The following colorectal cancer research updates extend from November 16th, 2017 to January 18th, 2018 inclusive and are intended for informational purposes only.

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**DRUGS / SYSTEMIC THERAPIES**


Regular aspirin use is linked to better survival among patients with colorectal cancer (CRC). Despite this fact, the timing of and the subgroup of CRC that would benefit the most from aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDS) in relation to survival remains unclear. A study examining 2,419 patients aged 18 to 74 years with invasive CRC were identified from population-based cancer registries in the United States, Canada, and Australia. Detailed epidemiologic questionnaires were given to all patients at enrollment and at 5-year follow-up. BRAF- and KRAS-mutation status, microsatellite instability, and CpG island methylator phenotype were also evaluated. Compared with non-users, post-diagnosis aspirin-only users had more favorable overall survival and CRC-specific survival. Overall survival and any NSAID use after diagnosis differed significantly by KRAS-mutation status. The use of any NSAID post-diagnosis was linked to improved overall survival only among participants with KRAS wild-type tumours but not among those with KRAS-mutant tumours. Thus, it was determined that regular use of NSAIDS after CRC diagnosis was significantly associated with better survival in individuals with KRAS wild-type tumours.  

https://clinicaltrials.gov/ct2/show/NCT02876224  


2. Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Oct 24/17)

In this non-randomized phase I trial, the safety, tolerability and pharmacokinetics of cobimetinib in combination with atezolizumab and bevacizumab among patients with metastatic colorectal cancer will be evaluated. Cobimetinib is an oral MEK kinase inhibitor which targets cell signalling involved in cell division and growth. Atezolizumab is an anti-PD-L1 antibody which targets the PD-L1 and PD-1 receptor to prevent suppression of the immune system against cancer cells. Bevacizumab is an antibody which interferes with the process of new blood vessel formation (angiogenesis) in cancer cells. All patients will have received at least 1 previous therapy with fluoropyrimidine and oxaliplatin or irinotecan. Cobimetinib will be administered orally while atezolizumab and bevacizumab will be given intravenously. In the first stage of the trial, patients will receive the drug combination until the disease progresses, unacceptable toxicity or withdrawal from the trial. In the second stage of the trial, the patients will be divided into two groups. The first group will receive the drug combination and undergo repeated tumour biopsy. The second group will receive atezolizumab and bevacizumab plus the cobimetinib dose that was given in stage I. For more information regarding the study, including inclusion and exclusion criteria, locations and contact information, visit: https://clinicaltrials.gov/ct2/show/NCT02876224. The study is open and recruiting patients as of Oct 24, 2017 in the U.S., U.K., and Spain.  


**SURGICAL THERAPIES**

3. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Nov.10/17)

The HAIP program is a first-in-Canada for individuals where colon or rectal cancer (colorectal cancer) has spread to the liver and cannot be removed with surgery. The program involves a coordinated, multidisciplinary team approach to care, with close collaboration across surgical oncology, medical oncology (chemotherapy), interventional radiology, nuclear medicine, and oncology nursing. The Hepatic Artery Infusion Pump (HAIP) is a small, disc-shaped device that is surgically implanted just below the skin of the patient, and is connected via a catheter to the hepatic (main) artery of the liver. About 95 percent of the chemotherapy that is directed through this pump stays in the liver, sparing the rest of the body from side effects. Patients receive HAIP-directed chemotherapy in addition to regular intravenous (IV) chemotherapy (systemic chemotherapy), to reduce the number and size of tumours. Drs. Paul Karanicolas and Yooj Ko are the program leads and happy to see patients eligible for the therapy.
Presently at Sunnybrook Odette Cancer Centre, HAIP is being used in patients with colorectal cancer that has spread to the liver that cannot be removed surgically, and has not spread to anywhere else in the body. Patients who have few (1-5) and very small tumors in the lungs may be considered if the lung disease is deemed treatable prior to HAIP. If you believe you may benefit from this therapy and/or would like to learn more about the clinical trial, your medical oncologist or surgeon may fax a referral to 416-480-6179. For more information on the HAIP clinical trial, please click on the link provided below.

http://sunnybrook.ca/content/?page=coloctal-colon-bowel-haip-chemotherapy

4. Living donor liver transplantation for unresectable colorectal cancer liver metastases (May 2017)

Approximately half of all colorectal cancer (CRC) patients develop metastases, commonly to the liver and lung. Surgical removal of liver metastases (LM) is the only treatment option, though only 20-40% of patients are candidates for surgical therapy. Surgical therapy adds a significant survival benefit, with a 5-year survival after liver resection for LM of 40-50%, compared to 10-20% 5-year survival for chemotherapy alone. Liver transplantation (LT) would remove all evident disease in cases where the colorectal metastases are isolated to the liver but considered unresectable.

Image Source: https://www.slideshare.net/AhmedAdel65/preoperative

While CRC LM are considered a contraindication for LT at most cancer centers, a single center in Oslo, Norway demonstrated a 5-year survival of 56%. A clinical trial sponsored by the University Health network in Toronto will offer live donor liver transplantation (LDLT) to select patients with unresectable metastases limited to the liver and are non-progressing on standard chemotherapy. Patients will be screened for liver transplant suitability and must also have a healthy living donor come forward for evaluation. Patients who undergo LDLT will be followed for survival, disease-free survival and quality of life for 5 years and compared to a control group who discontinue the study before transplantation due to reasons other than cancer progression.

https://clinicaltrials.gov/ct2/show/NCT02864485

5. Perioperative hepatic arterial infusion pump chemotherapy is associated with longer survival after resection of colorectal liver metastases: A propensity score analysis (Jan. 18/18)

The hepatic arterial infusion (HAI) therapy is a method for treating liver metastases in patients with colorectal cancer (CRC). A pump is implanted in the liver which delivers chemotherapy directly to the local tumours. A recent study aimed to investigate whether perioperative hepatic arterial infusion pump chemotherapy was associated with overall survival (OS) among patients who had a complete resection of colorectal liver metastases. Perioperative strategies aim to provide better conditions for patients before, during and after operation. Patients included in the study had undergone a complete resection of colorectal liver metastases between 1992 and 2012. All patients who had received HAI also received perioperative systemic chemotherapy. A total of 2,368 patients underwent a complete resection of colorectal liver metastases with a median follow-up of 55 months. The median OS for patients with HAI was 67 months vs. 44 months without HAI, despite the occurrence of more advanced disease in the HAI group. OS at 10 years was 38.0% vs. 23.8% without HAI. For patients who received modern systemic chemotherapy, the median OS was 67 months with HAI and 47 months without. A significant difference in median OS was observed for patients with node-negative CRC (cancer that has not spread to the lymph nodes) - 129 months with HAI vs. 51 months without. The study findings demonstrate that patients who received HAI had a median OS of approximately 2 years longer than patients without HAI. The association remained strong independent of the use of modern systemic chemotherapy. Patients with node-negative primary tumours seemed to benefit the most from HAI.


6. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Jan.18/18)

Magnetic resonance-guided focused ultrasound (MRg-FU) is a non–invasive, outpatient modality being investigated for the thermal treatment of cancer. In MRg-FU, a specially designed transducer is used to
focus a beam of low intensity ultrasound energy into a small volume at a specific target site in the body. MR is used to identify and delineate the tumour, focus the ultrasound beam on the target and provide real-time thermal mapping to ensure accurate heating of the designated target with minimal effect to the adjacent healthy tissue. The focused ultrasound beam produces therapeutic hyperthermia (40-42°C) in the target field causing protein denaturation and cell damage. Currently, there is no prospective clinical data reported on the use of MRg-FU in the setting of recurrent rectal cancer. Recurrent rectal cancer is a vexing clinical problem. Current retreatment protocols have limited efficacy. The addition of hyperthermia to radiation and chemotherapy may enhance the therapeutic response. With recent advances in technology, the investigators hypothesize that MRg-FU is technically feasible and can be safely used in combination with concurrent re-irradiation and chemotherapy for the treatment of recurrent rectal cancer without increased side-effects. The study is being offered at the Odette Cancer Centre. Here is the link to the study protocol:

https://clinicaltrials.gov/ct2/show/NCT02528175?term=magnetic+resonance+guided+focused+ultrasound&recr=Open&rank=1

SCREENING

7. Fatty liver index useful for predicting precancerous colon polyps (Dec 11/17)

The fatty liver index is a non-invasive method used to predict non-alcoholic fatty liver disease. New research has demonstrated that patients with a high fatty liver index showed a higher risk for colorectal adenomas, suggesting that the index may be useful for predicting the presence of adenomas in the gut. The study aimed to develop a simple indicator that can help screen individuals who have a higher risk of colorectal adenoma, and thus more likely to need a colonoscopy. The researchers calculated the fatty liver index by using 4 variables: BMI, waist circumference, triglycerides (TGs) and gamma-glutamyl transferase (GGT). GGT is an enzyme that is found in organs throughout the body but with the highest concentrations in the liver. It becomes elevated in the blood in the occurrence of diseases that cause damage to the liver or bile ducts. The researchers reviewed data on 2,976 patients older than 40 years who underwent abdominal ultrasonography and colonoscopy as part of their routine check-ups over a 6-year period. 31.3% had a colorectal adenoma – most often in the upper colon – 23.2% had metabolic syndrome and 50.8% had a fatty liver. Patients with BMI greater than 25 kg/m², those with fatty liver, and those older than 60 years showed a higher risk for colorectal adenoma. A fatty liver index greater than 30 was associated with an increased risk for colorectal adenoma, whereby patients with a score greater than 30 showed significantly more colorectal adenomas and more advanced colorectal adenomas compared with patients who had a score lower than 30. In addition, the researchers found an increasing prevalence of colorectal adenoma with each increasing quartile of fatty liver index. The study is the first of its kind to examine the relationship between the fatty liver index and the prevalence of colorectal adenomas, suggesting that high fatty liver index may be a promising tool to better predict the presence of colorectal adenoma.

https://www.healio.com/gastroenterology/liver-biliary-disorders/news/online/%7b25848500-1c5-4676-9491-f0af32697a0%7d/fatty-liver-index-useful-for-predicting-precancerous-colon-polyps


Molecular diagnostic testing has become an integral part of the evaluation of patients with metastatic colorectal cancer (CRC). In-depth mutational testing, including next-generation sequencing has been helpful in identifying mutations that have unclear clinical or prognostic implications. Such mutations include the BRAF mutations which occur outside of a region called codon 600 (non-V600 BRAF mutations). A study published in the Journal of Clinical Oncology aimed to better identify the clinical, pathologic, and survival implications of non-V600 BRAF mutations in patients with metastatic CRC. Of a total of 9,643 patients with metastatic CRC, 208 (2.2%) were identified with non-V600 BRAF mutations, accounting for 22% of all BRAF mutations identified. Cancers with non-V600 BRAF mutations compared to cancers with V600 BRAF mutations were found in patients who were younger (58 vs. 68 years, respectively), predominantly male (65% vs. 46%, respectively), among patients with fewer advanced tumours (13% vs. 64%, respectively) or right-sided primary tumours (36% vs. 81%, respectively). It was found that median overall survival among patients with non-V600 BRAF-mutant metastatic CRC was significantly longer compared to patients with both V600 BRAF-mutant metastatic CRC and wild-type BRAF metastatic CRC (60.7 vs. 11.4 vs. 43.0 months, respectively). Thus, molecular diagnostic testing has enabled patients with non-V600 BRAF molecular subtype CRC to be better defined, identifying them as a clinically distinct subgroup of CRC with an excellent prognosis.

http://ascopubs.org/doi/abs/10.1200/JCO.2016.71.4394?term=magnetic+resonance+guided+focused+ultrasound&recr=Open&rank=1


9. Prep-free capsule for colorectal cancer screening receives CE mark (Jan.15/18)

A capsule known as C-Scan has received a CE mark from the European Commission for its use as a preparation-free colorectal cancer (CRC) screening tool. The capsule does not require any bowel preparation, fasting or sedation, which
its manufacturer, Check-Cap, suggests could increase the number of adults who undergo screening for CRC. The C-Scan capsule is ingested and then emits ultra-low dose X-rays which are combined with a wireless tracking system. Together, these generate structural information of the colon wall. Physicians are then able to identify pre-cancerous polyps and other abnormalities by creating 2D and 3D maps of the colon. Despite being the third most common cancer diagnosed in men, as well as women, and causing the second most deaths, CRC screening rates remain low. Not requiring any prep for the test is a key validation of C-Scan and its potential as a convenient and comfortable option for identifying polyps in the colon.

https://www.healio.com/gastroenterology/therapeutics-diagnostics/news/online/%7Bde63ae46-5aa0-4853-a01b-51c02f7473d6%7D/prep-free-capule-for-colorectal-cancer-screening-receives-ce-mark

10. New biomarkers for colorectal cancer (Jan 11/18)

Early detection and classification of disease is important for colorectal cancer (CRC), when the disease is more manageable and more likely to respond to treatment. Biomarkers are measurable biological indicators for a disease, such as changes in the amounts of proteins that occur in the presence of certain illnesses. Such biomarkers are powerful tools which can help to diagnose a condition, identify the stage of the disease, and determine a patient’s risk of their disease coming back. They are powerful tools in choosing a personalized treatment plan that minimizes unnecessary treatments and side effects.

In a study conducted by a research team at the University of Luxembourg, a new promising biomarker for CRC was discovered which might allow oncologists to classify patients into ‘high’ and ‘low’ risk groups. By classifying patients in this way, it may help oncologists to better choose the adequate treatment regimens for a given patient. Using an analysis of publicly available gene expression data, the team identified the protein family named ‘Myosin’ - in particular the protein ‘MYO5B’ - as a potential prognostic marker in CRC. Members of this family are known to play a role in cellular trafficking and have been linked to several types of cancer. The team’s analysis demonstrates that the concentration of MYO5B decreases as the disease progresses, and that CRC patients with low expression of MYO5B had significantly lower chances of disease and metastasis-free survival. The study was able to identify MYO5B as a promising biomarker in CRC, particularly in early stages (stage I and II) which may be able to help indicate patients with stage II CRC for adjuvant chemotherapy.

https://www.sciencedaily.com/releases/2018/01/180111101419.htm

11. Candirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Nov 2/17)

15% of cancer survivors are estimated to experience mood problems even one year post-treatment. The CanDirect research study aims to support cancer survivors with mood problems by providing study participants with a self-care toolkit designed to help users better manage their mood and anxiety as well as phone coaching for a maximum duration of 6 months. Participation is open to eligible adult survivors residing in Quebec and Ontario who have completed cancer treatment for a non-metastatic cancer and who are experiencing depressive symptoms. For additional information, please click on the following link:

https://clinicaltrials.gov/show/NCT02890816

12. Colon cancer often misdiagnosed in young patients (Dec 15/18)

The US non-profit, Colorectal Cancer Alliance, surveyed 1,535 young-onset colorectal cancer (CRC) survivors over 1 month to better understand the challenges faced by young people with CRC. They received responses from 26 countries that demonstrated the global issue of CRC affecting young individuals under the age of 50, demanding more research and deliberate action. The survey results demonstrated that young CRC survivors faced many barriers to screening due to their age, and that most were initially misdiagnosed and then diagnosed with late-stage disease. Indeed, it has been observed that CRC rates in individuals younger than 50 is increasing. 82% of respondents were initially misdiagnosed, and 73% presented with late-stage disease. 67% saw at least two doctors before receiving a cancer diagnosis, 62% had no family history of CRC, and 15% said an ER visit led to a colonoscopy and their CRC diagnosis. It was reported that there were many challenges related to symptoms being taken seriously by doctors when seeking a diagnosis, finding age-appropriate support, and sexual function during and after treatment. The survey puts the spotlight on the experience of young-onset CRC patients and survivors who are currently experiencing suboptimal care due to a misunderstanding of their disease. Further research and data are very much in need in order to properly address this growing issue which is expected to affect young people in more than 1 in 10 colon cancer diagnoses and 1 in 4 rectal cancer diagnoses by 2030.
13. Young-onset colon cancers often genetic despite no family history (Dec 14/17)

A recent study has found that one in five patients who are diagnosed with colorectal cancer (CRC) younger than 50 years of age showed an inherited genetic predisposition to the disease, despite more than half of these patients lacking a clinical or family history that would typically indicate the need for genetic testing. Normally, when someone is diagnosed with cancer and there is no family history of the disease, doctors will think that the likelihood of an inherited factor is small. The study findings, however, demonstrated that this is not the case among young CRC patients. Even in the absence of a family history of cancer, the prevalence of inherited factors is so high that it makes sense to test everyone. In the study, of the 85 total patients who showed germline mutations associated with a hereditary cancer syndrome, only 51% reported a CRC diagnosis in a first-degree relative. As such, the study findings highlight the limitations of the currently-used algorithms for identifying individuals who should undergo genetic testing. The researchers suggest that the people that were being tested for genetic predisposing factors in the past were probably just tip of the iceberg, and that many more people who do not necessary meet the strict criteria for genetic testing may still be at high risk for CRC. Indeed, the strict criteria that insurance companies have in place to decide who qualifies for genetic testing often require multiple relatives over two generations who were diagnosed with CRC. In the case of young people, these criteria will undoubtedly lead to missed cases. New multigene panel testing technology which is used for genetic screening is highly effective though far costlier and often not covered by insurers, which would mean a $300-$2,000 out-of-pocket expense. Insurance companies are not covering the new technology because they still consider them experimental. Further research and data to support the new screening methods are needed in order to demonstrate their superiority and the real effects they have on morbidity and mortality, and to make these methods more accessible and affordable for those that are really in need.

14. Young adult colorectal cancer clinic available at Sunnybrook (Jan.18/18)

A recent study led by University of Toronto doctors has observed a rise in colorectal cancer rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing colorectal cancer rates in young people come after decades of declining rates in people over 50, which have occurred most likely due to increased use of colorectal cancer screening (through population-based screening programs) which can identify and remove precancerous polyps. Patients diagnosed under the age of 50 have a unique set of needs, challenges and worries. They are unlike those diagnosed over the age of 50. Dr. Shady Ashamalla (colorectal cancer surgical oncologist), and his team at the Sunnybrook Health Sciences Centre understand the needs of this patient population.

Dr. Ashamalla belongs to a multidisciplinary team of experts in the Young Adult Colorectal Cancer Clinic who will work with young colorectal cancer patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Their needs and concerns will be addressed as they relate to:

- Fertility concerns and issues
- Young children at home
- Dating/intimacy issues
- Challenges at work
- Concerns about hereditary cancer
- Relationships with family and friends
- Psychological stress due to any or all of the above

The team of experts consist of:

- Oncologists (medical, surgical, radiation)
- Social workers
- Psychologists
Nutrition/ Healthy Lifestyle

15. Coffee may improve survival in colon cancer (Dec 13/17)

Two large prospective cohort studies found that patients with colorectal cancer (CRC) who drank either caffeinated or decaffeinated coffee showed a lower risk for CRC-specific death and overall death. The benefits appeared to be the strongest among patients who drank at least two cups per day both before and after their diagnosis. 1,599 patients who were diagnosed with stage I or II CRC during follow-up in the Nurses’ Health Study (1984-2012) and the Health Professionals Follow-up Study (1986-2012) reported their coffee consumption before their CRC diagnosis and between 6 months and 4 years after diagnosis. After adjusting for demographic, lifestyle and other factors, analysis showed that patients who drank four or more cups of coffee per day were 52% less likely to die of CRC and 30% less likely to die of any cause compared to those who did not drink coffee. The researchers also observed these benefits among those who drank at least two cups per day, and those who maintained this level of consumption before and after CRC diagnosis showed significantly lower odds of CRC-specific death and all-cause mortality compared to patients who consistently drank less that two cups per day before and after diagnosis.


Existing research has pointed towards coffee’s protective anti-inflammatory and insulin-sensitizing properties and the anti-cancer compounds it contains including polyphenols, diterpenes, melanoidins, and antioxidants as being responsible for the beverage’s beneficial effects. These properties may improve CRC survival by equilibrating systemic disturbances or by promoting an anti-carcinogenic microenvironment that is inhibitory to tumour progression. The researchers also found that the beneficial association of post-diagnostic coffee intake with survival appeared to be strongest among stage III patients compared to stage I or II patients. In conclusion, further research is necessary to confirm the research findings and to better understand the underlying mechanism that drives coffee’s benefits to CRC survival.

https://www.healio.com/gastroenterology/oncology/news/online/%7b04bb77f-eb11-4fd1-a00d-31eab89f94b%7d/coffee-may-improve-survival-in-colon-cancer?nc=1

16. High fiber intake tied to improved colon cancer survival (Nov 3/17)

According to two prospective studies, high fiber intake is linked to improved survival among patients diagnosed with colorectal cancer (CRC) even among those who increase their fiber intake after their diagnosis. A recent study in JAMA Oncology found that each 5g/day increase in fiber intake was linked to a 22% reduction in cancer-specific mortality and a 16% reduction in overall mortality, with the strongest effect seen with whole-grain foods. Curiously, no association was found with daily fruit fiber intake. The study found that the maximum benefit was seen among patients who consumed about 24g/day of fiber. The fact that fiber or related substances may be protective is important because it sheds light on the processes by which colon cancer may spread, providing the oncology community with targets for new disease interventions. Researchers suggest that the protective effect of fiber could manifest, for example, on insulin pathways, and this may be a potential target for treatment in the future. Additionally, it may be possible that fiber may form a substrate for bacteria in the gut to produce anti-inflammatory compounds and cancer-protective metabolites.

In the studies, the research team found that mortality was lower for patients who increased their fiber intake after diagnosis: each 5g increase per day was linked with an 18% reduction in CRC-specific mortality and 14% reduction in all-cause mortality. These findings support the nutritional recommendations of maintaining sufficient fiber intake among CRC survivors.
17. With these special bacteria, a broccoli a day can keep the cancer doctor away (Jan 10/18)

Researchers from Singapore have engineered bacteria that target colorectal cancer cells and convert a substance found in certain vegetables into an anticancer agent. This cancer-targeting system is based on an engineered form of *E. coli Nissle*, a harmless type of bacteria that colonizes the gut. The team was able to engineer the bacteria into a probiotic that attached itself to the surface of colorectal cancer cells and secreted an enzyme to convert a dietary substance found in cruciferous vegetables such as kale or broccoli into a powerful anticancer agent. Then, any cancer cells nearby would take up this anticancer agent and be killed, while normal cells remained unaffected by the toxin. It was found that the mixture of engineered probiotics with a broccoli extract or water containing the dietary substance killed more than 95% of colorectal cancer cells in a petri dish. They also found that the mixture was specific to colon cancer cells, having no effect on cells from other types of cancer such as stomach or breast cancer.


The researchers have envisioned these probiotics to be used in two ways: first, as prevention, and second, to clean up the cancer cells remaining after surgical removal of tumours. They may also be able to be used as a dietary supplement along with their broccoli to prevent colorectal cancer or to reduce recurrence after cancer surgery.


18. A Phase III study on the impact of a physical activity program on disease-free survival in patients with high risk stage II or stage III colon cancer: a randomized controlled trial (CHALLENGE) (Nov.15/17)

The purpose of this study is to compare the disease-free survival of patients involved in a physical activity program (designed to increase physical activity participation) who also receive general health education materials (about diet and physical activity) to patients who receive the general health education materials only. This study is being done because, as of yet, there is no conclusive evidence that physical activity will decrease the likelihood of colon cancer recurrence. This study will also obtain important information about the impact of physical activity on patients’ physical functioning, body composition, quality of life, fatigue, mood, cytokines and the insulin pathway, and their influence on prognosis, as well as cost-effectiveness.

**Eligibility:** Medically fit colon cancer patients (high risk stage II and stage III) who have completed adjuvant chemotherapy within the past 60-180 days. Current physical activity levels must not meet the recommended guidelines (≥150 minutes of moderate-to-vigorous or ≥75 minutes of vigorous exercise/week). Following registration, and prior to randomization, patients must successfully complete at least two stages of a submaximal exercise test to ensure they are able to safely exercise at a moderate to vigorous intensity.

**Participation:** Limited to invited centres. For more information, visit the link below: https://scooby.ctg.queensu.ca/tum_bank/tum.php?g_cmd=trial_info&g_trial_cd=CO21

19. High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (Jan. 18/18)

A large body of evidence suggests that high blood levels of Vitamin D decreases the risk of developing cancer, especially colorectal cancer. Very little is known about what role optimum blood levels of Vitamin D can play in the treatment of cancer. The purpose of this clinical trial is to study the therapeutic effect and the safety of high-dose vitamin D supplementation in stage 4 (metastatic) colorectal cancer patients. Who is eligible to participate? Anyone who has a stage four colorectal cancer diagnosis, living in Ontario or British Columbia, may be eligible to participate. All participants need to have access to a Lifelabs facility for blood and urine collections. What is involved? This 40-month study involves regular lab tests and follow up phone calls. Participation is fully voluntary, and participants may withdraw at any time. Participants will be randomly assigned to either a high-dose vitamin D treatment group or a control group. Participants in both groups may continue all other cancer treatments including chemotherapy. Treatment group: Participants in the treatment group receive daily oral high dose Vitamin D supplementation provided free of charge through the clinical study. They also receive daily calcium supplementation 1000mg daily as per guidelines, provided free through the clinical study. Participants will have monthly blood and urine tests for monitoring purposes. All laboratory tests are free of charge. Participants also need to be available for a 15-minute phone consultation with a study coordinator every 2 months. Control group: Participants in the control group will continue their usual amount of Vitamin D and/or calcium if they wish to do so. No supplements will be provided through the study. Participants will be asked to provide a small blood and urine sample at the beginning of the study, every 8 months and at the end of the
study. These blood and urine tests will be free of charge. Contact person: If you have any further questions regarding this study or you are interested in participating in this study, please contact us: **British Columbia**: 604-734-7125, toll free 1-888-734-7125 or [vitDstudy@inspirehealth.ca](mailto:vitDstudy@inspirehealth.ca) **Ontario**: 613-792-1222, toll free 1-855-546-1244 or [research@oicc.ca](mailto:research@oicc.ca)