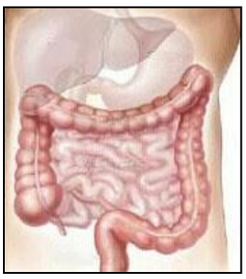
COLORECTAL CANCER RESEARCH

Month Ending September 17, 2010



The following colorectal cancer research update extends from August 14 – September 17, 2010 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Study Involving New Agent NGR-hTNF For Patients Who Have Failed Standard Therapy (Aug. 17/10)

NGR-hTNF is a new agent consisting of two parts: a tumour homing peptide (NGR) and the human Tumour Necrosis Factor (hTNF). The resulting molecule has unique activity, including a direct biological antitumour activity and an increase of vascular permeability (the ability to get into the blood vessels). It can be administered either as a novel single agent therapeutic option, or as part of a combination therapy with most chemotherapy regimens. Thirty-three patients with progressive disease at study entry received NGR-hTNF every 3 weeks. The median number of prior treatment regimens was three (range, 2–5). One-quarter of patients had previously received four or more regimens and two-thirds targeted agents. Progression-free survival (PFS) was the primary study objective. NGR-hTNF was well tolerated. One partial response and 12 stable diseases were observed, yielding a disease control rate of 39.4%. Median PFS and overall survival were 2.5 months and 13.1 months, respectively; whereas in patients who achieved disease control the median PFS and overall survival were 3.8 and 15.4 months, respectively. In an additional group of 13 patients treated with the same dose with a weekly schedule, there was no increased toxicity and 2 patients experienced PFS longer than 10 months. The investigators concluded that based on tolerability and preliminary evidence of disease control in heavily pretreated CRC patients, NGR-hTNF deserves further evaluation in combination with standard chemotherapy.

Santoro, Amando, et al., Phase Ii study of NGR-hTNF, a selective vascular targeting agent, inpatients with metastatic colorectal cancer after failure of standard therapy. European J of Cancer. Published online August 16, 2010.

2. New Clinical Trial Involving MK-2206 For Kras Wild Type, PIK3CA-Mutated CRC (Aug. 24/10)

The purpose of this study is to test a new drug called MK-2206 for metastatic colorectal cancer. This drug is being tested in a subgroup of patients with colorectal cancer whose tumors have changes in certain genes that may make them more likely to respond to this new medication. As tumors develop, the cells within the tumor acquire mutations within genes, allowing them to grow more effectively. Tumors will be tested for mutations involving two genes – KRAS and PIK3CA. Patients whose tumors have a normal copy of the KRAS gene and a mutation within the PIK3CA gene will be eligible to participate in this study. This study is a phase 2 study being conducted at Sloan Ketterig. The goal of a phase 2 study is to find out what effects, good and/or bad, a new treatment has against a certain type of cancer. More information may be sought at http://techcombo.com/2010/08/25/new-clinical-trial-on-colorectal-cancer-recruiting-123/

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3. Using Metformin – A Diabetes Drug - For CRC Treatment (Aug. 29/10)

Metformin is widely used in the treatment of diabetes mellitus type 2 where it reduces insulin resistance and diabetes-related complications. Studies show that metformin treatment is associated with a reduction in cancer risk. The metformin treatment also increases complete tumour response rates following neoadjuvant chemotherapy (chemotherapy administered before surgery) for breast cancer, suggesting a potential role as an anti-cancer drug. Diabetes mellitus type 2 is associated with insulin resistance, elevated insulin levels and an increased risk of cancer and cancer-related mortality. Reduction of insulin resistance by the oral anti-diabetic drug metformin is an attractive anti-cancer strategy. This review discusses the role of diabetes mellitus type 2 and insulin resistance in the evolution of cancer, the preclinical rationale and potential mechanisms of metformin's anti-cancer effect and the current and future clinical developments of metformin as a novel anti-cancer drug.

***Jalving, M., et al., Taking Away The Candy for Cancer. Eur J Cancer*. 2010 Sept; 46(13):2369-80**

4. Drug Treating Melanoma PLX4032 May Help CRC Patients (Aug. 30/10)

Research on treating metastatic melanoma points to an approach that may help colon cancer patients as well. A new targeted therapy called PLX4032, also referred to as RG7204, has caused tumors to shrink in 80% of the 81 patients enrolled in two phases of the melanoma study. These results have been published in a recent issue of the New England Journal of Medicine. These results for melanoma are exciting for colon cancer patients because PLX4032, the medication being tested, targets a gene that appears to play an important role in how colon cancer grows (BRAF gene) and responds to treatment

too. One ongoing clinical trial is looking at how this drug may help both melanoma and colorectal cancer patients. Results are not available for this trial yet but more information may be found on this clinical trial at http://clinicaltrials.gov/ct2/show/NCT00405587

Flaherty, Keith T., et al., Inhibition of Mutated, Activated BRAF in metastatic melanoma. New England J of Medicine. 2010; 363: pp. 809-819.

5. Gene Mutations (KRAS, BRAF, NRAS and PIK3CA) on Efficacy of Erbitux (Sept. 3/10)

A mutation in the gene known as *KRAS* is associated with resistance to anti-epidermal growth factor receptor (EGFR) antibodies, such as erbitux and vectibix. Hence, the tumours of patients with metastatic colorectal cancer are now profiled for seven *KRAS* mutations before receiving these therapies. However, most patients with *KRAS* wild-type tumours (no mutation) still do not respond. Investigators studied the effect of other downstream mutations (***BRAF, NRAS and PIK3CA***) on the efficacy of erbitux in patients with chemotherapy-refractory metastatic colorectal cancer treated with erbitux plus chemotherapy. According to the data, *KRAS* mutants did not derive benefit compared with wild types, with a response rate of 6.7% versus 35.8%, a median progression free survival (PFS – time before the disease got worse) of 12 weeks versus 24 weeks, and a median overall survival of 32 weeks versus 50 weeks. In *KRAS* wild types, carriers of *BRAF* and *NRAS* mutations had a significantly lower response rate than did *BRAF* and *NRAS* wild types, with a response rate of 8.3% in carriers of *BRAF* mutations versus 38.0% in BRAF wild types; and 7.7% in carriers of *NRAS* mutations versus 38.1% in *NRAS* wild types. *PIK3CA* exon 9 mutations had no effect, whereas exon 20 mutations were associated with a worse outcome compared with wild types, with a response rate of 0.0% versus 36.8%, a median PFS of 11.5 weeks versus 24 weeks, and a median overall survival of 34 weeks versus 51 weeks. [**Exons** are interrupted pieces of genetic material DNA]. If *KRAS* is not mutated, assessing *BRAF, NRAS*, and *PIK3CA* exon 20 mutations (in that order) gives additional information about outcome. While confirming the negative effect of *KRAS* mutations on outcome after cetuximab, researchers showed that *BRAF, NRAS*, and *PIK3CA* exon 20 mutations are significantly associated with a low response rate to anti-EGFR therapies. Response rates could be improved by additional testing of *BRAF, NRAS*, and *PIK3CA* exon 20 mutations in a *KRAS* wild-type population.

DeRoock, W, et al., Effects of Kras, braf, nras, and pik3ca mutations on the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory metastatic colorectal cancer: a retrospective consortium analysis. Lancet Oncolo. 2010 Aug 1. 11(8): pp. 753-762

6. VEGF-Trap Trial Continues (Sept. 8/10)

The Phase 3 VELOUR clinical trial of aflibercept or VEGF Trap in patients with metastatic colorectal cancer will continue to completion as planned, with no modifications due to efficacy or safety concerns as relayed by the sponsoring companies Sanofi-aventis and Regeneron. The main objective of the VELOUR study is to evaluate the safety and effectiveness of aflibercept as a second-line treatment in combination with folinic acid, 5-fluorouracil, and irinotecan. While the primary endpoint is improvement in overall survival, secondary endpoints include progression-free survival, response to treatment, and safety. Aflibercept or VEGF Trap is an anti-angiogenesis inhibitor with a unique mechanism of action. It prevents the growth of tumour blood vessels. This agent binds all forms of Vascular Endothelial Growth Factor-A or VEGF-A, as well as VEGF-B and placental growth factor or PIGF, additional angiogenic growth factors that appear to play a role in tumor angiogenesis (the formation of tumor blood vessels) and inflammation. The therapy has been shown to bind VEGF-A, VEGF-B, and PlGF with higher affinity than their natural receptors.

http://www.rttnews.com/content/BreakingNews.aspx?Id=1413197

7. Angiozyme Enters Phase III Trials in India (Sept. 9/10)

Bio-pharmaceutical company Actis Biologics Ltd has entered the third phase of human trials on its promising biotech molecule Angiozyme, targeting colorectal cancer. The drug works by cutting blood supply to the cancerous cells, in a targeted method, as opposed to chemotherapy that works akin to carpet bombing – killing the good cells along with the bad,. Regulatory clearance from the Drug Controller General of India has been received and the Phase-III trial will be done on 150 patients. The trial will be multi-country and multi-centric, and if completed without an incident, it will be another 18 months before the drug is in the market. A substantial part of the trial will be done in India and six centres have been finalized. It is for the first time in the world that a biotech molecule based on anti-sense technology is entering phase III trial. Phase III trials involve monitoring patients on the drug for its efficacy, safety and adverse events. Angiozyme is administered as an injectable, similar to an insulin shot, and as a result it reduces the inconvenience associated with chemotherapy, that includes hospitalization and other side effects.

http://www.blonnet.com/2010/09/10/stories/2010091051160300.htm

8. Aspirin & NSAIDs on Risk & Survival From CRC (Sept. 16, 2010)

Previous studies have shown that aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) lower colorectal cancer (CRC) risk. However, the lowest effective NSAID dose, treatment duration, and effects

on survival have not been defined. In this study, researchers explored the relationship between NSAID dose and duration, CRC risk and overall CRC-specific survival.

The relationship between NSAID use and CRC risk was examined in 2279 cases and 2907 controls. Patients completed food-frequency and lifestyle questionnaires. NSAID categories were low-dose aspirin (75 mg), non-aspirin NSAIDs (NA-NSAIDs) and any NSAID. Users were defined as taking >4 tablets/week for >1 month. In all, 354 cases (15.5%) were taking low-dose aspirin compared to 526 controls (18.1%). Low-dose aspirin use was associated with decreased CRC risk, evident after 1 year and increasing with duration of use. NA-NSAID and any NSAID use were also inversely associated with CRC. Researchers concluded that this was the first study to demonstrate a protective effect against CRC associated with the lowest dose of aspirin (75 mg per day) after only 5 year use in the general population. NSAID use prior to CRC diagnosis does not influence survival from the disease.

Din, Farhat, et al., Effect of aspirin and NSAIDs on risk and survival from colorectal cancer. GUT. Doi: 10.1136/gut.2009.203000

SURGICAL THERAPIES

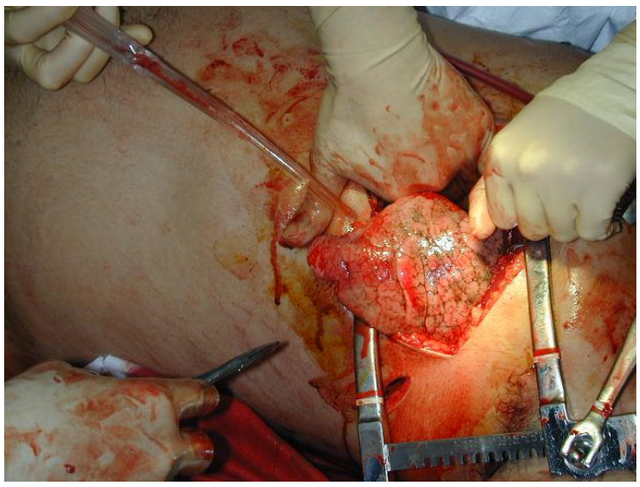
9. Primary Resection is Better For Incurable Metastatic Colorectal Cancer (Aug. 16/10)

This study investigated survival in patients treated with FOLFOX followed by primary site resection or palliative surgery for incurable metastatic colorectal cancer. Between 2001 and 2009, a total of 98 patients with colorectal adenocarcinoma and non-resectable metastases were diagnosed and treated with the new systemic agent chemotherapy regimen FOLFOX (5FU, oxaliplatin, leucovorin). Primary site resection was carried out in 38 patients, creation of a colostomy or bypass without resection was carried out in 36 patients, and 23 were not operated on because of advanced disease. The survival times of patients in the 3 different groups were analyzed. There were no differences between the patients regarding their general condition, concurrent disease, or tumor stage. The median survivals of the three groups were **30.6, 20.8, and 12.7 months**, respectively. The postoperative complication rate was higher in the primary site resection group than in the palliative surgery group. According to the researchers, the results indicate that there are benefits from primary site resection for incurable metastatic colorectal cancer with systemic chemotherapy.

Tanoue, Y, et al., Primary Site resection is superior for incurable metastatic colorectal cancer. World J of Gastroenterology. 2010 July; 16(28): pp. 3561-3566

10. Lung Mets Surgery (Aug. 20/10)

Few patients with lung metastases from colorectal cancer are candidates for surgical therapy with a curative intent, and it is difficult to identify those who may benefit the most from surgery. The aim of this study was to determine the impact of various parameters on survival after pulmonary metastasectomy for colorectal cancer. Researchers looked at 40 patients, with an average age of 63.5 years, who had undergone surgery to remove colon cancer tumors that had spread to the lungs. The factor that had the biggest impact on length of life after lung surgery was whether or not the person also had colon cancer tumors that had spread to the liver. In people without metastasis to the liver, the median survival time was 87 months or 7.25 years. Some in this group lived 139 months after lung surgery or 11.6 years. Although survival was shorter for people with colon cancer that had previously spread to the liver, even this group had a median survival of 40 months or 3.3 years. The ultimate goal for advanced (metastatic) colon cancer is a complete cure - an outlook that is improving greatly.

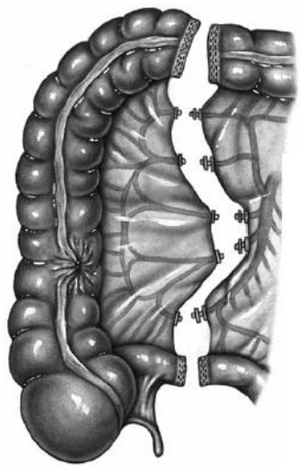


Researchers maintain that a history of previous liver metastases is certainly not a contra-indication for pulmonary metastasectomy, but the data presented indicates that these patients have a higher risk of tumor recurrence and a decreased survival in comparison with patients who underwent surgery for lung-only CRC metastases. These results are clinically relevant, since the incidence of isolated lung metastases without associated liver metastases is low (<10%); and researchers maintain that a history of previously resected liver metastases should be considered a poor prognostic factor in the small subset of CRC patient candidates for pulmonary metastasectomy.

Landes, Ulrich, et al., **Predicting** ***survival after pulmonary metastasectomy for colorectal cancer: previous liver metastases matter. BMC Surgery. 2010. 10:17.***

11. Elements that Predict Post-Operative Complications and Early Mortality After Colorectal Cancer Surgery (Aug. 29/10)

This study analyzed a group of elderly patients with colorectal cancer as it relates to those elements capable of predicting post-surgical complications and early death. Patients 70 years or older electively operated for all stages of colorectal cancer from 2006 to 2008 in three hospitals were consecutively included. The following elements were addressed before surgery: personal and instrumental activities of daily living [IADL], comorbidity (the simultaneous appearance of 2 or more ailments), medications, nutrition, cognition, and depression.



The associations were analyzed. After analyzing the data, investigators concluded that in elderly patients with colorectal cancer, severe comorbidity, IADL-dependency, depression, and impaired nutrition appeared to be the most important elements predictive of post-operative complications and early mortality.

Kristjansson, SR, et al., Which elements of a comprehensive geriatric assessment (CGA) predict post-operative complications and early mortality after colorectal cancer surgery? J of Geriatric Oncology. 2010 Jul 21; Epub ahead of print.

RADIATION / INTERVENTIONAL RADIOLOGY

12. PET & Colorectal Cancer (Aug.1 5/10)

Colorectal cancer (CRC) is a major cause of cancer-related morbidity and mortality. Molecular imaging using positron emission tomography (PET) is now an integral part of multidisciplinary cancer care and in this review, researchers discuss the role of PET in CRC including well established indications in the assessment of recurrent disease and emerging applications such as **initial staging, monitoring therapy efficacy and using PET for radiotherapy planning**.

With rapid advancement in imaging technology, they also discuss the future potential of combining PET and magnetic resonance imaging and the use of novel radiotracers. The researchers maintain that the role of PET in CRC continues to evolve. While it is well established in the assessment of recurrent and residual CRC and in patients prior to potential curative metastasectomy (surgery for metastatic disease), the benefits of FDG PET in particular for staging in rectal cancer, in the assessment of therapy efficacy as well as providing early prognostic information in patients receiving neoadjuvant treatment are emerging. PET also has the potential to assist in planning radiotherapy. FDG PET performed for indications other than CRC can detect incidental focal colonic uptake which has a significant rate of pre-malignancy and malignancy that warrants further investigations. With the increasing appreciation and understanding of the underlying molecular processes involved in the evolution of cancer, functional imaging using PET and different radiopharmaceuticals will enable *in vivo* assessment of tumour biology that would allow clinicians to target, individualize and monitor therapy.

Lin, Michael, et al., Positron emission tomography and colorectal cancer. Critical Reviews in Oncology Hematology. Published online July 12, 2010.

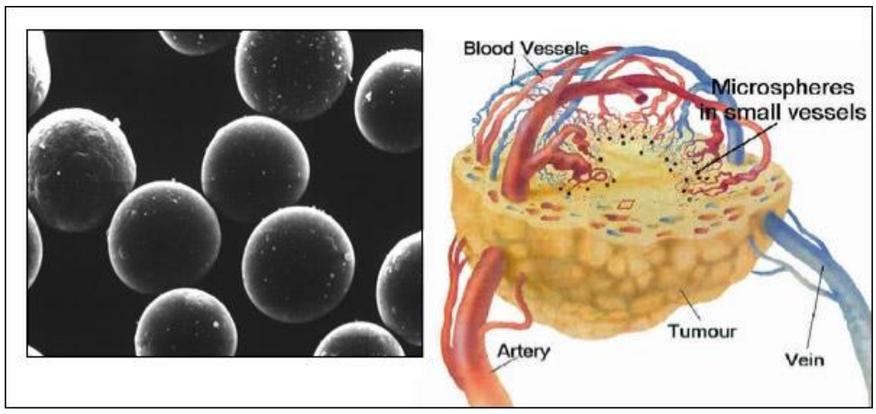
13. The Role of PET/CT in Recurrent Colorectal Cancer (Aug. 15/10)

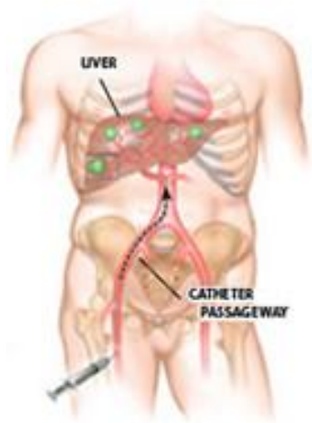
The aim of this study was to examine the clinical applicability of positron-emission tomography/computed tomography (PET/CT) for diagnosing local recurrence of colorectal cancer. From August 2003 to August 2008, 256 patients with colorectal cancer underwent PET/CT scanning for staging or restaging. Local recurrence was detected in 22 patients postsurgically. Of the 22 patients, 21 underwent positive glucose uptake from pet/ct and were diagnosed with local recurrence by PET/CT; the results were negative in one case. The sensitivity, specificity, positive predictive value (the probability that a person with a positive test result has, or will get, the disease), and negative predictive value (the proportion of patients with negative test results who are correctly diagnosed) for local recurrence were 95.5%, 100%, 100%, and 99.6%, respectively. CT/MRI scans yielded the following results: positive, 10 cases (45.5%); suspected positive, 11 cases (50.0%); negative, 1 case (4.5%). In the suspected positive cases, not only imaging but also colonoscopy and tumor markers among other techniques were used for definitive diagnosis. Investigators concluded that PET/CT has high sensitivity and specificity for diagnosing local recurrence of colorectal cancer and would be useful especially in the case of locally recurrent colorectal cancer suspected to be positive by CT/MRI.

Bamba, Yoshiko, et al., management of local recurrence of colorectal cancer: the role of pet/ct. Abdominal Imaging. DOI: 10.1007/s00261-010-9639-z

14. Microspheres to Treat Liver Metastases (Aug. 19/10)

Radioactive yttrium-90 labeled resin microspheres (Sirspheres) appear to be a safe and effective treatment for patients with colorectal cancer liver metastases who have failed available chemotherapy options, according to the final results of a prospective clinical multi-centre phase II trial conducted by the Italian Society of Locoregional Therapies in Oncology (SITILO) and published in the British Journal of Cancer. Yttrium Y 90 glass microspheres are an injectable formulation of yttrium Y 90 consisting of glass microspheres containing the radioisotope yttrium Y 90. When injected into the tumor vascular bed, yttrium Y 90 glass microspheres occlude (cut the flow) tumor blood vessels and deliver a cytotoxic dose of beta radiation to the tumor site, thereby reducing the tumor burden.





The results of the 52-patient study revealed that the liver mets completely disappeared in one patient (2%), and 11 (22%) patients had a partial response involving at least a 30% reduction in tumour size. A further 12 (24%) patients had stable disease. The liver tumours shrank sufficiently in two patients (4%) to enable potentially curative surgery to be performed. The median overall survival was 12.6 months for all patients in the trial, with significantly longer survival in the 24 (48%) patients that responded to SIR-Spheres or who had stable disease compared to non-responders (median 16 months versus 8 months), and 40% of the responders remaining alive at two years compared to none of the non-responders. Mild-to-moderate side effects consisting mostly of fever and pain were reported in 16% of patients in the first 48 hours and 22% in days 3 to 30. Investigators concluded that the results reveal that radioembolization using SIR-Spheres is a promising therapy for patients with colorectal cancer liver metastases who have failed chemotherapy. The prolonged 12.6-month median survival and encouraging tumour response reported in the SITILO study compares favourably with the clinical trial results of second- or third-line chemotherapy, even though three-quarters of the patients had previously received at least four different combinations of chemotherapy drugs and therefore had a poor prognosis with no other treatment options available.

Cosimelli M, et al., multi-centre phase II clinical trial of yttrium-90 resin microspheres alone in unresectable, chemotherapy refractory colorectal liver metastases. British J of Cancer 2010; 103: pp. 324-331

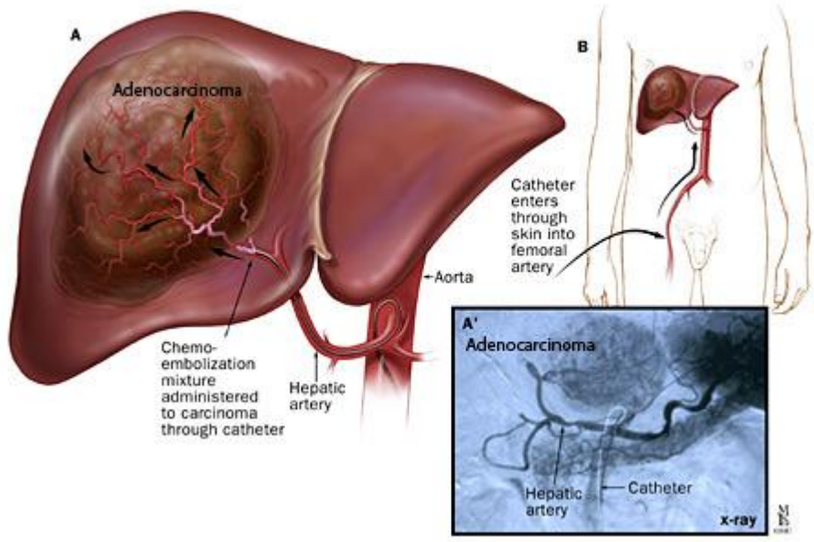
15. Microspheres To Treat Inoperable Liver Mets (Aug. 19/10)

Using the innovative technique of radioembolization to treat patients with inoperable colorectal cancer liver metastases who have failed all standard-of-care chemotherapy options can more than double the time until their disease progresses, according to the final results of a Phase III randomized controlled trial published in the Journal of Clinical Oncology. The prospective, randomized trial compared a protracted infusion of 5-fluorouracil (5FU) chemotherapy to the same chemotherapy in combination with radioembolization, also known as selective internal radiation therapy (SIRT), using 90Y-resin microspheres. The trial was designed to assess the efficacy and safety of this combination in patients with liver metastases from colorectal cancer and was conducted at three Belgian university hospitals. The trial recruited 46 patients who had failed all other standard-of-care treatments. The time to the progression of liver metastases - the primary endpoint of the study - increased significantly from a median of 2.1 months in patients receiving 5FU alone to 5.5 months in patients receiving radioembolization plus 5FU. The risk of progression was 62% lower in patients receiving radioembolization plus 5FU. The time to progression of disease anywhere in the body was also significantly longer, from a median of 2.1 months in the 5FU control arm to 4.5 months in patients in the radioembolization/5FU arm. Control of liver metastases was also significantly increased in patients receiving radioembolization plus 5FU, from 35% to 85%. More patients in the 5FU-only control arm experienced severe side effects than those receiving radioembolization plus 5FU (26% versus 5%).

Henlisz, A, Phase III trial comparing protracted intravenous fluorouracil infusion alone or with yttrium-90 resin microspheres radioembolization for liver-limited metastatic colorectal cancer refractory to standard chemotherapy. J of Clinical Oncology 2010; 28: pp. 3687-3694

16. Chemoembolization for Colorectal Liver Mets (Sept. 9/10)

Unresectable colorectal liver metastases have a 1- and 2-year survival of 55% and 33% with current systemic therapies. In this study, the authors evaluated response and survival after transarterial chemoembolization. Chemoembolization is a procedure in which the blood supply to a tumour is blocked and anticancer drugs are administered directly into the tumor, permitting a much higher concentration of drugs to be in contact with the tumor for a longer period of time, while depriving the tumor of oxygen and nutrients. The procedure is used to treat cancer originating in the liver (primary liver cancer) as well as cancer that has metastasized (spread) to the liver from another area such as the colorectum.



Chemoembolization with cisplatin, doxorubicin, mitomycin C, ethiodized oil, and polyvinyl alcohol particles was performed at monthly intervals for 1 to 4 sessions in this study. Cross-sectional imaging and clinical and laboratory evaluation were performed before treatment, 1 month after treatment, and then every 3 months. A second cycle was performed for intrahepatic recurrence. Toxicity was assessed and response was evaluated. A total of 245 treatments were performed over 141 cycles on 121 patients. Ninety-five of 141 treatment cycles were evaluable for response: 2 (2%) partial response, 39 (41%) stable disease, and 54 (57%) progression. Median time to disease progression (TTP) in the treated liver was 5 months, and median TTP anywhere was 3 months. Median survival was 33 months from diagnosis of the primary colon cancer, 27 months from development of liver metastases, and 9 months from chemoembolization. Survival was significantly better when chemoembolization was performed after first- or second-line systemic therapy (11-12 months) than after third- to fifth-line therapies (6 months). Presence of extrahepatic metastases did not adversely affect survival. The investigators concluded that chemoembolization provided local disease control of hepatic metastases after 43% of treatment cycles. Median survival was 27 months overall, and 11 months when initiated for salvage after failure of second-line systemic therapy.

Albert, Marissa, et al., Chemoembolization of colorectal liver metastases with cisplatin, doxorubicin, mitomycin c, ethiodol, and polyvinyl alcohol. Cancer. Sept. 10, 2010. Doi: 10.1002/cncr.25387.

SCREENING

17. Breath Test to Detect Colorectal Cancer (Aug. 18/10)

A new nanosensor array breath test identified people with lung, breast, colorectal and prostate cancers, according to new study findings published in the *British Journal of Cancer*. These findings build on earlier research suggesting that a sensor made with gold nanoparticles could detect lung cancer in breath. The 'NA-NOSE' concept has the potential to reduce cancer mortality by enabling widespread, trustworthy screening, especially suitable for high-risk populations. According to the researchers, tumor growth is accompanied by changes that may lead to the emission of volatile organic compounds. Therefore, they set out to determine whether the test would identify lung, breast, colorectal or prostate cancers in the breath of 177 volunteers aged between 20 and 75 years. The researchers identified six of the 33 most common volatile organic compounds for lung cancer; five of the 54 most common for breast cancer; six of the 39 most common for colon cancer; and four of the 36 most common for prostate cancer. Healthy vs. cancerous breath patterns were identified regardless of age, gender, lifestyle and other confounding factors. If these initial results can be confirmed in large scale studies, this new technology could become a simple tool for early diagnosis of cancer along with imaging. It could also be an easy way to assess and monitor the effectiveness of cancer treatment and detect relapses earlier.

http://www.hemonctoday.com/article.aspx?rid=67697

18. Virtual Colonoscopy Can Detect More Cancers (Aug. 20/10)

Colonoscopy is an important tool to detect colorectal cancer. In recent years, virtual colonoscopy, which involves a CT scan of the colon instead of the invasive, optical inspection of the colon, has been shown to be as effective as traditional colonoscopy. This study suggests that virtual colonoscopy may even be superior because it can identify cancers outside of the colon. In a study of 2,277 patients who underwent virtual colonoscopy, almost half were found to have some suspicious lesions outside the colon. Further testing showed that 240 of those lesions were considered medically significant, such as being some type of cancer. After further evaluation, 19 surgeries were performed to identify six cancers (one lymphoma, three renal cell cancers and two lung cancers) and one aortic aneurysm.

Virtual colonoscopy essentially allows for an examination of the entire abdomen and pelvis, unlike traditional colonoscopy, which is limited to the interior of the colon and rectum. While virtual colonoscopy is not as accurate as a regular CT scan of the abdomen for identifying cancers in the abdomen, it's ability to pick up some types of cancers outside the colon while primarily looking for colorectal cancer make it an attractive alternative to traditional colonoscopy. The obvious problem with this approach, however, is the extra cost of having to explore suspicious lesions outside the colon (that may turn out to be nothing significant) and the resulting anxiety felt by patients who have to undergo further testing. The study's authors suggest that the minimal additional cost may be worth it to identify other types of cancer.

Ganesh R. et al., Extracolonic Findings on CT Colonography Increases Yield of Colorectal Cancer Screening. Am. J. Roentgenol., Sep 2010; 195: 677 - 686.

PSYCHO-SOCIAL

19. Survival Time is Increased with Early Palliative Care (Aug. 20/10)

Should cancer care focused on quality of life wait until all treatment ends? Or can it be integrated with medical treatment as soon as someone is diagnosed with a life-threatening illness? In a study of 150 advanced lung cancer patients, starting palliative care along with standard life-prolonging treatment when patients were first diagnosed not only improved their mood and quality of life, it actually increased the time they lived. Although patients who received early palliative care received less aggressive treatment at the end of life, they lived almost 3 months longer than patients who didn't have such early support. Newly diagnosed lung cancer patients at Massachusetts General Hospital were invited to participate in a randomized clinical trial where they either received standard medical treatment for their cancer or had early palliative care along with that treatment. Ten patients (14 percent) in the standard treatment arm who asked for it were able to receive care from the palliative team, but were not switched to the palliative arm of the trial. Researchers measured quality of life, mood, and survival time in both groups. They also looked at aggressive care at the end of life and whether patient's preferences for resuscitation were recorded in the outpatient electronic medical record. Palliative care was provided by a team of specialists who followed the guidelines of the National Consensus Project for Quality Palliative Care. Such teams are becoming more common in hospitals and some outpatient settings in the United States and are not limited to hospice programs. More than 80 percent of large hospitals have them. Multidisciplinary, they include professionals in the fields of medicine, nursing, social work, chaplaincy, counseling, nutrition, and rehabilitation.

The team paid special attention to:

- assessing physical and psychosocial symptoms
- establishing goals for care
- assisting with decision making regarding treatment
- coordinating care on the basis of the individual needs of the patient

Palliative care is both a philosophy of care and an organized, highly structured system for delivering care. Palliative care expands traditional disease-model medical treatments to include the goals of enhancing quality of life for patient and family, optimizing function, helping with decision making, and providing opportunities for personal growth. As such, it can be delivered concurrently with life-prolonging care or as the main focus of care. Far from being focused on dying, the Guidelines continue, Palliative care affirms life by supporting the patient and family's goals for the future, including their hopes for cure or life-prolongation, as well as their hopes for peace and dignity throughout the course of illness, the dying process, and death. The investigators concluded that among patients with metastatic non–small-cell lung cancer, early palliative care led to significant improvements in both quality of life and mood. As compared with patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life but longer survival.

Temel, Jennifer, et al., Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer . New England J of Medicine. Volume 363, Number 8, August 19, 2010.

Kelley, Amy, et al., Palliative Care – A Shifting Paradigm. New England J of Medicine. Volume 363, Number 8, August 19,2010 Editorial.

20. Personality Traits Do Not Increase Cancer Risk (Sept. 1/10)

According to this study, personality has nothing to do with a person's risk of developing cancer or cancer recurrence. We can all breathe a sigh of relief that personality traits, such as anxiety, neuroticism, or being extroverted or introverted do not have a relationship with cancer risk or risk of recurrence in people who have been treated for the disease. According to experts, the idea that personality traits can increase cancer risk goes back to ancient Greek times. A few poorly designed studies in the 1960s and 70s suggested there might be a personality-cancer connection. These early, and now discredited, studies led to an "industry" of sorts that promoted the importance of "optimism and a fighting spirit" for better cancer survival. While this approach may be encouraging to some, others with cancer find it overwhelming. The study offers reassurance that you don't need to "have the fighting spirit" to survive cancer. The study followed more than 60,000 cancer survivors for up to 30 years each and concluded that personality had no connection with either cancer risk, or risk of dying after cancer diagnosis.

Nakaya, Naoki, et al., Personality traits and cancer risk and survival based on Finnish and Swedish registry data. Amer J of Epidemiology. Vol. 172, Issue 4: pp. 377-385

OTHER

21. More Young Patients Being Diagnosed with Rectal Cancer (Aug. 27/10)

According to the results of this study, rectal cancer rates are increasing in people under the age of 40, although rates of colon cancer have remained stable in younger people. It isn't clear why, but rectal cancer rates in this young group of men and women began increasing in 1984, rising about 3.8% per year. Increases were similar for both sexes and all races. A research team studied 7,661 patients under 40 with colon or rectal cancer, including 1,922 with rectal cancer between 1973 and 2005. More than half of the cases, 52%, were in patients from 35 to 39, with 28% from 30 to 34, and 20% under 30. Looking through the medical literature, the study authors couldn't find an explanation for why rectal cancer was going up while colon cancer wasn't. Screening or lifestyle issues couldn't be identified as a possible reason. Both rectal and colon cancer are rare in people under 40 with slightly over 1 case of colon cancer for every 100,000 people in the United States and less than 0.5 cases of rectal cancer. This compares to 34.5 new colon cancer cases per 100,000 people and 13.4 new rectal cancer cases in the overall US population of all ages. Because the overall incidence of rectal cancer in this age group is so low, the authors do not recommend changes in screening guidelines. However, they do urge that symptoms of rectal cancer, including rectal bleeding, be followed up. The lead author of the study, recommends, "We suggest that in young people presenting with rectal bleeding or other common signs of rectal cancer, endoscopic evaluation should be considered in order to rule out a malignancy. This is in contrast to what is frequently done, which is to attribute these findings to hemorrhoids. More frequent endoscopic evaluation may be able to decrease the documented delay in diagnosis among young people". The researchers concluded that the incidence of rectal and rectosigmoid cancer appears to be increasing in patients aged less than 40 years. Patients presenting with rectal bleeding or other alarming signs or symptoms should be evaluated with this finding in mind.

Meyer, Joshua, et al., Increasing incidence of rectal cancer inpatients aged younger than 40 years. Cancer. Volo. 116, Issue 18: pp. 4354-4359.

22. Clinical Trial on Polyposis Patients Recruiting (Aug. 27/10)

The study, NCT01197901, involving COX and EGFR inhibition in familial polyposis patients is currently recruiting participants. The purpose of the trial is to determine in a randomized, placebo-controlled, phase II trial if the combination of sulindac and erlotinib causes a significant regression of duodenal and colorectal adenomas in familial adenomatous polyposis (FAP) and attenuated FAP patients. More information may be found at http://clinicaltrials.gov/ct2/show/NCT01187901

http://clinicaltrials.gov/ct2/show/NCT01187901

23. Overweight May Affect CEA Levels (Aug. 29/10)

Carcinoembyronic antigen (CEA) is a protein produced by some cancers, including colon cancer. Colon cancer is one of the cancers that produces CEA and therefore blood levels of the protein can be measured to help guide treatment. CEA levels can be checked before and after surgery, radiation, or chemotherapy to see how these treatments are working. If CEA levels are not decreasing as expected, different treatment options may be attempted. In this way, measuring blood levels of CEA can be an important part of colon cancer care. Researchers, however, have identified one group of people for

whom CEA levels may not provide a good indication of how treatments are working: People who are overweight or obese. The study looked at the connection between body mass index (BMI) (weight adjusted for height) and CEA levels in 2,845 people who underwent colon cancer surgery between 1995 and 2009. A BMI between 20 and 24.9 is considered normal weight, 25 to 29.9 is overweight, and 30 and above is obese (calculate your BMI). The researchers found that being overweight renders lower CEA levels than would otherwise be in normal weight people with colon cancer. It turns out that the heavier a person is, the more plasma they have in their bodies. Plasma is a clear, liquid component of blood. And more plasma means that levels of proteins in blood, like CEA, can become diluted. The researchers concluded that in overweight and obese people, CEA levels may be a less sensitive and accurate way to track how a person with colon cancer is responding to treatment. If you are overweight and you're being treated for colon cancer, ask if CEA levels are being used to track your response to treatment. If they are, ask how your doctor can account for the fact that your CEA levels may appear lower than they otherwise would due to your higher body weight. Your doctor may be able to perform other tests in addition to CEA, such as scans or imaging studies, to better track your response to treatment. And even if you won't be undergoing other tests, just knowing that extra body weight will need to be factored in when you and your doctor discuss your treatments can be helpful.

Choi, Gyu-Seog, et al., Influence of obesity on the serum carcinoembyronic antigen value in patients with colorectal cancer. Cancer, Epidemiology, Biomarkers & Prevention. Published Online First August 20, 2010; doi: 10.1158/1055-9965.EPI-10-0569

NUTRITION & HEALTHY LIFESTYLE

24. Body Mass Index, Physical Activity & Diet Affect Colorectal Cancer Recurrence (Aug. 15/10)

The role of dietary and other lifestyle factors in colorectal cancer recurrence and survival is largely unknown. This study conducted a review to summarize the evidence from studies that examined the association of body mass index (BMI), physical activity, and nutrition with colorectal cancer recurrence and survival. BMI, physical activity, and nutrition mostly referred to the time at or before diagnosis. According to the results, there may be an association between higher BMI and body fatness before or at the time of diagnosis and a higher all-cause mortality or colorectal cancer–specific mortality or recurrence, although results may differ by sex, tumor location, and molecular subtype. There may also be a relation between higher leisure-time physical activity after diagnosis and a lower all-cause or colorectal cancer–specific mortality. For dietary factors, statistically significant associations were only shown for single foods, nutrients, and dietary patterns in single studies. Researchers concluded that only a paucity of data is available on the effect of dietary and other lifestyle factors on colorectal cancer recurrence and survival. Thus far, no clear conclusions can be drawn. Future studies are warranted, particularly on post diagnosis BMI and diet.

Vrieling, Alina, et al., The role of body mass index, physical activity, and diet in colorectal cancer recurrence and survival: a review of the literature. Am J Clin Nutrition. Doi: 10.3945/ajcn.2009.29005

25. Bacteria & Colorectal Cancer (Aug. 23/10)

Scientists have found increased immune response to antigens (proteins on the surface of a bacterium that stimulates the production of an antibody) produced by a particular intestinal bacteria in patients with polyps and early stage I or II colorectal cancer. Antibodies against the bacterium *Streptococcus bovis* antigen RpL7/L12 were higher in the blood of polyp and early cancer patients than healthy individuals. However, the increased immune response had disappeared in patients with more advanced stage III or IV cancer. Scientists were led to believe that *Streptococcus bovis* and RpL7/L12 is unique in its ability to cause early polyps to become cancerous. Researchers concluded, “These findings are indicative of an increased exposure to antigen RpL7/L12 during early stages of colon carcinogenesis and suggest that intestinal bacteria such as S. bovis constitute a risk factor for the progression of premalignant lesions into early stage carcinomas. Clearly, the current findings emphasize the necessity for further studies on the possible etiologic relationship between intestinal bacteria and human colorectal cancer”.

Boleij, Annemarie, et al., Increased exposure to bacterial antigen RpL7/L12 in early stage colorectal cancer patients. Cancer. Vol. 116, Issue 17, pp. 4014-4022.

26. Metabolic Syndrome Linked to Colorectal Cancer in Men (Aug. 24/10)

According to the results of this study, there was an association between metabolic syndrome and colon and rectal cancers in men, but this association was not observed in women. Metabolic Syndrome Metabolic syndrome is a cluster of conditions — increased blood pressure, elevated insulin levels, excess body fat around the waist or abnormal cholesterol levels — that occur together, increasing the risk of heart disease, stroke and diabetes. A person has metabolic syndrome when they have a combination of three or more certain health risks. These health risks include:

- high blood pressure
- high blood sugar levels
- excess body weight
- low levels of "good" cholesterol (HDL)

- high levels of *triglycerides* (a type of fat found in the blood)

The term "metabolic" refers to the biochemical processes involved in the body's normal functioning. To assess the relationship between metabolic syndrome and colon and rectal cancers, the researchers analyzed data from a multicenter case-controlled study conducted in Italy and Switzerland. They examined 1,378 cases of colon cancer, 878 cases of rectal cancer and 4,661 controls. Colorectal cancer risk was elevated in men but not in women with metabolic syndrome. Findings were similar when colon and rectal cancers were analyzed separately, according to the researchers. These findings weigh in favor of a combined role of factors involved in metabolic syndrome in the etiology of male colorectal cancer, according to the researchers.

Montella, M, et al., Metabolic Syndrome linked to colon and rectal cancer in men. Abstract #432. Presented at Union of International Cancer Control (UICC) World Cancer Congress: Aug. 18-21, 2010. Shenzhen, China.

27. Body Mass Index Increases Risk of Colorectal Adenomas in Men With Lynch Syndrome (Aug. 24/10)

High body mass index (BMI) is an established risk factor for sporadic colorectal cancer. Still, the influence of BMI on hereditary colorectal cancer (eg, Lynch syndrome [LS]), is unknown. Lynch syndrome, often called hereditary nonpolyposis colorectal cancer (HNPCC), is a type of inherited cancer of the digestive tract, particularly the colon (large intestine) and rectum. People with Lynch syndrome have an increased risk of cancers of the stomach, small intestine, liver, gallbladder ducts, upper urinary tract, brain, skin, and prostate. Women with this disorder also have a high risk of cancer of the endometrium (lining of the uterus) and ovaries. The objective of this study was to assess whether BMI is associated with colorectal adenoma occurrence in persons with LS. A study of 486 patients with LS was conducted. Patients were divided between those who had and those who did not have a history of colorectal cancer (CRC) neoplasms, to determine whether there is an association between BMI and colorectal adenoma occurrence in LS patients. Associations between BMI, height, weight, weight change, and risk of colorectal adenomas were explored. Researchers found a statistically significant association between current overweight (≥ 25 kg/m^2) and developing colorectal adenomas among men in the group with no history of colorectal cancer. Men with Lynch syndrome (LS) and a body mass index (BMI) of 25 kg/m² or more may be at increased risk for developing colorectal adenomas. This association was not observed among women, nor was it observed in the group having a history of colorectal cancer. Researchers concluded that excess body weight increased the risk of colorectal adenomas in people with LS. This increased risk was seen only in men.

Botma, Akke, et al., Body mass index increases risk of colorectal adenomas in men with lynch syndrome: the GEOLynch Cohort study. J of Clin Oncology. Published online before print August 23, 2010, doi: 10.1200/JCO.2010.28.0453 JCO.2010.28.0453

28. Vitamin Use Does Not Decrease Colorectal Cancer Recurrence (Aug. 30/10)

According to the results of this study, patients with stage III colon cancer who used multivitamins during and after adjuvant chemotherapy did not experience a lower recurrence rate or improved survival. Researchers studied 1,038 patients with stage III colon cancer who were enrolled during 1999 to 2001 in the Cancer and Leukemia Group B trial of adjuvant chemotherapy.

The patients were surveyed about their use of multivitamins during and six months following adjuvant chemotherapy, and were followed until 2009 for cancer recurrence and death. The 49.9% of patients who reported taking multivitamins during chemotherapy had no significant associated benefits compared to those who didn't take multivitamins. The researchers found that use of multivitamins during chemotherapy was not significantly associated with disease-free survival, recurrence-free survival, or overall survival. In addition, no benefits were seen for use of multivitamins six months after adjuvant chemotherapy, for taking more vitamin tablets, or for longer duration of vitamin use before cancer diagnosis. The rates of grade III and higher gastrointestinal toxicity were not improved by multivitamin use. "These results are consistent with a conference statement from the National Institutes of Health that concluded there was insufficient evidence to recommend either for or against the use of multivitamins for chronic disease prevention. Nonetheless, further research is needed to assess the utility of individual vitamins in patients with established colorectal cancer," the authors conclude.

Ng, Kimmie, et al., Multivitamin use is not associated with cancer recurrence or survival in patients with stage III colon cancer: findings from CALGB 89803. J of Clinical Oncology. Published online before print August 30, 2010, doi: 10.1200/JCO.2010.28.0362 JCO.2010.28.0362

29. Coffee & Colorectal Cancer Risk (Sept. 2/10)

The Finns are among the heaviest coffee drinkers in the world, with each person in Finland consuming more than twice as much coffee every year as the average European and nearly three times as much as Americans. Yet, when more than 60,000 Finns were followed for more than 18 years, there was no difference in colon or rectal cancer between those who drank more than 10 cups a day and those who didn't drink coffee at all.

Researchers tracked 60,041 Finnish men and women, aged 26 to 74 at enrollment, for an average of 18 years. None had cancer when they began the study. During that time there were 538 cases of colon cancer and 234 cases of rectal cancer. Comparing the group who drank more than 10 cups of coffee a day and those who didn't drink coffee at all, there was no difference in risk for colon or rectal cancer for men, women, or men and women together. Researchers concluded: In this study, we found no association between coffee consumption and the risk of colorectal, colon and rectal cancer.

Bidel, S. et al., Coffee consumption and risk of colorectal cancer. European J of Clin Nutrition. (2010); 64: pp. 917-923.

30. Smoking Affects Colorectal Cancer (Sept. 7/10)

Smoking has definitely been linked to ailments of the lungs. People who smoke have over 10 times the risk of lung cancer compared to never-smokers. This figure is so attention-grabbing that many people forget that smoking can increase risk of other cancers as well.

A large meta-analysis, which is a type of study that combines results from many smaller studies, examined the connection between smoking and colon cancer. The results are persuasive, to say the least. Current smokers had more than twice the risk of being diagnosed with an adenoma compared with never-smokers. An adenoma is a growth in the colon that can develop into colon cancer if not found and removed through tests such as a colonoscopy. Also of interest: The risk was strongest for "high-risk" adenomas - the type of growths that are *most likely* to go on to become cancer. When people quit smoking, their risk of cancer, heart disease, and stroke begin to drop measurably. In some cases, disease risks drop within hours of quitting. No matter how long you've used tobacco, you can improve your health by quitting. Learn more about how you can free yourself from smoking for good from About.com.

Iodice, Simona, et al., Cigarette smoking and adenomatous polyps: a meta-analysis. Gastroenterology. Vol. 134, Issue 2: pp. 388-395.

31. Meat-Based Diets Increase Mortality (Sept. 9/10)

This study found that men and women who eat a high protein diet which consisted of a high percentage of meat and cheese had a higher risk of early death. The study found, on the other hand, that those that eat a high protein diet which consisted of mostly plant-based protein had a lower risk than average of early death. The study included more than 85,000 women and 44,500 men studied for a period of 20 to 26 years. Lifestyle factors like alcohol intake, exercise, and multivitamin use were taken into account as well and the participants all started with a clean bill of health--no cancer, diabetes, or heart disease.

According to the study, a low-carbohydrate diet based on animal sources was associated with higher all-cause mortality in both men and women, whereas a vegetable-based low-carbohydrate diet was associated with lower all-cause and cardiovascular disease mortality rates. Increased cancer mortality was most prevalent in **colorectal** and lung cancer. The increase in colorectal cancer is the most obvious because ingesting a diet comprised mainly of meat and cheeses tends to compromise your ability to go to the bathroom. Meat and cheese without whole grains, fruits, and an abundance of vegetables tend to constipate. The key to good health is good digestion because without it, things can't keep moving through the digestive system and toxins build up, causing disease. This is why dietary fiber is so important to our health. Higher protein diets based on plant proteins like beans, lentils, and nuts are not only lower in fat and sodium, but they're higher in dietary fiber. And the more meat and processed cheeses you eat, the more the body must ingest the hormones, antibiotics, and other chemicals that go along with them.

Fung, Teresa, et al., Low Carbohydrate diets and all-cause and cause-specific mortality two cohort studies. Annals of Internal Medicine. September 7, 2010, 153 (5)

32. Obese CRC Women Have Increased Mortality (Sept. 9/10)

Postmenopausal women diagnosed with colon cancer may be at increased risk of death if they fail to maintain a healthy body weight before cancer diagnosis, according to this study.. The researchers found that women considered "underweight" or "obese," or who had increased abdominal obesity prior to cancer diagnosis seemed to face a greater risk of mortality. Maintaining a healthy body weight is beneficial for postmenopausal women. This may also be beneficial for those diagnosed with colon cancer later in life. Abdominal obesity may be a useful indicator of higher colon cancer mortality. "It is too early to say whether a decrease in weight characteristics after diagnosis will also decrease mortality risk; at that point it may be too late, according to researchers. Therefore, it's best to maintain a normal, healthy body weight throughout life. Researchers extracted data which included 1,096 women diagnosed with colon cancer who were observed over a maximum 20-year period. During that time, 493 died, of which 289 died from colon cancer. Women classified as obese, with a BMI of at least 30 kg/m2, had a 45% increased overall mortality rate. The few women classified as underweight, with a BMI less than 18.5 kg/m2, had an 89% increased mortality rate compared to those with normal BMI. Furthermore, women with high waist-to-hip ratio had a 30 to 40% greater risk of colon cancer related death. Researchers maintain that the "exact mechanisms underlying the link between obesity and higher mortality of colon cancer patients are unknown." "Obese people may be diagnosed at later stage, have different treatment or more comorbidities". However, the facts that the increased abdominal obesity was associated with colon cancer mortality and those associations persisted after correcting for age, stage at cancer diagnosis and comorbidities suggest that obesity could have a direct biological effect. Obese women, especially those with higher abdominal obesity, have higher hormone levels and may have more aggressive cancer. These women have been already known to have a higher risk of developing colon cancer. Researchers encouraged further investigation of the potential effect of obesity, in particular, abdominal obesity, on the prognosis after colon cancer diagnosis.

Prizment, Anna E., et al., Survival of women with colon cnacer in relation to precancers anthropometric characteristics: the Iowa women's health study. Cancer Epidemiology, Biomarkers, & Prevention. September 2010, 19 (9)