFA to treat cancer that had spread to the liver from the colon or rectum, they did complete a review of existing studies and called for more research into the usefulness of RFA to improve outcomes for patients with liver metastases from colorectal cancer. In reviewing existing medical literature, the panel focused on three important points:

- The effectiveness of RFA versus surgical resection for those tumors that could be surgically removed (*resectable*).
- The usefulness of RFA to treat tumors that could not be surgically removed (*unresectable*).
- RFA approaches (*open, laparoscopic, or percutaneous*).

RFA uses metal probes and low frequency electric current to heat and destroy tumor tissue. Radiofrequency also seals small blood vessels to reduce bleeding risk. Because heat is confined to the cancerous tissue, patients don't feel it and normal liver tissue is protected. RFA can be performed during an open surgery, laparoscopically, or through the skin, percutaneously. During all treatments, good imaging is critical to be able to see the tumor being ablated. CT scans, MRI, or ultrasound can be used during percutaneous RFA, but intraoperative ultrasound is used during an open or laparoscopic operation. *Postablation syndrome* occurs in about 30 to 40% of patients, usually beginning three days after an RFA procedure and lasting about five days. Patients experience low-grade fever, chills, malaise, achiness, pain, and nausea and vomiting. It is more common when large tumor volumes are treated and is probably due to inflammation as treated tissues die. Other complications from RFA were relatively low and were more common in open as opposed to percutaneous methods. There were fewer complications among more experienced doctors and in hospitals with more RFA experience. The Expert Panel also included an Appendix to help doctors discuss options with patients when managing liver metastases from colorectal cancer. Panel members concluded that there is a compelling need for more research to determine the efficacy and utility of RFA to increase local recurrence-free, progression-free, and disease-free survival as well as overall survival for patients with colorectal hepatic metastases. Clinical trials have established that hepatic resection can improve overall survival for patients with resectable colorectal hepatic metastases.

Wong, Sandra L., et al., American Society of Clinical Oncology 2009 Clinical Evidence Review on Radiofrequency Ablation of Hepatic Metastases From Colorectal Cancer. J of Clinical Oncology, Vol. 28, No. 3 (January 20, 2010): pp. 493-508

SCREENING

34. Blood Test Developed to Detect Colorectal Cancer

(Jan. 16/10)

A blood test that helps to detect colorectal cancer is now available. The ColoVantage test detects changes in DNA shed into the blood stream from colon and rectal tumors. It will be offered in the US by Quest Diagnostics. In preliminary results from a clinical trial of nearly 8,000 people, the blood test found colorectal cancer in about 50%. Previous studies have identified cancer at all stages in 70% of those who had it. The test is over 90% specific with few false positives. Developed by the German firm Epigenomics, the molecular test is based on changes in DNA called *methylation*. If the test finds methylation of the SEPTIN9 gene in blood, patients are referred for colonoscopy and further evaluation for possible colorectal cancer. The goal is to find cancer in the early stages when it is most curable. In describing the use of the molecular test, investigators claimed that the big issue in colorectal cancer screening remains that far too few people make use of it. Stool tests and colonoscopy are still not sufficiently accepted by patients. In this situation a simple blood test makes a lot of sense as it is easy to use for the patients and quickly done. And who wouldn't accept to undergo colonoscopy if the blood test already indicated a high risk of having colorectal cancer. The test has not yet been approved by the FDA in the United States.

www.abbott.com/global/url/

35. Oral Sodium Phosphate Laxative Inducing Elevated Phosphate Levels (Jan. 18/10)

Colon cleansing is used widely for colonoscopic exploration and colonic surgery. Oral sodium phosphate (OSP) solution is the osmotic laxative most commonly used for this purpose. It is known that OSP can induce severe hyperphosphatemia (elevated level of blood phosphate) and hypocalcemia (low level of calcium in the blood) due to excessive absorption of phosphates, and there have been reports of deaths and irreversible dialysis-requiring renal insufficiency. However, no prospective studies have investigated the prevalence of hyperphosphatemia in low-risk patients. This research article addresses this issue. A research team from Argentina recruited one hundred individuals aged 35-74 years to study the frequency of hyperphosphatemia following the administration of OSP. They found that in low-risk, well-hydrated patients, hyperphosphatemia following standard OSP doses was related to weight. Their results suggest performing preoperative evaluation aimed at avoiding administration of OSP laxatives to patients at risk; reducing the dose of OSP in patients with low weight; and avoiding dehydration with an adequate oral intake of clear liquids.

Casais MN, et al., Hyperphosphatemia after sodium phosphate laxatives in low risk patients: Prospective study. World Journal of Gastroenterology, 2009; 15 (47): 5960 DOI: [10.3748/wjg.15.5960](https://doi.org/10.3748/wjg.15.5960)

36. New Biomarkers Identified To Help Predict Spread of CRC (Jan. 15/10)

Scientists in China are reporting the discovery of two proteins present in the blood of people with colon cancer that may serve as the potential biomarkers for accurately predicting whether the disease will spread. Surgery is the main method of treating the disease. However, half of colon cancer patients undergoing surgery develop a recurrence of the disease within 5 years due to its spread, or metastasis, to other parts of the body. The spread of colon cancer can be difficult to detect and there are currently no reliable chemical markers in the body for predicting its spread, the scientists say. In an effort to identify useful biomarkers for tracking the spread of colon cancer, the scientists compared proteins produced by primary, or original, tumor cells to those of metastasized cells that came from a single individual with colon cancer. They identified two proteins that occurred at significantly higher levels in the metastatic cells than in the primary cancer cells. The two proteins could serve as potential biomarkers in a blood test for predicting the spread of colon cancer, allowing earlier intervention and treatment, the scientists say

Xue, Hua, et al. Identification of Serum Biomarkers for Colorectal Cancer Metastasis Using a Differential Secretome Approach. Journal of Proteome Research, 2010; 9 (1): 545 DOI: [10.1021/pr9008817](https://doi.org/10.1021/pr9008817)

37. Genomic Health Launches Colorectal Cancer Test For Stage II Colorectal Cancer (Jan. 28/10)

Genomic Health Inc. announced the availability of a new 12 gene test to assess disease recurrence in stage II colorectal cancer. The test is called Oncotype Dx and it could help physicians and their patients with stage II colorectal cancer assess disease reoccurrence. The 12 gene lab developed test had its clinical results presented at this year's GI ASCO as an independent predictor of recurrence risk in stage II colon cancer patients. The higher the recurrence score, the more likely the disease is to recur. The score range is from 1-100 and Canadians may now access the test through their physicians to determine if adjuvant therapy should be part of their treatment plan. The test may be in a position to prevent stage II colon cancer patients from having to undergo unnecessary toxic adjuvant therapy (chemo after surgery). For more information, please visit Genomic Health Inc at www.genomichealth.com

<http://www.glgroup.com/News/Genomic-Health-Launches-Colorectal-Test-46275.html>

38. Cancer Blood Test Being Developed (Feb. 8/10)

The National Cancer Institute recently shared information about exciting new research that may lead to blood tests for **many different types of cancer**. This type of blood test would be a very important advance in the way cancers are detected. An easy, simple blood test to find cancer early would be so important in the fight against this disease. It would allow doctors to discover cancers early, when they are most treatable. There are two barriers to detecting cancer early, when it is more easily treatable:

- There is a lack of technology to detect certain cancers. As an example, ovarian cancer is difficult to detect, the symptoms are vague and easy to miss, and there are no good screening tests to catch this cancer early. Pancreatic cancer also is difficult to detect. No standard screening tests are available to find pancreatic cancer before it has spread. Survival rates for these cancers are lower than for many other cancers - the cancers for which good screening tests *do* exist, such colorectal.
- Technology to detect the cancer exists, but it is invasive or uncomfortable, so people tend to shy away from them.. As an example, colonoscopy to detect colon cancer is reasonably good at finding the disease. However, preparation for the test involves completely emptying (cleansing) the colon. Many people find this unpleasant, though not painful. Due to the discomfort experienced preparing for a colonoscopy, as well as fear and embarrassment about the test itself, many people do not access a colonoscopy as often as recommended by their doctor.

In the new research, scientists from Denmark found that the body may produce something called an antibody in response to cancer. An antibody is a protein made by the immune system when harmful substances such as bacteria, viruses, and parasites enter the body. The Danish researchers discovered that in some people with cancer, the body produces antibodies against their own cancer. The goal is to use these auto- or self- antibodies to create a blood test to detect cancer very early, before the tumor is able to spread. There shall be more information forwarded on cancer autoantibodies as it is published.

www.cancer.gov/newscenter

PSYCHO-SOCIAL

39. Wellness Coaching Help Cancer Survivors

(Jan. 15/10)

New research is showing that wellness coaching, a relatively new type of health intervention, had significant, immediate, and lasting impact in reducing anxiety and depression, while simultaneously improving quality of life and increasing other healthy lifestyle behaviors. The American Cancer Society recommends survivors maintain a healthy weight and engage in healthy lifestyle habits to reduce risk of recurrence, mortality, and other chronic diseases, yet the majority do not, according to recent research. This study looked at the initial and longitudinal benefits that wellness coaching might have with cancer survivors. Investigators are maintaining that it is the first research published utilizing this methodology as a single intervention, which has promising results and potential application in other areas. Randomized controlled trials are required to confirm the results of this study, but investigators are encouraged with the initial results. The idea to apply this methodology to cancer survivorship came in 2004, when wellness coach and fitness professional, Pam Schmid was diagnosed with breast cancer. She was a leader in the new field of wellness coaching and recognized the wide reaching benefits coaching might offer survivors, after struggling personally with the challenges treatment brought her way. Some health behaviors can reduce risk of recurrence or dying of their cancer as much as 50%. It's critical to support survivors to do the things they can do to not only improve their risks but to improve their quality of life. In this observational cohort study of 30 breast, prostate, and colorectal cancer survivors, participants received six coaching sessions over a three month period. They were followed for a year after the intervention to evaluate the sustainability of changes through the wellness coaching. Wellness coaches are credentialed professionals who are trained and certified as coaches. In this study, a fitness professional certified as an ACSM (American College of Sports Medicine) Health Fitness Instructor and Wellness Coach (through Wellcoaches Corporation -in partnership with ACSM) served as the coach. Participants were coached in three different states via telephone. Survivors reported in questionnaires that they increased their fruit and vegetable consumption, increased their physical activity and had a reduction in weight and BMI that was sustained one year after the intervention ended. The most helpful aspect reported was the motivation and feedback they received as they worked towards their goals.

- All sessions were conducted by phone
- Agenda/goals were client directed
- Survivors developed a wellness vision and three month goals
- Follow-up sessions supported consistent progress towards their vision/goals
- Expertise was given in a "just-in-time" method only as needed
- Utilized a strength-based approach

http://www.pamschmid.com/healthyandfitaftercancer/index_assets/OfficialCopy_LongitudinalBenefitsofWellnessCoachingInterventionsforCancerSurvivors_final.pdf

40. Insomnia During Cancer Care

(Feb. 1/10)

New research on 823 people receiving chemotherapy reveals that far more patients experience insomnia than previously thought. The researchers found that insomnia was at least twice as common in people receiving chemotherapy as compared with the general population. About 80% of those receiving chemotherapy had symptoms of insomnia or had insomnia syndrome at some point during treatment.

Younger people, those less than 58 years old, had a higher risk of insomnia compared with people over 58. The researchers noted that insomnia is common and under-treated among patients with cancer receiving chemotherapy. Getting more sleep should be a priority when undergoing treatment. It may seem impossible to improve sleep, but a few steps can help.

- *Don't ignore it.* If cancer treatment is affecting your sleep, talk to your doctor. Getting enough sleep is an important part of helping your body heal and tolerate treatment. Lack of sleep may also decrease immune function. Poor immune function, as measured by white blood cell count can make it harder to recover after each cycle of chemotherapy. Your doctor can help you decide if temporary use of a sleep medication will be helpful. Many people worry about becoming addicted to sleep medication, but short term use is safe for most people. And sleep aids can help "reset the clock". In a sense, these medications, when used occasionally, may help your body "remember how to sleep."
- *Help yourself.* Even if you decide not to take any sleep medications, you can do a lot to help yourself sleep better. Try cutting back on caffeine. For a start, don't have caffeine after noon. Also, if possible, keep yourself to 1-2 caffeinated beverages per day total. This includes coffee, colas, some teas, and energy drinks. Set up a relaxing ritual to signal "bedtime". For many people, following the same, soothing routine at night helps their brain and body wind down and sleep well. The routine might be reading a bit, having a cup of non-caffeinated tea such as chamomile, praying, or meditating. Just be sure whatever you read won't wind you up. When reading before bed, avoid upsetting topics like politics, war, and disaster. Cut down on TV and computer time. Researchers have found that light from electronic equipment can suppress melatonin, a hormone your body needs to produce for good quality sleep. Go TV- and computer-free for at least an hour before bed.

http://journals.lww.com/oncology-times/Fulltext/2010/01250/Insomnia_More_Common_in_Patients_Receiving.2.aspx

41. **Feeling A Sense of Loss After Cancer Treatment**

(Feb. 8/10)

Many people assume that immediately after cancer treatment, a person will want to do nothing but celebrate. And given that a diagnosis of cancer can leave a person reeling and confused, it may come as a surprise to know that many people actually end up "missing" their cancer treatment once it is completed. There are many reasons for a sense of let down after cancer treatment, but the important thing to know is that these feelings are normal. It's normal to miss aspects of your care after cancer treatment ends. Certainly, nobody misses things such as lower blood cell counts and the days lost to medical appointments. However, if asked, many cancer survivors admit that they miss their cancer healthcare providers -- the doctors and nurses who gave them so much in the care process. And certainly, the security and stability of the same appointments, at the same time, on a regular schedule can be comforting. One of the best ways to deal with a sense of loss and let down after cancer treatment is to admit that it's normal -- plain and simple. For someone who has never experienced cancer and its aftermath, the assumption may be that these feelings mean that you "wished" to be sick or like to play "the victim." Nothing could be further from the truth. It is a part of the human condition to process traumatic experiences in a variety of ways. Missing treatment certainly is within the realm of normal regarding what it takes to get through cancer. Beyond the first step -- acknowledging that missing treatment is normal -- you can undertake additional positive actions to cope with your feelings of loss after cancer treatment:

- **Reach out to your health care team after cancer treatment**
Pick up the phone to leave a message; it will likely be hard to get through to your doctor or nurse directly. Or, write a short note to your doctor and/or nurses to say "thanks" for a job well done. Let them know that you appreciate their hard work in making your treatment as successful as possible. Your healthcare provider will be thrilled by the acknowledgment, and you'll feel better too.
- **Seek "after cancer treatment" resources**
Find out if there are specific resources, such as support groups or educational sessions, specifically for people who have completed their cancer treatment. You don't need to sign on for years of group attendance. Often, you can use this sort of resource as much or as little as you need as you work through your feelings about being a cancer survivor.
- **Consider volunteering**
Volunteering is a great way to give back for some people. You know yourself best and if you don't feel ready, it's OK to admit that you don't want to "be around cancer" just yet. It's also alright if you never want to volunteer. Just know that this is an option. If you do want to volunteer, explore your options, which can range from a one-time project (such as helping organize a cancer center event) to a long-term commitment to be a "cancer buddy" or mentor to someone else who's been diagnosed with cancer. Before signing on, just make sure you feel physically and emotionally up to the task.
- **Explore the Internet**
Many people find that online support groups, chat boards, or email lists about cancer are a great resource. You may be surprised at how helpful this type of connection can be. You can tap into these resources any time day or night, and it allows you to take part a little or a lot. It's all up to you. You can start right here at About.com by visiting our Colon Cancer Forums.

- **Ask for a referral**

If you really feel out of sorts and feel as if your life will never return to "normal," seek professional help. There is no shame in asking your primary health care provider for a referral to a mental health care specialist. This doesn't mean you're "crazy" or "can't cope." It simply means you're smart enough to seek help when you need it, which is the best way to find the tools and skills needed to cope effectively with difficult situations.

- **Moving On After Cancer Treatment**

In the end, one of the most important things to know -- something that can help you cope with feelings after cancer treatment ends -- is that these feelings are normal. With time, you can move into a new phase and figure out ways to reclaim the joy in your life while honoring the challenging journey you've been through.

Miller, K, Merry, B, Miller, J. Seasons of survivorship revisited.. The Cancer Journal 2008 14:369-74

OTHER

42. Differences Between Right and Left Sided Colon Cancers (Jan. 17/10)

More evidence is emerging that right-sided colon cancers are different in significant ways from those on the left side of the colon. Information from 17,641 colon cancer patients in this study, found that people with cancers on the right side of the colon were older, had more chronic illness, and were more likely to be women. There were significantly more deaths in this group. While the rate of metastatic cancer spread was similar for both right and left sided tumors, spread to the liver or lungs was more common in the **left-sided cancers** and peritoneal carcinomatosis from **tumors on the right**. Right-sided tumors were more often poorly differentiated and found in nearby lymph nodes (*stage III*). Even after adjusting for risk factors, survival was worse for cancers on the right side. Right-sided tumors (*proximal*) included those in the ascending and transverse colon, while the left side includes the descending and sigmoid colon nearest to the rectum (*distal*). Investigators concluded that they found that right- and left-sided colon cancers are significantly different regarding epidemiological, clinical, and histological parameters. Patients with right-sided colon cancers have a worse prognosis. These discrepancies may be caused by genetic differences that account for distinct carcinogenesis and biological behavior. The impact of these findings on screening and therapy remains to be defined.

Benedix et al., Diseases of the Colon and Rectum, Volume 53, Issue 1, pp 57-64, January 2010.

43. Sexual Function in Colorectal Cancer Survivors (Jan. 25/10)

Findings from clinical and research studies suggest that the overall health-related quality of life of many colorectal cancer survivors is good. However, many survivors report significant sexual dysfunction after treatment that may adversely affect their quality of life in survivorship. This article examined studies investigating sexual function in men and women treated for colorectal cancer. Also included are data on the prevalence and nature of sexual dysfunctions in colorectal cancer survivors, the impact of specific treatment modalities for colorectal cancer on sexual function, and the management of sexual dysfunction in men and women. Published studies investigating sexual dysfunction after colorectal cancer treatment generally have been limited conceptually and methodologically. However, findings suggest that the prevalence of sexual dysfunction among colorectal cancer survivors is high. Sexual dysfunction is often a long-term and late effect of treatment for colorectal cancer. The assessment and management of sexual dysfunction in men and women treated for colorectal cancer should be standard practice throughout treatment and in survivorship.

Donovan, Kristine, et al., Sexual Function in Colorectal Cancer Survivors. Cancer Control: J of the Moffitt Cancer Centre. 2010; 17(1): pp. 44-51.

44. Avoiding Blood Clots (Feb. 11/10)

One of the potential side effects of some types of chemotherapy is blood clots. Blood clots should be taken very seriously. If a blood clot occurs in an area of the body supplying blood to a vital organ, such as the lungs or brain, it can be life threatening. Some people are given blood thinners during treatment, specifically to head off a blood clot before it occurs. Fortunately, these medications are very effective. If you are taking blood thinners as part of your cancer care, you should take these medications exactly as prescribed. New research has now identified a specific combination of cancer treatment medications that may increase the risk of developing blood clots. This is very important information. It can help your doctor determine whether you are at high risk of a blood clot. He or she can then manage your care better and reduce the chances you get a clot. The researchers found that a combination of the chemotherapy medication bevacizumab (Avastin,) and a type of red blood cell building medication called an erythropoietin stimulating agent (ESA), increases the risk of life-threatening blood clots. But even this isn't the full picture. In addition to this combination of medications, other things can up the risk as well. The researchers found that people who have any of the following are at higher risk of blood clots:

- Having had a blood clot in the past
- Having heart disease or a history of heart disease

- Being obese
- Using hormone therapy; examples include the birth control pill and hormone replacement therapy that some women use around the time of menopause

If you have any of these risk factors - a history of blood clots or heart disease, you are obese, or you are using hormones - talk to your doctor about whether you need to be extra careful about blood clots. Ensure your doctor knows if you have a history of heart disease or blood clots, or if you are using hormones. This information is important. Your doctor may decide on a different, safer course of treatment when considering all of these factors together.

Roddy, Julianna, et al., Thromboembolic events in patients with colorectal cancer receiving the combination of bevacizumab-based chemotherapy and erythropoietin stimulating agents. Amer J of Clinical Oncology: Feb. 2010; Vol. 33, Issue 1: pp. 36-42

NUTRITION & HEALTHY LIFESTYLE

45. Vitamin D Recommendations Should Be Increased (Jan. 15/10)

The latest research on Vitamin D is reinforcing what many health experts have been saying about vitamin D for years: The current recommendations for vitamin D intake in the United States are set too low. These recommendations, called the Recommended Dietary Allowance (RDA) or the Dietary Reference Intake (DRI), are not high enough to ensure enough vitamin D for good health in most people. In this study, investigators suggest that people of European ancestry with a high sun exposure need 1300 IU per day of the vitamin during the winter. People of African ancestry with low sun exposure would require much higher intakes, from 2100 to 3100 IU per day throughout the year. These suggested levels for vitamin D intake are 6.5 to 15.5 times higher than the current "adequate intake" of 200 IU per day. These levels are 3.25 to 7.75 times higher than the current RDA of 400 IU. Irrespective of the number used for comparison, it's clear that current recommendations may be too low to ensure people get enough vitamin D. This recommendation is problematic because low levels of vitamin D have been linked to increased risk of the following conditions and diseases:

- Osteoporosis
- several types of cancer, including colon cancer
- autoimmune diseases, such as MS and rheumatoid arthritis
- muscle weakness and falls in elderly people
- respiratory and other infections, including influenza (flu)
- heart disease

In publishing their findings, the researchers noted another recent study showing that 94% of Chinese adults between 50 and 70 years old enrolled in the study were vitamin D deficient. This is not just an American issue. Low levels of vitamin D may be increasing the rates of many diseases around the world. These study findings, the Chinese research, and previous research showing that many cancer patients are low in vitamin D, suggest many people could benefit from a vitamin D supplement. Eating more vitamin D-rich foods is a good idea, but vitamin D isn't found in too many places. The only natural source of vitamin D is fatty fish, such as wild-caught salmon. Fortified foods such as cereals, orange juice, and dairy will help you get additional vitamin D from your food. Beyond this, you may need a supplement to get your body the D it needs. Some people should not take vitamin D for medical reasons. If possible, get your blood levels of vitamin D checked. A blood test will let you know for certain whether you do or do not need a vitamin D supplement at this time. If your vitamin D levels come back low, ask your doctor how much vitamin D you should take, how long to take it, and when your blood should be rechecked to see if the supplements are working.

Hall, LM, et al., Vitamin D intake needed to maintain target serum 25-hydroxyvitamin d concentrations in participants with low sun exposure and dark skin pigmentation is substantially higher than current recommendations. J of Nutrition. Published online ahead of print, doi: 10.3945/jn.109.115253

46. Mango Is Helpful in Preventing and Stopping Colon Cancer (Jan. 15/10)

According to the results of this study, mango fruit has been found to prevent or stop certain colon and breast cancer cells in the lab. Scientists examined the five varieties most common in the U.S.: Kent, Francine, Ataulfo, Tommy/Atkins and Haden. Though the mango is an ancient fruit heavily consumed in many parts of the world, little has been known about its health aspects. The National Mango Board commissioned a variety of studies with several U.S. researchers to help determine its nutritional value. If you look at what people currently perceive as a super-food, people think of high antioxidant capacity, and mango is not quite there at least in comparison with antioxidants in blueberry, acai and pomegranate. But the team checked mango against cancer cells anyway, and found it prevented or stopped cancer growth in certain breast and colon cell lines. It has about four to five times less antioxidant capacity than an average wine grape, and it still held up fairly well in anticancer activity. If you look at it from the physiological and nutritional standpoint, taking everything together, it would be a high-ranking super food.

Scientists maintain that it would be good to include mangoes as part of the regular diet. Investigators tested mango polyphenol extracts in vitro (in a test tube) on colon, breast, lung, leukemia and prostate cancers. Polyphenols are natural substances in plants and are associated with a variety of compounds known to promote good health. Mango showed some impact on lung, leukemia and prostate cancers but was most effective on the most common breast and colon cancers. What researchers found is that not all cell lines are sensitive to the same extent to an anticancer agent. But the breast and colon cancer lines underwent apoptosis, or programmed cell death. Additionally, they found that when they tested normal colon cells side by side with the colon cancer cells, that the mango polyphenolics did not harm the normal cells. The researchers did further tests on the colon cancer lines because a mango contains both small molecules that are readily absorbed and larger molecules that would not be absorbed and thus remain present in a colon. They found the normal cells weren't killed, so mango is not expected to be damaging in the body. That is a general observation for any natural agent, that they target cancer cells and leave the healthy cells alone, in reasonable concentrations at least.

<http://agnews.tamu.edu/dailynews/storylisting.php?listby=&page=1&id=>

47. **Obesity Linked to Colon Cancer** (Jan. 25/10)

According to research, obesity is one of the most important risk factors for colon cancer. Health experts estimate that at least 13,200 cases of colon cancer diagnosed in the US each year are due to obesity. Many experts believe this number is much higher. New research has added another piece to the puzzle of how obesity causes cancer. Using animal models of cancer development, the researchers narrowed in on inflammation as one of the main ways through which obesity can lead to cancer development. You may understand two common kinds of inflammation:

- A fever that accompanies an illness
- The swelling and pain that occur with an injury

These are forms of acute inflammation - the kind you can see and feel. But it's another form of inflammation that appears to link obesity and cancer. It is the chronic, low-grade inflammation that can occur in the body everyday. To get an idea of what chronic inflammation is, consider that every cell in the body conducts conversations with the cells around it. When inflammation is in balance, these conversations are like a pleasant chat with a neighbor or friend. When inflammation is out of control, cellular communication becomes aggressive. The communication becomes a shouting match, and even may lead to pushing and shoving. Inflammation turns up the tone and volume of cellular conversations to damaging levels. And the damage caused by excessive inflammation has been linked to the development of cancer. Additionally, low-grade inflammation is linked with many of the other diseases that plague modern humans: heart disease, diabetes, stroke, hypertension, arthritis, chronic pain, allergies, auto-immune diseases, and more. The good news is that inflammation can be dampened down in the body by following the following:

1. **Focus on healthy body weight and shape.** As this researcher shows, obesity is a prime cause of inflammation. Carrying excess fat increases the risk of cancer. Carrying that fat around the mid-section is most damaging.
2. **Avoid tobacco.** Tobacco most definitely increases inflammation. Cigarettes, pipes, smokeless tobacco (chew), and any other form of tobacco increase cancer risk..
3. **Eat the right foods.** The key to keeping inflammation in check is a plant-based diet. You don't have to be a vegetarian to reap the benefits of a plant-based diet. You do have to get the majority of your calories from minimally-processed, whole plant foods - vegetables, fruit, whole grains, legumes (beans and peas), nuts, and seeds. A good goal is to have three-fourths of every meal or snack come from plant foods
4. **Exercise regularly** There is no single panacea for warding off cancer, but exercise comes pretty close. Moving your body moderately to vigorously for a minimum of 20-30 minutes most days of the week is the goal. This alone can keep inflammation in check
5. **Get a Good Night's Rest** Many people don't realize that lack of sleep affects us in so many negative ways. Poor sleep habits ratchet up inflammation. Not getting enough sleep is indirectly linked to cancer, because it can cause obesity. Lack of sleep is directly linked to increased cancer risk as well.

<http://www.newswise.com/articles/view/560371/>

48. **Vitamin D Cuts Colon Cancer Risk** (Jan. 23/10)

High levels of vitamin D in the blood appear to be linked to lower risks of colorectal cancer, although it's not clear if higher intake of the vitamin actually prevents the disease, according to the researchers in this study. Scientists found that those with the highest levels of vitamin D in their blood had as much as a 40% lower risk for developing colorectal cancer than those with the lowest levels. The research is based on a study of more than 520,000 people from 10 countries in Western Europe. The study participants gave blood samples and filled out diet and lifestyle questionnaires between 1992 and 1998. They were then tracked for several more years to see what happened to them. During the follow-up period, 1,248 were diagnosed with colorectal cancer. These participants were compared with a similar group of 1,248 people who were not diagnosed with the disease. The researchers cautioned that it's not clear if there are risks from consuming high levels of vitamin D, which is available in supplements. It's also not known whether supplements are necessary if people reach certain levels through a healthy diet, exercise and moderate exposure to sunlight. The study authors noted that current recommendations for preventing colorectal cancer include exercising, not smoking, reducing obesity and abdominal fat, and limiting consumption of alcohol and red and processed meats.

Jenab, Mazda, et al, Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case control study. BMJ, January 2010.

49. **Diabetes and Cancer Risk** (Feb. 1/10)

Consistently high blood sugar is the key feature of diabetes and been determined to be the cause of bad health. When not managed properly with exercise, a healthy diet, medications, and/or insulin, high blood sugar levels can lead to kidney damage and failure, blindness, circulatory problems and the need for amputations, and increased risk of heart disease, stroke, possibly cancer, and more. But even among people who have blood sugar levels within the normal range, those with higher levels may have a higher risk of cancer. In this study, additional evidence is provided that more blood sugar equals more cancer risk. The study subjects' average age was 45 years. The group was followed for 10 years to look at the connection between blood sugar levels and cancer risk. Researchers considered and "controlled for" other factors that also can affect cancer risk, including smoking and overweight/obesity. For men, each 18 point (milligrams per deciliter - mg/dL) increase in blood sugar levels was associated with a 5% increased risk of getting cancer and a 15% higher risk of dying of cancer. For women, each 18 mg/dL increase in blood sugar levels was associated with an 11% increased risk of getting cancer and a 21% higher risk of dying of cancer. This study points to a clear connection between higher blood sugar levels and higher cancer risk. Fortunately, there are many things you can do to keep your blood sugar in the low end of the healthy range:

- **Manage Diabetes:** If you do have diabetes, work closely with your health care team to manage your diabetes properly. If you need medications, be sure you take them exactly as prescribed. Check your blood sugar often and ask your doctor how to adjust your medications if needed.
- **Move More:** One of the single best ways to lower blood sugar is to exercise regularly. Exercise helps your body use insulin more effectively. Insulin is the hormone that regulates (controls) blood sugar levels. The more effectively your body responds to insulin, the more likely your blood sugar levels will be in the healthy range. And even if you don't lose weight through exercise, you still benefit. Exercise alone will help.
- **Lose Weight:** If you are overweight, make losing weight a priority. You don't need to lose it all to benefit either. Just losing 5-10% of your initial weight will improve blood sugar levels. For example, if you weigh 250 pounds, losing 12 to 25 pounds will improve blood sugar levels. Even if you don't reach the "ideal" healthy body weight, you still benefit from even losing a small amount of weight.
- **Sleep Enough:** Lack of sleep is a surefire way to make blood sugar levels soar. When you don't get enough sleep, your body releases stress hormones which increase blood sugar levels. Even worse, lack of sleep makes your body less responsive to insulin. Even when you produce plenty of insulin, lack of sleep ensures your body can't use it very well.

Stocks T, et al. Blood Glucose and Risk of Incident and Fatal Cancer in the Metabolic Syndrome and Cancer Project (Me-Can): Analysis of Six Prospective Cohorts. PLoS Med 6(12): e1000201. doi:10.1371/journal.pmed.1000201

50. **Dietary Polyamines Linked to Colorectal Cancer** (Feb. 2/10)

Polyamines, which are concentrated in foods such as orange juice, meat, green peas and corn, may be associated with an increased risk of colorectal cancer, according to research presented at the American Society of Clinical Oncology's Gastrointestinal Cancers Symposium, held from Jan. 22 to 24 in Orlando, Florida. Researchers investigated the association between polyamine intake and the efficacy of a polyamine-inhibiting regimen of difluoromethylornithine (DFMO) plus sulindac to prevent precancerous

colorectal adenomas in 188 patients. Compared to patients with the lowest polyamine intake, the researchers found that those with the highest intake were significantly more likely to present with adenomas larger than 1 cm (43.6% vs. 26.4%) and advanced adenomas (52.7% vs. 35.9%). They also found that DFMO/sulindac was associated with a reduced adenoma risk only in patients with a lower polyamine intake. Controlling dietary polyamines may be an effective strategy for preventing the occurrence of colorectal adenomas and colorectal cancer the authors conclude.

ASCO GI Symposium 2010: Abstract #279. Raj, KP, et al., Role of dietary polyamines in a phase III clinical trial of DFMO and sulindac for prevention of metachronous colorectal adenomas: A potential target for colon cancer chemoprevention.

51. Exercise Can Help in Cancer Care (Feb. 5/10)

Even after diagnosis, the power of exercise may still positively impact the health of those with cancers of the colon and rectum. While it is known that exercise may help prevent cancer, less is known about the effects of exercise in people who already have cancer. In this study, 668 men with nonmetastatic colorectal cancer participating in the Health Professionals Follow-up Study were assessed for the amount they exercised after a diagnosis of colorectal cancer and were followed to see if exercise helped them live longer. Men filled out questionnaires about recreational physical activities, including time spent walking, running, bicycling, lap swimming, doing yoga, or other activities. Men who exercised more frequently after their diagnosis of colorectal cancer had a lower risk of death caused by colorectal cancer or any other cause compared with men who exercised less frequently or not at all. Exercise may help reduce the risk of death from cancer by improving immune system function, reducing inflammation, or other mechanisms. The authors state that this hopeful study should lead to further research trials to determine the benefits of exercise in cancer survivors

Meyerhardt, Jeffrey, et al., Physical Activity and Male Colorectal Cancer Survival. Arch Intern Med 2009;Vol. 169, No. 22: pp. 2102–8

52. Blueberries and Probiotics Protect Against Colitis and Cancer (Feb. 9/10)

According to Swedish researchers, protecting yourself against intestinal disease such as colitis and colorectal cancer can be accomplished by adding blueberries to your diet and that effect can be magnified by adding probiotics to the picture. Blueberries are rich in antioxidants and other nutrients, and numerous studies have suggested that compounds found in this fruit may help combat cancer. In a review article from the University of California, Los Angeles, for example, the authors noted that there is overwhelming evidence suggesting that the polyphenols, lignans, stilbenoids, and other components in blueberries and similar berries can repair cell damage resulting from oxidative stress and inflammation. In this latest study, scientists from Lund University set out to determine whether various types of dietary fiber and probiotics (e.g., lactobacillus and bifidobacteria) could help alleviate and prevent the risk of ulcerative colitis and colorectal cancer. They compared diets of blueberry husks, rye bran, and oat bran both with and without the addition of probiotic bacteria. The authors found that adding probiotics protected the liver and reduced inflammation-inducing bacteria in the intestinal tract while the population of health-promoting bacteria (e.g., lactobacillus) increased. They also noted that when blueberries were consumed along with probiotics, the content of butyric acid and propionic acid increased in the blood. Previous research has shown that these two substances enhance the immune system and are important energy sources for intestinal cells. Another reason for the positive impact of blueberries, according to the authors, is that the blueberry fiber is not broken down a great deal in the large intestine. This means that substances that cause inflammation, and thus inflammatory bowel diseases such as colitis, do not make contact with the intestinal lining. Instead, they become embedded in the fiber and can then be transported out of the body in feces.

http://www.lu.se/o.o.i.s?id=15111&news_item=4472

53. Green Tea Discovered to Prevent Colorectal Cancer in Women (Feb. 9/10)

This study found that women, who regularly drank green tea, lowered their risk of developing both colon and rectal cancers compared with women who drank green tea infrequently or not at all. More than 69,700 Chinese women between the 40 and 70 years old were enrolled in the study regarding their tea consumption. The women were followed for a total of six years. In that time, 256 cases of colorectal cancer were identified. Scientists claim that a significant dose-response relationship was found for both the amount of tea consumed and duration in years of lifetime tea consumption. The reduction in risk was most evident among those who consistently reported to drink tea regularly at both the baseline and follow-up surveys. This study suggests that regular consumption of green tea may reduce CRC risk in women.

Yang, G., et al., Prospective cohort study of green tea consumption and colorectal cancer risk in women. Cancer Epidemiology Biomarkers and Prevention. <http://cebp.aacrjournals.org/content/16/6/1219.abstract>

54. History of Early Smoking Can Compromise Disease Free Survival (Feb. 9/10)

Patients with stage III colon cancer who had a smoking history of 12 or more pack years before they were 30 had almost a 40% increased risk of having their cancer return within three years compared to patients who had never smoked. Among the 1,045 study participants, 46% had never smoked, 44% were past

smokers, and 10% were currently smoking. Disease-free survival (time before disease got worse) three years after treatment was about 18% greater for people who had never smoked than for past smokers.

McCleary, Nadine, et al., Impact of smoking on patients with stage III colon cancer. Cancer. Vol. 116, Issue 4, pp. 957-966.