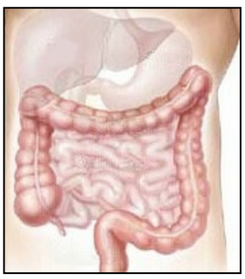
Colorectal Cancer Association of Canada

COLORECTAL CANCER RESEARCH UPDATES

Month Ending March 13th, 2015



The following colorectal cancer research update extends from January 17th, 2015 – March 13th, 2015 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Ramucirumab Meets Primary Endpoint (Jan. 17/15)

Patients with progressive metastatic colorectal cancer had modest but statistically significant improvement in overall survival and progression-free survival (PFS) with second-line ramucirumab (Cyramza) and chemotherapy Folfiri. The addition of ramucirumab to FOLFIRI chemotherapy led to a median overall survival (OS) of 13.3 months versus 11.7 months with FOLFIRI plus placebo. The median PFS was 5.7 months with ramucirumab compared with 4.5 months with placebo. All of the patients had progressed during or after first-line treatment with chemotherapy plus bevacizumab (Avastin). The trial met its primary endpoint, demonstrating a statistically significant improvement in overall survival for ramucirumab and FOLFIRI versus placebo and FOLFIRI. Ramucirumab, in combination with FOLFIRI, was well tolerated in patients with metastatic colorectal cancer. Overall, the adverse events were considered manageable.

About Ramucirumab

In colorectal cancer, tumor growth involves multiple molecules and signaling pathways, including vascular endothelial growth factor (VEGF) and VEGF receptor 2 (VEGFR2), which mediate tumor angiogenesis (the formation of new blood vessels). Both VEGF and VEGFR2 are established therapeutic targets in colorectal cancer, as reflected in the approved indication for bevacizumab.

Ramucirumab is an anti-VEGFR2 antibody that targets the receptor's extracellular domain to prevent ligand binding and receptor activation. The drug was FDA approved for the treatment of advanced gastric cancer or adenocarcinoma of the gastroesophageal junction last year.

Gastrointestinal Cancers Symposium

Source Reference: Tabernero J, et al "RAISE: A randomized, double-blind, multicenter phase III study of irinotecan, folinic acid, and 5-fluorouracil (FOLFIRI) plus ramucirumab (RAM) or placebo (PBO) in patients (pts) with metastatic colorectal carcinoma (CRC) progressive during or following first-line combination therapy with bevacizumab (bev), oxaliplatin (ox), and a fluoropyrimidine (fp)" GiCS 2015; Abstract 512.

2. Cetuximab plus FOLFIRI only Effective in RAS WT mCRC (Feb.10/15)

Molecular testing of all tumors for *RAS* mutations in patients with metastatic colorectal cancer should be standard practice to help guide decisions about use of anti-epidermal growth factor receptor (anti-EGFR) therapy, according to a reassessment of results from the phase 3 CRYSTAL study. In the CRYSTAL study, researchers compared the combination of FOLFIRI with the anti-EGFR antibody cetuximab (Erbitux) to FOLFIRI alone as a first-line therapy for metastatic colorectal cancer. Results showed the combination was associated with significant improvements in OS, PFS and objective response rate among patients with *KRAS* exon 2 wild-type tumors, but researchers observed no efficacy benefit for the combination in patients who harbored KRAS exon 2 mutations. Two other studies — the phase 2 OPUS trial, which combined cetuximab with FOLFOX4, and the PRIME trial, which evaluated the combination of the EGFR antibody Panitumumab (Vectibix) and FOLFOX4 — revealed patients with KRAS wild-type tumors derived benefits from the combinations but those with KRAS mutations did not.

In the current analysis, researchers conducted a post hoc investigation of the CRYSTAL study to measure the efficacy of the cetuximab–FOLFIRI combination vs. FOLFIRI alone in patients with other *RAS* mutations. The investigators took existing DNA samples from wild-type tumors and re-analyzed them for mutations in four additional *KRAS* codons and six additional *NRAS* codons. A ≥5% mutant allele cutoff was used to determine the mutation. Of the 666 original patients with *KRAS* exon 2 wild-type tumors, 430 (64.6%) were evaluable. From that cohort, 14.7% (63 patients) were identified with other *RAS* mutations. In that sample, researchers continued to observe a significant benefit with the cetuximab combination in *RAS* wild-type tumors. However, they reported no difference in efficacy between the cetuximab–FOLFIRI combination and FOLFIRI alone in tumors with other *RAS* mutations. The safety profile of the combination was similar in all *RAS* subgroups. Despite these data, researchers suggested that — because of the small sample size — there still is not enough evidence to conclude that other *RAS* mutations have a negative predictive value. They reached this conclusion after they evaluated treatment outcomes in *RAS* subgroups defined according to a threshold of 0.1% mutant-to-wild-type sequences. For that analysis, the researchers moved 23 patients initially included in the *RAS* wild-type group to the *RAS*-mutant group.

Van Cutsem, E, et al., Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and* RAS *Mutations in Colorectal Cancer J Clin Oncol. 2015; 2014.59.4812.

3. Analysis Confirms Safety of Regorafenib in mCRC (Feb.15/15)

Toxicities among patients with metastatic colorectal cancer (mCRC) who responded best to regorafenib were “broadly similar” to the overall study population, according to a post hoc analysis of the pivotal phase III CORRECT trial presented at the 2015 Gastrointestinal (GI) Cancers Symposium. The results of this exploratory subgroup analysis support the clinical benefit and tolerability of regorafenib as a treatment option for patients with metastatic colorectal cancer. CORRECT randomized 760 patients with mCRC in a 2:1 ratio to the oral multikinase inhibitor regorafenib (n = 505) or placebo (n = 255). Overall, treatment with regorafenib improved overall survival (OS) by 1.4 months (6.4 vs 5.0 months) and progression-free survival (PFS) by 0.2 months (1.9 vs 1.7 months;). Based on these data, the FDA approved regorafenib in September 2012 for use in patients with previously treated mCRC.

The subgroup analysis presented at the GI Symposium in January included 98 patients (19.4%) treated with regorafenib who had PFS >4 months. Forty-seven percent of these patients were KRAS-mutation positive and 44% were KRAS wild-type. Patients in this best responder subgroup received a median of 6 cycles of regorafenib, with 92% receiving ≥5 cycles and 20% receiving >8 cycles. Overall, 34% of patients had their regorafenib dose reduced and 87% had dose interruptions. The resulting mean daily dose was 139 mg, or 81% of the planned dose. The review of toxicities in the subgroup found that these patients mostly experienced adverse events (AEs) at comparable rates to those in the overall trial population, despite exposure to regorafenib for over twice as long as the overall group. All patients with longer PFS experienced AEs; the most common grade ≥3 AEs were

- hand-foot skin reaction (20%),
- hypertension (17%),
- diarrhea (17%), and
- fatigue (16%).

Although the AE profile of regorafenib was similar in both populations, some AEs did occur more frequently in patients treated with regorafenib for >4 months. Rates of all-grade diarrhea, hand-foot skin reaction, and weight loss were ≥15% higher in the subgroup with longer PFS than in the overall CORRECT population. Rates of grade ≥3 diarrhea and hypertension (17% each) in the longer PFS population were twice as high as in the overall population. According to Axel Grothey, prospective validation of these AE findings among the best responders is needed, in conjunction with biomarker analysis from real-life clinical experience."While adverse events across both populations were broadly similar, some did occur more frequently in patients with longer exposure, an observation that is possibly related to the longer duration in this subgroup. Analyses to identify clinical and molecular markers in these patients are ongoing."

Grothey A, Falcone A, Humblet Y, et al. Subgroup analysis of patients with metastatic colorectal cancer (mCRC) treated with regorafenib (REG) in the CORRECT trial who had progression-free survival (PFS) longer than 4 months. J Clin Oncol 33, 2015 (suppl 3; abstr 710)

http://www.onclive.com/web-exclusives/Analysis-Confirms-Safety-of-Regorafenib-in-mCRC-Among-Best-Responders

4. Personalized Onco-Genomics Program At BC Cancer Agency Leads to Unique Breakthrough (Mar.12/15)

The Personalized Onco-Genomics (POG) Program at the BC Cancer Agency has identified a life-altering treatment option for a patient with advanced cancer. With BC Cancer Foundation funding, the BC Cancer Agency set forth with a world-leading clinical study as POG began integrating genomic sequencing into patient care and clinical decision-making for 30 individuals with advanced and hard-to-treat cancers. With an additional $5 million raised through the BC Cancer Foundation's *2014 Inspiration Gala* presented by Encana, POG is expanding and will enroll 300 patients with incurable cancers. Trish, a vibrant mother of a 27-year-old son and former costume designer in the film industry, has been through the gamut of treatments for her aggressive colorectal cancer. Over the past five years she has weathered; chemotherapy, three complicated surgeries and radiation therapy. She had been given a "two-year sentence," her description for the terminal stage of disease. When her medical oncologist, Dr. Howard Lim, at the BC Cancer Agency, introduced the option of enrolling in POG, Trish says: "I didn't care what it entailed, I thought, 'bring it on.'" Dr. Lim describes her results as unique, as a number of patients with seemingly similar advanced colorectal cancer do not have the same degree of protein "up-regulation" that's driving Trish's cancer. The protein function is a critical piece of knowledge in her care as there's a drug on the market—commonly used to treat high blood pressure—that targets the protein. "I noticed a big change in my energy about a week after starting to take the drug," says Trish. Her husband John Givins echoes the dramatic improvement, as he spent the past year caring for his wife and helping her through excruciating pain caused by the tumours enveloping her spine. Within weeks, her tumour markers dropped to normal and a PET/CT scan didn't turn up any evidence of cancer. Dr. Lim emphasizes the value in POG is that every patient is their own personalized clinical trial, allowing the research team to rapidly translate the results into care. John says that POG has taught them to be brave and to live with purpose. "We are grateful for the time, money and dedication invested in the POG Program, through the BC Cancer Foundation and BC Cancer Agency. It has given me and Trish quality time together with our family and friends and the hope that we will finally slay the cancer dragon," he says. When asked what POG has meant to Trish, she keeps it simple: "This has meant my life." And, while the results have been rapid and dramatic, Trish, John and Dr. Lim take it all step-by-step as the treatment is a first for cancer care, and the long-term effects remain unknown. To learn more about POG or to make a donation supporting the future of this world-leading clinical research program, visit **www.bccancerfoundation.com/POG**

http://bccancerfoundation.com/about-us/news/bc-cancer-agency%E2%80%99s-pog-program-leads-unique-breakthrough-patient%E2%80%99s-treatment

SURGICAL THERAPIES

5. Surgery May Not Be Necessary for Some Patients with Rectal Cancer (Jan. 19/15)

A retrospective review of clinical data on 145 patients with stage I-III rectal cancer indicates that patients with a *complete response*, defined as complete disappearance of the tumor after treatment with chemoradiation and systemic chemotherapy, had similar 4-year survival rates regardless of whether they had immediate surgery or pursued a watch-and-wait surveillance approach. The findings add to growing evidence suggesting that, with frequent follow-up examinations after initial chemotherapy and radiation, select patients with rectal cancer can achieve excellent outcomes while avoiding the risks and

complications of rectal surgery. “We believe that our results will encourage more doctors to consider this watch-and-wait approach in patients with clinical complete response as an alternative to immediate rectal surgery, at least for some patients,” said senior study author Philip Paty, MD, a surgical oncologist at the Memorial Sloan-Kettering Cancer Center in New York, New York. “From my experience, most patients are willing to accept some risk to defer rectal surgery in hope of avoiding major surgery and preserving rectal function.” Paty stated that in approximately 40% to 50% of patients with stage I rectal cancer and 30% to 40% of patients with stage II-III cancer, tumors disappear clinically after initial treatment with chemoradiation and systemic chemotherapy. He suggested that those patients are potential candidates for the watch-and-wait approach. By avoiding rectal surgery, patients are spared its risks, including impaired bowel and sexual function, which can substantially diminish quality of life.

In the present report, researchers retrospectively analyzed data that were collected at Memorial Sloan-Kettering Cancer Center between 2006 and 2014. Patients with stage I-III rectal cancer who received radiation and chemotherapy (neoadjuvant therapy) and who experienced complete tumor regression were either followed by watchful waiting (nonsurgical management) or underwent rectal surgery. Patients undergoing the watchful-waiting approach were initially followed at 3- to 4-month intervals by digital rectal and endoscopic examinations and at 6-month intervals by cross-sectional imaging. Median follow-up in this report is 3.3 years. Rectal surgery was deferred in 73 patients who achieved a clinical complete response after chemotherapy and radiation (no cancer detected on physical examination, endoscopy, or imaging). Among those 73 patients, 74% experienced durable tumor regression and avoided rectal surgery; 26% eventually underwent rectal surgery to treat tumor regrowth. In a nonrandomized comparison, researchers found that the outcomes achieved in this group of patients were similar to the outcomes of 72 patients who underwent standard rectal surgery and experienced a pathologic complete response (no viable cancer cells found on microscopic examination of surgically removed tissue): the 4-year overall survival rate was 91% in the no-surgery group vs. 95% in the standard-surgery group. No significant differences were noted in the number of distant recurrences between the two groups. According to the authors, this is one of the largest experiences of its kind, building on prior evidence from research conducted in Brazil and the Netherlands. Nonsurgical management of rectal cancer is becoming increasingly accepted as a standard option worldwide. A prospective phase II study has recently begun enrolling patients at 20 institutions across the United States, and nonsurgical management will be offered to patients whose tumors fully disappear after initial chemotherapy and radiation.

http://www.oncologynurseadvisor.com/surgery-may-not-be-necessary-for-some-patients-with-rectal-cancer/article/393058/

PSYCHOSOCIAL

6. Most Cancer Patients Involve Family in Treatment Decisions (Mar.12/15)

Family members often play an important role in providing care for patients with cancer, but which patients are more or less likely to involve family members in decisions regarding their care is not well known. A new study provides some insights and may help physicians understand patients' preferences regarding their care. Researchers surveyed 5284 patients with a new diagnosis of lung or **colon cancer**, and asked participants how they involved their families in decisions about their care. Only 1.5 percent of patients reported family-controlled decisions. Among the remaining patients, 49.4 percent reported equally sharing decisions with family, 22.1 percent reported some family input, and 28.5 percent reported little or no input from their families. Non-English speaking Asian patients and Spanish-speaking Hispanic patients were more likely to report equally shared decisions with their families than other patients. Also, patients who were married, female, older, and insured more often equally shared decision-making with their families than their counterparts. Patients who were veterans were the least likely to share decision-making with their families. "Understanding how patients vary in their inclusion of family members in decisions--by ethnicity, language spoken, marital status, sex, age, insurance status, and veteran status--may help physicians to better assess their patients' preferences for engaging family members in decisions," said Dr. Hobbs, lead investigator. "As we move to more patient-centered models of care, such assessments may help doctors personalize the care they offer their patients." Dr. Hobbs noted that as therapies for cancer patients improve, they are also becoming increasingly complex, making it challenging for patients and providers to determine the optimal therapy for each patient. With this in mind, knowing how patients make decisions and understanding the role that families play in decision-making is crucial for optimizing patient participation in treatment decisions. "Our study suggests that not all patients wish to include family in the same way. By raising awareness of these preferences, we hope that physicians will be aware of these variations and elicit their patient's preference on how they wish to include, or not to include, families in decision-making."

Gabriela S. Hobbs, et al., The role of families in decisions about cancer treatments.* CANCER*, February 2015 DOI: 10.1002/cncr.29064

OTHER

7. RAS Mutations Predicted Metastatic Spread, Survival in Colorectal Cancer (Jan.19/15)

Patients with *RAS*-mutant metastatic colorectal cancer demonstrated significantly higher incidence of brain, bone and lung metastasis than those who had *RAS* wild-type metastatic disease, according to study results. RAS mutation also was significantly associated with shorter median overall survival (OS), results showed. "I first noticed that a few patients with brain metastasis had the *KRAS* mutation," **Nancy Kemeny, MD**, a medical oncologist at Memorial Sloan Kettering Cancer Center, told *HemOnc Today.* "Since brain metastases are rare, I thought we should look at all our patients with *KRAS* mutations and see if they had a higher chance of getting metastases to the brain or other areas. We have confirmed this concept in a larger study of more than 900 patients with the same results — significantly more brain metastases occurred in patients with *KRAS* mutations, as did lung and bone metastases." Kemeny and colleagues evaluated genomic data on RAS and *PIK3CA* mutations from 918 patients with metastatic colorectal cancer. Overall, 477 patients had wild-type *RAS* and 441 had *RAS* mutations. *RAS* mutations included those at *KRAS* exon 2 (n=394), at *KRAS* exon 3 or 4 (n=29), and in *NRAS* (n=18). Researchers also identified *PIK3CA*-activating mutations in 76 (9.7%) of 786 eligible patients. Patients who had wild-type *RAS* demonstrated significantly longer median OS following diagnosis of metastatic disease than those who had *RAS* mutations (81 months vs. 47 months). Results indicated *RAS* mutations were significantly associated with shorter OS. Among patients who did not have metastases in these sites at the time of the diagnosis of metastatic disease, those who harbored *RAS* mutations demonstrated significantly higher incidence of metastases in the lung (32.5% vs. 19%), bone (8.8% vs. 4.4%) and brain (1.4% vs. 0.2%) at 2 years. The incidence of liver metastases was comparable between patients with and without *RAS* mutations (12% vs. 14.3%). Analyses indicated *RAS* mutations were significantly associated with the risk for brain metastases), bone metastases and lung metastases. PIK3CA mutations were not associated with OS, nor were they associated with liver, lung or bone metastases. However, PIK3CA mutations were associated with an increased occurrence of brain metastasis. "Our findings have implications for understanding the biologic effects of *RAS* activation in metastatic colorectal cancer and suggest *RAS* mutations not only affect initiation of disease but also progression," Kemeny and colleagues wrote. "An understanding of this pattern of spread may help inform physicians' assessment of symptoms in patients with metastatic colorectal cancer and alert physicians to have a lower threshold to evaluate neurologic or bony-related symptoms in patients with *RAS*-mutant metastatic colorectal cancer."

http://www.healio.com/hematology-oncology/gastrointestinal-cancer/news/online/%7B230a0f72-0c35-46e9-b31e-15ae62b3f4f5%7D/ras-mutations-predicted-metastatic-spread-survival-in-colorectal-cancer

8. **Colon Cancer Patients With Left-Sided Tumours Have Better Survival Rates** (Feb.20/15)

The two halves of the human colon have different embryonic origins and gene expression patterns, and these differences may also play a role in cancer biology, according to this study. To determine if there is an association between right or left colon primary tumor location and prognosis in metastatic colorectal cancer (CRC), as well as efficacy of the antiangiogenic agent bevacizumab (avastin), researchers used data from a prospective pharmaco-genetic study and two randomized phase III trials. Overall survival (OS) and progression-free survival (PFS) were assessed in 2027 patients with metastatic CRC according to tumor location. Given the prognostic impact of BRAF mutational status and mucinous histology and their association to right-sided CRC, the prognostic impact of primary tumor location was also assessed in a subgroup of 200 patients from the prospective PROVETTA study, with full information on BRAF status and details on histology. Over the three studies, about 70% of patients had left-sided primary tumors and had better survival outcomes than those with right-sided tumors. In the PROVETTA study, right-sided tumor location also had a negative prognostic value independent of BRAF mutation status or histological type. However, the efficacy of bevacizumab was independent of tumor location, although right-sided tumors were associated with development of chemo-resistance, suggesting biological differences. The researchers point out that the analysis was exploratory and that data on BRAF mutation status and mucinous histology were not available from the two randomized trials. However, they conclude that ." ..side of origin could be of added value in clinical decision-making, and should be considered an important stratification factor for future randomized trials." In an editorial, Howard S. Hochster, M.D., notes that the study was of patients with metastatic disease and therefore may not apply to patients with resected primary tumors. In addition, because this was a pooled analysis of three studies, there were no untreated control patients and selection bias may have influenced the results. However, Dr. Hochster concludes that "This interesting analysis gives rise to some important and testable biological hypotheses."

F. Loupakis, D. Yang, L. Yau, et al.. Primary Tumor Location as a Prognostic Factor in Metastatic Colorectal Cancer.* JNCI Journal of the National Cancer Institute, *2015; 107 (3): dju427 DOI: 10.1093/jnci/dju427

NUTRITION & HEALTHY LIFESTYLE

9. Prolonged Survival in mCRC Linked to High Pretreatment Vitamin D (Jan.17/15)

Patients with metastatic colorectal cancer (mCRC) with high levels of plasma **vitamin D** prior to first-line systemic therapy lived a median of 8.1 months longer than those with low vitamin D levels, according to a preplanned analysis of prospective clinical trial data. Median overall survival among patients who fell into the highest vitamin D quintile at baseline, with a median 25-hydroxyvitamin D (25[OH]D) level of 27.5

ng/mL, was 32.6 months, as compared with 24.5 months among patients in the lowest quintile, with a median 25(OH)D level of 8.0 ng/mL (Progression-free survival outcomes bolstered the overall survival results, showing a 2.1-month improvement with high versus low vitamin D at baseline. The median time to disease progression reached 12.2 months among patients in the highest quintile versus 10.1 months among patients in the lowest quintile. "Even after controlling for known prognostic factors and potential confounding factors, we still saw a significant relationship between higher vitamin D levels and improved outcome," said Kimmie Ng, MD, MPH, of the Dana-Farber Cancer Institute, the lead investigator of this cohort study. Patients with mCRC are frequently deficient in vitamin D. This is potentially worrisome given that vitamin D inhibits cell proliferation and angiogenesis, induces cell differentiation and apoptosis, and exerts anti-inflammatory effects—all relevant processes in cancer. In addition, epidemiologic data support a strong link between low plasma 25(OH)D levels and the risk of CRC. Dr. Ng and colleagues previously published a cohort study in which they observed a strong association between plasma 25(OH)D and survival among patients with all stages of CRC. "In exploratory subgroup analyses, we found that the survival associated with higher plasma 25(OH)D levels seemed to be greater in more advanced stages of disease," she noted. The current study represents a larger, more rigorous evaluation of the potential influence of vitamin D levels on patient outcomes, specifically in mCRC. The findings were derived from data collected during the CALGB/SWOG 80405 trial, more commonly known as Alliance. This randomized, controlled, phase III study compared the efficacy and safety of three different biologic therapies—cetuximab, bevacizumab, and cetuximab plus bevacizumab—in combination with first-line chemotherapy in patients newly diagnosed with mCRC. Investigators could pick the chemotherapy backbone, which consisted of either FOLFOX or FOLFIRI. Overall survival was the primary endpoint of interest. Among the 2,334 patients included in the Alliance trial, 1,043 had plasma 25(OH)D measured prior to initiation of study treatment, all of whom completed self-administered questionnaires to evaluate their dietary and lifestyle behaviors. The median plasma 25(OH)D level in the overall population was 17.2 ng/mL. "For reference, vitamin D deficiency is defined as a level less than 20 ng/mL," Dr. Ng explained. Individuals in the cohort were split into quintiles based on their vitamin D levels. No significant differences were found between quintiles with regard to patients' history of prior adjuvant therapy, the chemotherapy backbone they received, or their assigned biologic therapy. However, black race, worse general physical condition, higher body mass index, lack of supplemental vitamin D intake, and lower physical activity, among other factors, were all tied to lower vitamin D levels. "It is often raised that high vitamin D levels may simply be a surrogate of more favorable disease or healthy lifestyle. One of the great benefits of working with the 80405 cohort was that we had very detailed information on patient and tumor characteristics, response and survival times, as well as multiple diet and lifestyle factors," Dr. Ng said. Using this detailed information, the investigators controlled for multiple variables that could potentially confound the results—routine variables such as age, sex, race, and body mass index, but also other relevant factors, including the season during which the patient's blood was drawn, the patients' geographic region of residence, physical activity, and *RAS* mutation status. After accounting for multiple variables, patients with the highest levels of vitamin D still showed a 35% improvement in the risk of mortality, as compared with individuals with the lowest. Progression-free survival was also still improved among patients with the highest vitamin D levels, as compared to patients with the lowest levels. Further data exploration revealed that the survival benefit associated with higher plasma vitamin D was consistently seen across all patient subgroups examined. Although these provocative data suggest that vitamin D confers possible protective effects in mCRC, it is too early to recommend vitamin D as a treatment adjunct. A prospective trial evaluating vitamin D therapy is needed to confirm the possible benefits.

Ng K, Meyerhardt JA, Wu K, et al. Circulating 25-hydroxyvitamin d levels and survival in patients with colorectal cancer. J Clin Oncol. 2008;26:2984-2991.

http://gicasym.org/prolonged-survival-mcrc-linked-high-pretreatment-vitamin-d

10. Vitamin D Linked to Lower Bowel Cancer Risk (Jan.16/15)

Researchers say they have demonstrated the mechanism that appears to give Vitamin D the power to protect some people from developing colorectal cancer – otherwise known as bowel cancer. A US study has found that vitamin D boosts the immune system's vigilance against tumour cells. "People with high levels of vitamin D in their bloodstream have a lower overall risk of developing colorectal cancer, says Dr Shuji Ogino from Harvard School of Public Health and Brigham and Women's Hospital, the study's senior author. "Laboratory research suggests that vitamin D boosts immune system function by activating T cells that recognise and attack cancer cells." To try to prove the link between vitamin D, the immune system and bowel cancer rates, Dr Ogino and colleagues drew on data from 942 people enrolled in two long-term health projects. Of these, 318 had colorectal cancer and 624 were free from the disease. All the participants had given blood samples during the 1990s before any of them had developed cancer. The investigators tested these samples for 25-hydroxyvitamin D, a substance produced in the liver from vitamin D. They found that patients with high amounts of this substance had a lower-than-average risk of developing colorectal tumours that were enriched with immune system cells. "This is the first study to show evidence of the effect of vitamin D on anti-cancer immune function in actual patients, and vindicates basic laboratory discoveries that vitamin D can interact with the immune system to raise the body's defences against cancer," says Dr Ogino. "In the future, we may be able to predict how increasing an individual's vitamin D intake and immune function can reduce his or her risk of colorectal cancer."

Ogino, Shuji, et al., Plasma 25-hydroxyvitamin D and colorectal cancer risk according to tumour immunity status Gut: doi./10.1136/gutjnl-2014-30885

http://www.webmd.boots.com/vitamins-and-minerals/news/20150116/vitamin-d-lower-bowel-cancer-risk

11. Study Finds Link Between Colon Cancer and Sedentary Habits (Jan.20/15)

According to this study, there is a serious risk of illness or even premature death from too much sitting on a regular basis. Importantly, it appears this tendency cannot be erased by regular physical exercise. Using data from 47 previous studies, the research team concluded that continued daily sitting was correlated to an increased risk of heart disease, diabetes, and cancer, including **colorectal cancer**. Importantly, even if the subjects being evaluated exercised on a regular basis, they still faced lower health outcomes if they sat for long periods of time. Nonetheless, participants who did little or no exercise had an even higher risk of developing these malignancies. "We found the association relatively consistent across all diseases. A pretty strong case can be made that sedentary behavior and sitting is probably linked with these diseases," maintained the study author. "When we're standing, certain muscles in our body are working very hard to keep us upright. Once we sit for a long time . . . our metabolism is not as functional, and the inactivity is associated with a lot of negative effects", he *added*. According to the authors, prolonged sitting included periods of 8 to 12 daily hours. Researchers noted that many daily sedentary activities such as driving, computer usage and watching TV, should not account for more than 4 to 5 hours of an individual's daily routine. "We found that exercise is very good, but it's what we do across our day. Exercise is just one hour in our day, if we're diligent; we need to do something when we're not otherwise exercising, like finding excuses to move around, take the stairs, or carry groceries rather than use the [shopping cart] at the supermarket". Concerning cancer incidence, the team found that **colon**, breast, uterine and ovarian cancers were the ones with a higher association to sedentary habits.

http://coloncancernewstoday.com/2015/01/21/study-finds-link-colon-cancer-sedentary-habits/

Biswas, Aviroop, et al.,Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med. 2015; 162(2):123-132. doi: 10.7326/M14-1651

12. Vegetarian Diet Linked to Reduced Risk of Colorectal Cancer (Mar.11/15)

Eating a vegetarian diet was associated with a lower risk of colorectal cancer compared with nonvegetarians. Colorectal cancer is the second leading cause of cancer death in the United States and Canada. Although great attention has been paid to screening, primary prevention through lowering risk factors remains an important objective. Dietary factors have been identified as a modifiable risk factor for colorectal cancer, including red meat which is linked to increased risk and food rich in dietary fiber which is linked to reduced risk, according to the study background. Among 77,659 study participants, study authors identified 380 cases of colon cancer and 110 cases of rectal cancer. Compared with non-vegetarians, vegetarians had a 22 percent lower risk for all colorectal cancers, 19 percent lower risk for colon cancer and 29 percent lower risk for rectal cancer. Compared with nonvegetarians, vegans had a 16 percent lower risk of colorectal cancer, 18 percent less for lacto-ovo (eat milk and eggs) vegetarians, 43 percent less in pescovegetarians (eat fish) and 8 percent less in semivegetarians, according to study results. "If such associations are causal, they may be important for primary prevention of colorectal cancers. … The evidence that vegetarian diets similar to those of our study participants may be associated with a reduced risk of colorectal cancer, along with prior evidence of the potential reduced risk of obesity, hypertension, diabetes and mortality, should be considered carefully in making dietary choices and in giving dietary guidance," the study concludes.

Michael J. Orlich, et al., Vegetarian Dietary Patterns and the Risk of Colorectal Cancers*. JAMA Internal Medicine*, 2015; DOI: 10.1001/jamainternmed.2015.59