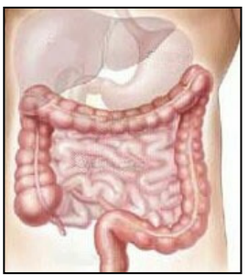
Colorectal Cancer Association of Canada

COLORECTAL CANCER RESEARCH UPDATES

Month Ending August 17th, 2014



The following colorectal cancer research update extends from June 21st, 2014 – August 17th, 2014 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Active Maintenance Improves Progression Free Survival (PFS) in mCRC (Jun.24/14)

Two active maintenance regimens following disease stabilization with standard induction therapy demonstrated superior disease-free outcomes compared with no treatment in patients with metastatic colorectal cancer (mCRC), according to findings of a phase III trial. Patients who received maintenance treatment with fluoropyrimidines plus bevacizumab or bevacizumab monotherapy experienced progression-free survival (PFS). Researchers evaluated whether maintenance with no therapy or bevacizumab monotherapy was non-inferior to fluoropyrimidines plus bevacizumab following successful induction treatment. Progression-free survival was improved with active maintenance treatment but it is too soon to tell if there is an effect on overall survival. The trial enrolled 840 patients with mCRC who received 24 weeks of induction treatment with fluoropyrimidines, oxaliplatin, and bevacizumab. After

completing this treatment, 473 patients who did not experience disease progression were randomized into one of the following arms:

- Arm A, standard maintenance treatment with fluoropyrimidines and bevacizumab (n= 141);
- Arm B, bevacizumab monotherapy (n= 153); or
- Arm C, no treatment (n= 153).

The initial induction therapy regimen would be re-administered if any patients exhibited disease progression. The primary endpoint of the trial was time to failure of strategy (TFS), which included the time of first induction treatment and duration of maintenance until disease progression. Secondary endpoints included time to first progression (PFS1) and overall survival (OS). Following initial induction therapy, the response rate [RR=complete response (CR) + partial response (PR)] was 60% in arm A and B versus 59% in arm C. The best response of stable disease was reported for 40% of patients in arms A and B versus 41% of patients in arm C. After being assigned to a maintenance strategy, patients achieved median PFS1 in arms A, B, and C of 6.2, 4.8 and 3.6 months, respectively. PFS1 from start of induction was 11.7 months, 10.2 months and 9.0 months in arms A, B, and C, respectively. TFS favored arm A over arm C, but did not reach statistical significance. No statistically significant difference was observed between arms A and B in TFS. Few patients terminated maintenance because of unacceptable toxicity; 8%, 5% and 1% of patients in arms A, B, and C discontinued for this reason. However 58%, 79%, and 86% of patients in arms A, B. and C discontinued because of disease progression. The re-induction rate was low overall at 37%; upon first progression only 24% of patients in arm A and 47 % of patients in both arms B and C, received re-induction. Rates for grades 1, 2, and 3 toxicity during maintenance were similar across all 3 arms. After 200 documented events, preliminary OS was 23.4 months from randomization, without significant difference between treatment arms. The researchers concluded that bevacizumab alone is non-inferior to bevacizumab combined with fluoropyrimidines as maintenance but no active maintenance is inferior to combination maintenance. In addition, immediate re-induction rates upon first progression were too low to accept this strategy. “I suspect, but we do not know, that irinotecan toxicity was a factor in patients’ decisions to forego re-induction therapy,” Arnold remarked.

Arnold et al. A Phase III Trial of Fluoropyrimidines (FP) Plus Bevacizumab (BEV) or no Treatment as Maintenance Strategy Following a Standard Combination of FP, Oxaliplatin (OXO), and BEV as First-line Treatment for Patients With Metastatic Colorectal Cancer (mCRC). Presented at: the ESMO 16th World Congress on Gastrointestinal Cancer; June 25-28, 2014; Barcelona, Spain. Abstract AIO KRK 0207.

2. Erbitux Betters Avastin in mCRC Subgroup (Jun.25/14)

Merck Serono, the biopharma division of Merck, used the World Congress on Gastrointestinal Cancer (WCGC) to post early positive data from its FIRE-3 study, which was initiated to compare the two drugs erbitux and avastin in patients with metastatic colorectal cancer (mCRC). Previous FIRE-3 data posted by Merck Serono had demonstrated that there was no statistical difference between Erbitux (cetuximab) plus FOLFIRI chemotherapy and Avastin (bevacizumab) plus FOLFIRI chemotherapy in the overall mCRC population. However, new data presented at the Congress suggests that Merck's drug may be superior in the subset of patients with RAS wild-type mCRC – a form of mCRC associated with a genetic mutation that is thought to count for 50 per cent of advanced / metastatic colorectal cancer cases. The data showed that Erbitux had a significantly higher overall response rate in these patients, at 72.5 per cent compared to 55.5 per cent for Avastin. There was a similar difference in the rate of early tumour shrinkage; 69.2 per cent of Erbitux patients achieved this result compared to 47.4 per cent of Avastin patients. In addition, Erbitux recorded an improved median 'depth of response' – the maximum tumour per cent-shrinkage observed in a patient. Prof Will Steward, head of cancer studies and molecular medicine at Leicester Royal Infirmary in the UK, said the data indicates “a correlation between early tumour shrinkage, depth of response and overall survival and may in part explain why we are seeing the overall survival benefit in the Erbitux over the bevacizumab arm in this RAS wild-type patient population”.

http://www.pmlive.com/pharma_news/erbitux_betters_avastin_in_bowel_cancer_subgroup_581659

3. Survival Benefit from Panitumumab (Vectibix) in Wild Type KRAS mCRC (July 9/14)

Patients with wild-type (WT) *KRAS* metastatic colorectal cancer (mCRC) had extended progression-free survival (PFS) following a regimen of panitumumab (Vectibix) plus FOLFOX4 (i.e. leucovorin, fluorouracil and oxaliplatin) compared with those treated with FOLFOX4 alone. Objective response rates were higher, and a trend toward improved overall survival (OS) was noted. In this international, multisite Phase III study, 1,183 patients with previously untreated mCRC were randomized to receive panitumumab plus FOLFOX4 (arm 1) or FOLFOX4 alone (arm 2). Preliminary results led to the further investigation of patients based on *KRAS* status. Investigators confirmed that mCRC patients with mutated (MT) *KRAS* mCRC had better results when treated with FOLFOX4 without the addition of panitumumab. Patients with WT *KRAS* mCRC had improved PFS and OS in arm 1 compared with those treated in arm 2. In these patients, median PFS was 10 months in arm 1 versus 8.6 months in arm 2. Median OS was 23.9

months in arm 1 versus 19.7 months in arm 2. The updated final analysis of median OS confirmed these numbers. Results for patients with MT *KRAS* mCRC favored the administration of FOLFOX 4 alone. In the final analysis of these patients, median OS was 15.5 months in arm 1 and 19.2 months in arm 2.

http://www.clinicaloncology.com/ViewArticle.aspx?d=Reviews+and+Commentaries&d_id=543&i=July+2014&i_id=1082&a_id=27746

4. Addition of Targeted Biological Agents to First Line Chemo Increases Complete Response (Jul.11/14)

This study assessed whether the addition of monoclonal antibodies (MoAbs) to first-line chemotherapy for advanced colorectal cancer (CRC) increases the complete response (CR) compared with controls. PubMed was reviewed for randomized clinical trials (RCTs) with approved MoAbs (bevacizumab, cetuximab and panitumumab) vs non-MoAbs as first-line therapy for patients with advanced CRC. The incidence and ratio of CR events were calculated in patients assigned to MoAbs compared with controls. A total of 3790 patients from nine RCTs were included for analysis. The overall incidence of CR in patients treated with MoAbs was 2.4% compared with 1.3% in controls. Comparison of the different types of MoAbs showed that the incidence of CR was higher for bevacizumab than for cetuximab. The addition of MoAbs to chemotherapy significantly increased the OR of obtaining a CR compared with controls. No significant differences in the OR were observed in any of the subgroups. The investigators concluded that the CR is a rare event in advanced CRC; however, the addition of MoAbs to first-line chemotherapy significantly increases the curative rate of metastatic disease compared with controls.

Qi WX, et al., Does the addition of targeted biological agents to first line chemotherapy for advanced colorectal cancer increase complete response? A systematic review and meta-analysis. Colorectal Dis 2014 Sep;16(9):O300-7. doi: 10.1111/codi.12647.

5. High Risk for Chemo-Induced Diarrhea (Jul.30/14)

Chemotherapy-induced diarrhea occurred frequently in patients undergoing treatment for colorectal cancer, especially during first exposure, which significantly affected quality of life, according to recent study data. As part of the multinational prospective TRIAD Burden of Illness Study, researchers evaluated patients with colorectal cancer undergoing standard chemotherapy to better understand the risk factors and burden associated with chemotherapy-induced diarrhea (CID). Patients received either FOLFOX (n=95; 530 cycles), FOLFOX plus monoclonal antibodies (n=10; 49 cycles) or FOLFIRI (n=9; 50 cycles). They graded CID severity on a 10-point scale and frequency on a 5-point scale in diaries using questions from the Oral Mucositis Daily Questionnaire through up to eight treatment cycles. Quality of life (QOL) was evaluated by the Functional Assessment of Cancer Therapy instrument; fatigue was assessed by the Functional Assessment of Chronic Illness Therapy scale. CID occurred in 89% of the FOLFIRI group, 56% of the FOLFOX group and 50% of the FOLFOX plus monoclonal antibodies group. Risk for CID was highest during the first cycle of chemotherapy (35%), dropping below 10% for cycles three through five. Compared with those in whom CID did not occur, patients with CID reported lower mean QOL scores (77.1 vs. 80.7). "The risk of CID is highest during the first exposure to chemotherapy, suggesting that some patients are more susceptible than others, and those patients at high risk may drop out of treatment earlier," the researchers concluded. "Identification of those patients at high risk for CID would enable prophylactic treatment that may reduce the incidence and severity of CID and could improve [QOL] among this high-risk group."

Keefe, DM, et al., Risk and outcomes of chemotherapy-induced diarrhea (CID) among patients with colorectal cancer receiving multi-cycle chemotherapy. Cancer Chemo and Pharma. 2014; doi:10.1007/s00280-014-2526-5.

SURGICAL THERAPIES

6. Palliative Resection Associated with Improved Survival in mCRC (Jun.24/14)

In patients with metastatic colorectal cancer (mCRC) receiving palliative care, initial treatment with surgical resection of the primary tumor followed by systemic treatment yielded a 4.7 month overall survival (OS) benefit compared with the same treatments administered in the reverse order, according to a retrospective analysis. Overall, the analysis showed vast differences in OS based on initial treatment in patients presenting with stage IV mCRC, with local curative treatment faring the best. Controversy remains as to the benefit of surgical resection of the primary tumor prior to treatment in stage IV colorectal cancer. Some studies have shown an extension of OS but these positive data are offset by reports of morbidity and mortality following surgery. Further, all the available data are from retrospective studies. This retrospective, population-based study used data from patients presenting with stage IV colorectal cancer enrolled in the Netherlands National Cancer Registries database from 2008 to 2011. Patients were stratified according to treatment received: curative treatment, palliative treatment, or best supportive care (BSC). The group receiving palliative care was further divided according to whether the first treatment administered involved resection of the primary tumor or systemic therapy. A total of

10,593 patients were identified by the researchers; however, 2360 patients did not meet the inclusion criteria and were excluded from the study. Among the remaining 8233 patients, 1510 (18.3%) received local curative treatment for metastasis and 2304 patients (28%) received BSC only. The median OS for patients receiving local curative treatment was 43.7 months compared with 2.1 months in patients receiving BSC. Among patients in the palliative treatment group, 1908 (23.2%) were initially treated with resection of the primary tumor, which was followed by systemic therapy in 949 patients (49.7%). The remaining 2511 patients in the palliative group initially received systemic treatment, followed by resection of the primary tumor in 145 patients (5.8%). Multivariate analysis showed that primary resection was done more often in patients aged <75 years, patients with colon cancer, and patients with one site of metastasis. ***OS was significantly improved in the group of patients initially treated with resection compared with those initially treated with systemic therapy: 16.6 months versus 11.9 months, respectively.***

't Lam-Boer J, et al. Palliative resection of the primary tumour is associated with increased survival in patients with synchronous metastatic colorectal cancer: a nationwide population-based study from The Netherlands. Presented at: ESMO 16th World Congress on Gastrointestinal Cancer; June 25-28, 2014; Barcelona, Spain. Abstract O-0014

SCREENING

7. Noninvasive Method Can Capture Circulating Tumor Cells From Blood Samples for Genetic Testing (Jul.10/14)

Okayama University medical researchers seek partners to commercialize their clinically proven non-invasive fluorescence virus-guided capture system of human colorectal circulating tumor cells (CTCs) from blood samples for genetic testing. This form of non-invasive companion diagnostics is important for personalized targeted cancer therapy. The key factor in capturing extremely low quantities of live CTCs from millions of background blood leukocytes is targeting the high telomerase activity of malignant tumor cells with green fluorescent protein (GFP) expressing telomerase specific replication adenovirus. This 'liquid biopsy' via a simple blood test could be carried out in real time and enables optimized and timely decisions for therapeutic intervention. In 1869 Thomas Ashworth first reported the presence of circulating tumor cells (CTCs) in patients with advanced cancer in his paper entitled: "A case of cancer in which cells similar to those in the tumors were seen in the blood after death. However, it is challenging to detect CTCs because there are very small quantities of CTCs in the bloodstream. The so-called CellSearch system is widely used to detect CTCs, where antibodies are used to target the major epithelial cell surface marker known as the epithelial cell adhesion molecule. Importantly, recent research has shown the existence of heterogeneous CTCs that have both epithelial and mesenchymal characteristics. This discovery has led to demand for the development of CTC capture systems that are able to detect CTCs irrespective of the epithelial cell marker for cancer treatment with molecularly targeted drugs. Another important fact is that currently, targeted cancer treatment for individual patients is carried out by analysis of primary tumors. The difficulties with this approach are that the primary tumors contain very few cells that cause metastasis or reoccurrence, and samples for analysis are obtained by needle core biopsies or surgical removal of tumor tissue—which are invasive procedures and prohibit the extraction of tissue from locations inaccessible by surgery. So there is the need for non-invasive methods capable of detecting CTCs independent of the epithelial cell marker.

Fujiwara, T. et al., Fluorescence virus-guided capturing system of human colorectal circulating tumour cells for non-invasive companion diagnostics. ***Gut*****, 2014; DOI**: ***10.1136/gutjnl-2014-306957***

http://www.sciencedaily.com/releases/2014/07/140710130510.htm

OTHER

8. Higher Death Rate for African Americans Explained (Jun.23/14)

In the U.S. African-American men and women are diagnosed with and die from colorectal cancers at higher rates than men and women of any other racial or ethnic background. Now, a new **study** from the University of Michigan may provide insight into this disparity. African-Americans with colon cancer are half as likely as European-American patients to have a type of colon cancer that is linked to better outcomes and more likely to have right-sided cancers, researchers discovered. Researchers conducted a study involving 503 people with colon cancer. The researchers began by identifying patients using the North Carolina Colon Cancer Study, which collected data on patients throughout central and eastern regions of the state and so includes both rural and urban areas, creating an adequate representation of both African-Americans and rural residents. Among the overall group, 45 percent were black and 55 percent were white and all had suffered from colon cancer. For this important public health study, scientists had examined tissue samples taken during surgery and assessed them for various markers. After analyzing the data from the North Carolina Colon Cancer Study, investigators found that 14 percent

of Caucasians and seven percent of African-Americans had a genetic marker known as microsatellite instability (MSI). "We know that patients with MSI colon cancer do better without chemotherapy. But these improved survival benefits are limited among African-Americans with colon cancer," said Carethers, explaining how MSI tumors are resistant to the chemotherapy drug 5FU, commonly used to treat colorectal cancers. These results, Carethers suggested, may help explain the overall disparity in cancer outcomes. Surprisingly, the researchers also found that African-American patients were more likely to have cancer develop on the right side of their colon. "Right-sided colon cancer may be the 'black ice' of the colon — unseen but potentially deadly," noted Carethers in a press release. Generally, right-sided colon cancer is easier to miss during screening and, when found, more likely to be more advanced than left-sided cancers. Armed with this knowledge about underlying genetics and right-sided development, scientists may be able to adjust their treatment practices and so correct any racial disparity in survival rates.

Murali B, Yang B, Basa R, et al. Influence of Race on Microsatellite Instability and CD8+ T Cell Infiltration in Colon Cancer.* PLOS One*. 2014.

9. Age Matters in Prognosis (Jul.14/14)

Age is a prognostic factor for both overall survival (OS) and progression-free survival (PFS) among patients diagnosed with metastatic colorectal cancer, according to the results of this study. The age effect did not vary by the sites of metastases, the type of therapy received, or the mutation status of the tumour. Compared with middle-aged patients, younger patients had a 19% increased risk of death and a 22% increased risk of progression. The oldest patients in the study had a 42% increased risk of death and a 15% increased risk of progression compared with their middle-aged counterparts. This was most pronounced 1 year after diagnosis. After adjusting for sex; liver, lung, or peritoneal metastases; and performance status, age remained marginally significant for OS and significant for PFS. Cathy Eng, MD, professor in the department of gastrointestinal medical oncology at the University of Texas MD Anderson Cancer Center in Houston, and colleagues analyzed a total of 20,023 patients who participated in 24 first-line colorectal cancer clinical trials that were part of the Aide et Recherche en Cancérologie Digestive (ARCAD) database. Fifteen percent (3,051) of the patients were younger than age 50.The incidence of metastatic colorectal cancer among younger patients (those younger than 50) has seen an uptick in the last few years, although the proportion is still relatively small (about 4.6%). In the United States, the median age of diagnosis of colorectal cancer is 72 and almost one-third of those diagnosed are older than 80. But the incidence of colorectal cancer has recently been shown to increase by about 1.5% every year for individuals aged 50 or younger, with those between the ages of 20 and 29 having the highest increase in incidence (5.6% per year for women and 5.2% per year for men).The median age of patients analyzed in this study was 62, and 4% were younger than age 40. Thirty-eight percent of the patients were female. “In contrast to prior studies, our analyses revealed that age was a significant predictor of OS, with the youngest and oldest patients showing worse survival than patients of middle age, with similar results seen for PFS,” the study authors concluded. The reasons for these differences may be the inclusion of a greater proportion of younger patients in the current study and the evaluation of age as a continuous, rather than a discrete, variable. The study suggested that both younger and older patients with metastatic colorectal cancer could represent a higher-risk population, according to the study authors. Although younger patients are generally healthier overall at diagnosis, a worse prognosis may reflect a different, more aggressive tumor biology or a general greater tumor burden.

Eng, Cathy, et al., Association of Age with survival in patients with metastatic colorectal cancer: analysis from the ARC AD clinical trials program. J of Clin Onc. Published online before print July 7, 2014. doi: 10.1200/JCO.2013.54.9329

10. Gut Bacteria Link to Colorectal Cancer (Jul 21/14)

Colorectal cancer has been linked to carbohydrate-rich western diets, but the underlying mechanisms have been unclear. A study published by Cell Press July 17th in the journal *Cell* shows that gut microbes metabolize carbohydrates in the diet, causing intestinal cells to proliferate and form tumors in mice that are genetically predisposed to colorectal cancer. Treatment with antibiotics or a low-carbohydrate diet significantly reduced tumors in these mice, suggesting that these easy interventions could prevent a common type of colorectal cancer in humans. Carbohydrates account for about half of the daily caloric intake of adults on a western-style diet, and previous studies have linked carbohydrate-rich diets to colorectal cancer in humans. This type of cancer is also frequently associated with mutations in a tumor suppressor gene called APC as well as the MSH2 gene, which plays a critical role in repairing DNA damage. However, it has been unclear why mutations affecting the DNA repair pathway are much more common in colorectal cancer compared with other cancers. Because gut microbes also contribute to the development of colorectal cancer, Researcher Martin and his team suspected that they could interact with diet to explain how the mutations could cause this type of cancer. To explore this question in the new study, Martin and his collaborators used mice that had APC and MSH2 mutations and thus were predisposed to develop colorectal cancer. Treatment with either antibiotics or a low-carbohydrate diet reduced cell proliferation as well as the number of tumors in the small intestines and colons of these mice. These two treatments also reduced levels of certain gut microbes that metabolize carbohydrates to

produce a fatty acid called butyrate. When the researchers increased butyrate levels in the antibiotic-treated mice, cell proliferation and the number of tumors increased in the small intestines. Taken together, the findings suggest that carbohydrate-derived metabolites produced by gut microbes drive abnormal cell proliferation and tumor development in mice genetically predisposed to colorectal cancer. "By providing a direct link between genetics and gut microbes, our findings suggest that a diet reduced in carbohydrates as well as alterations in the intestinal microbial community could be beneficial to those individuals that are genetically predisposed to colorectal cancer," Martin says.

Belcheva,, Antoaneta, et al., Gut Microbial Metabolism Drives Transformation of Msh2-Deficient Colon Epithelial Cells*. Cell*, 2014; 158 (2): 288 DOI: 10.1016/j.cell.2014.04.051

11. Genetic Testing of Tumor is Recommended for Colorectal Cancer Patients (Aug. 5/14)

Of the 143,000 patients diagnosed with colorectal cancer annually in the U.S., up to 25 percent have a familial risk of colorectal cancer. A new guideline from the U.S. Multi-Society Task Force on Colorectal Cancer recommends genetic testing of tumors for all newly diagnosed colorectal cancer patients. The task force makes specific surveillance and management recommendations for those affected by a genetic condition called Lynch syndrome, the most common cause of inherited colorectal cancer, accounting for approximately 3 percent, or more than 4,000, of the newly diagnosed cases in the U.S. each year. Universal genetic testing of the tumors for evidence of mismatch repair (MMR) deficiency of newly diagnosed colorectal cancer patients is recommended for several reasons:

1. Use of clinical criteria and prediction models to identify patients with Lynch syndrome have less than optimal sensitivity and specificity.
2. It has been shown to be cost effective for the diagnosis of Lynch syndrome.
3. It has greater sensitivity for identification of Lynch syndrome compared with other strategies, including Bethesda guidelines, or a selective tumor testing strategy.

Individuals whose tumor shows evidence of MMR deficiency, have a known MMR gene mutation in the family, who meet clinical criteria for Lynch syndrome, or who have a personal risk of greater than or equal to 5 percent chance of Lynch syndrome based on prediction models should undergo a genetic evaluation for Lynch syndrome. Germline genetic testing has the following advantages:

1. It can confirm a diagnosis of Lynch syndrome in the patient.
2. It can determine the status of at-risk family members in families in which disease mutation has been found.
3. It can direct the management of affected and unaffected individuals.

Patients with Lynch syndrome are at an increased risk of developing colorectal cancer, as well as cancers outside of the colon. The U.S. Multi-Society Task Force on Colorectal Cancer recommends that annual history, physical examination, and patient and family education regarding the risk of cancer should start between the ages of 20 and 25 years. In addition, the following recommendations are made for patients with or at risk of Lynch syndrome:

- Colorectal cancer: Colonoscopy screening every one to two years beginning at ages 20 to 25, or two to five years younger than the youngest age of CRC diagnosis in the family, if the diagnosis was before the age of 25.
- Endometrial cancer: Conduct pelvic exam screening and endometrial sampling annually starting between the ages of 30 and 35.
- Ovarian cancer: Start annual transvaginal ultrasound screening at ages 30 to 35. Hysterectomy and bilaterial salpingo-oophorectomy is recommended for women with Lynch syndrome at age 40 or after childbearing is complete.
- Gastric cancer: Screen via endoscopy with gastric biopsy beginning at ages 30 to 35. Continue every two to three years based on patient risk factors.
- Urinary cancer: Conduct annual urinalysis starting at ages 30 to 35.
- Routine screening of the small intestine, pancreas, prostate and breasts are not recommended.

There are two treatments recommended for patients affected with Lynch syndrome:

1. Removal of the large intestine: Colectomy with ileorectal anastomosis, which removes the large intestine and attaches the small intestine to the rectum, is the primary treatment for patients affected by Lynch syndrome who have colon cancer or precancerous colon polyps that cannot be removed by colonoscopy. Less extensive surgery can be considered for patients older than 60 to 65 years of age.

2. Aspirin therapy: There is growing evidence that the use of aspirin is beneficial in preventing cancer in Lynch syndrome patients. While the evidence is not conclusive, treatment of an individual patient with aspirin is a consideration after discussing patient-specific risks, benefits and uncertainties of treatment.

Douglas K. Rex. Guidelines on genetic evaluation and management of Lynch syndrome: A consensus statement by the U.S. Multi-Society Task Force on Colorectal Cancer.* Gastrointestinal Endoscopy*, 2014; 80 (2): 197 DOI: 10.1016/j.gie.2014.06.006

http://www.sciencedaily.com/releases/2014/08/140805132150.htm

NUTRITION & HEALTHY LIFESTYLE

12. Coffee May Raise Colon Cancer Risk in Men (Jun. 17/14)

A new Japanese study suggests that drinking too much coffee may increase risk of colon cancer in men, but not in women and high coffee consumption was linked with high risk of colon cancer in men. The study found a positive association between coffee consumption and risk of colon cancer in men. Specifically, compared with those who drank less than one cup of coffee per day, men used 2 to 3 cups of coffee per day were 26% more likely to develop colon cancer and those drinking more than 4 cups of coffee per day were at 79% increased risk for colon cancer. However, coffee drinking was associated neither with risk of colon cancer in women nor with risk of rectal cancer in men and women.

Yamada, H, et al., Coffee Consumption and risk of colorectal cancer: the japan collaborative cohort study. J Epidemiol. 2014 May 24.

13. Diets High in Dairy May Boost Colon Cancer Survival (Jun.24/14)

A diet rich in dairy products may slightly extend the lives of people diagnosed with colon cancer, a new study suggests. But at least one cancer doctor not involved with the study was skeptical of the research and its conclusions. The study found that people who ate the most dairy lived slightly longer and had a lower risk of dying from any cause. "If you are a colorectal cancer patient, calcium and milk consumption may improve your survival. But do not change your diet just yet before more research is conducted," said lead researcher Peter Campbell, who's with the American Cancer Society's epidemiology research program. The new study, he noted, showed only an association between dairy and survival -- it could not prove that dairy consumption was the direct cause of increased longevity. "If our findings are replicated in future studies, we may see changes in dietary guidelines for cancer survivors: patients might be encouraged to increase calcium and milk intake," Campbell added. But, Dr. Donald Abrams, an integrative oncologist at the University of California, San Francisco, and author of an accompanying journal editorial, had significant doubts about the study. "It's silly to look at milk in isolation, because [according to the study] the people who drank the most milk also were the leanest, did the most physical exercise, ate less red meat, and ate more fruits and vegetables," he said. "The message is it's the whole diet, not a single component." On a technical point, Abrams doesn't believe that a study such as this is meaningful. "Investigators are going to try to write as many papers as they can from their data and chop it up into little reductionist pieces, when it's much better to look at nutrition and diet more holistically," he said. The report was published online June 23 in the *Journal of Clinical Oncology*. For the study, Campbell's team collected data on almost 2,300 people diagnosed between 1992 and 2009 with colon cancer that had not spread beyond the colon. By 2010, among those in the study, 949 patients had died -- 408 from their cancer. The researchers found that those who ate the most dairy and therefore got the highest amount of dietary calcium lived slightly longer. The authors say their finding was "marginally statistically significant." In addition, those who drank the most milk had a 28 percent lower risk of dying from any cause, the researchers noted. The study authors believe the survival benefit may be from the calcium in dairy, not the vitamin D. They also suggested that calcium may hinder cancer-cell growth and its ability to settle in sites far away from the original cancer. What cancer patients eat does make a difference, Abrams noted. "They should eat a healthy diet and try to avoid the standard American diet," he said. Abrams would rather people skipped dairy altogether. Dairy is high in saturated fat, and affects hormones that might increase the risk of other cancers, he noted in his editorial. "I believe dairy should be avoided by all people, let alone people with cancer," he said. Abrams noted that studies find that people diagnosed with colon cancer who eat "meats and sweets" don't do as well in survival and cancer recurrence as patients who eat a diet rich in fruits and vegetables.

Peter Campbell, Ph.D., epidemiology research program, American Cancer Society; Donald Abrams, M.D., integrative oncologist, University of California, San Francisco; June 23, 2014, Journal of Clinical Oncology, online

http://www.webmd.com/colorectal-cancer/news/20140624/diets-high-in-dairy-might-boost-colon-cancer-survival-a-bit

14. Vitamin D Boosts Survival Chances for Colorectal Cancer Patients (Jul.8/14)

Colorectal cancer patients with high levels of vitamin D in their blood are more likely to survive the disease, according to research published. Scientists who studied almost 1,600 patients after surgery for bowel cancer found those with the highest levels of vitamin D have half the risk of dying of the disease compared with those with the lowest levels. The study is the first to correlate the long-term survival prospects of bowel cancer patients after diagnosis with total blood levels of vitamin D. Vitamin D, sometimes known as the "sunshine vitamin", is made in the body when the skin is exposed to sunlight and is found in foods such as fish liver oil, eggs and fatty fish such as salmon, herring and mackerel. It is known to boost the uptake of calcium and bone formation. Some observational studies have also

suggested a link between low levels of vitamin D and greater risks of many acute and chronic diseases. Malcolm Dunlop of the Medical Research Council Human Genetics Unit at the University of Edinburgh who led this study, said it suggested vitamin D supplements may be worth exploring for bowel cancer patients. "Our findings are promising but it is important to note that this is an observational study (and) we need carefully designed randomized clinical trials before we can confirm whether taking vitamin D supplements offers any survival benefit," he said. Dunlop's team tested blood samples from almost 1,600 patients after surgery for bowel cancer. They found the greatest benefit of vitamin D in patients with stage 2 cancers, when the tumor may be quite large but the disease has not yet spread. Three quarters of the patients with the highest vitamin D levels were still alive after five years, compared with fewer than two thirds of those with the lowest levels, they found. The team, whose work was published in the Journal of Clinical Oncology, said they now plan to set up a clinical trial to test whether taking vitamin D tablets in combination with chemotherapy can improve bowel cancer survival rates.

http://www.foxnews.com/health/2014/07/09/vitamin-d-boosts-survival-chances-for-bowel-cancer-patients-study-says/