The following colorectal cancer research updates extend from January 18th, 2018 to February 15th, 2018 inclusive and are intended for informational purposes only.

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1. **ASCO GI 2018: Adding Ipilimumab to Nivolumab enhances benefit in DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer (Jan 20/18)**

The combination of ipilimumab with nivolumab may be a promising new treatment option for patients with previously treated DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer (mCRC). In the CheckMate-142 study, the largest report of an immunotherapy regimen in patients with DNA mismatch repair-deficient/microsatellite instability-high mCRC, nivolumab provided lasting responses and disease control in pre-treated patients. Ipilimumab is a monoclonal antibody which targets normal and cancerous T immune cells and controls their activation and proliferation. Nivolumab is a targeted antibody therapy which blocks the interaction of the programmed cell death receptor (PD-1) with its ligands. This inhibits T cell proliferation and removes inhibition of the body’s immune response (including the anti-tumour response), resulting in decreased tumour growth. The nivolumab + ipilimumab combination in CheckMate-142 reported efficacy and safety in the subset of patients with DNA mismatch repair-deficient/microsatellite instability-high mCRC, with a preliminary response rate of 55% and a manageable safety profile. In preclinical and clinical settings, the drug combination was found to have enhanced activity over nivolumab monotherapy alone. In the study, of the 119 patients treated with the drug combination, tumour burden was reduced in 77% of patients. The 1-year progression-free and overall survival rates were 71% and 85%, respectively. Grade 3–4 treatment-related adverse events occurred in 32% of patients, with no treatment-related deaths reported. Statistically significant and clinically meaningful improvements were observed in patient-reported outcomes, including functioning, symptoms and quality of life. In this study, nivolumab + ipilimumab provided improved clinical benefit compared to nivolumab alone with a manageable safety profile and offers a potential new treatment option among previously treated patients with DNA mismatch repair-deficient/microsatellite instability-high mCRC. Future directions aim to understand the underlying mechanisms of the drug combination in this population and to seek biomarkers, with the goal of increasing the treatable population.

http://www.practiceupdate.com/c/63338/32/1?elsca1=emc_conf&ASCOGI2018Post1&elsca2=emai&elsca3=practiceupdate_onc&elsca4=201805_ASCOGI2018Post1&elsca5=conference&id=NTU2MjE4MDA1NzQ5&lsid=10332481


2. **No survival benefit with Bevacizumab maintenance in CRC (Jan 28/18)**

A recent study found that Bevacizumab (Avastin) therapy alone did not improve survival when used as maintenance treatment after initial chemotherapy in metastatic colorectal cancer (mCRC). The phase III PRODIGE 9 trial demonstrated that in 491 patients randomly assigned to bevacizumab maintenance or observation (i.e. no treatment) after frontline treatment with FOLFIRI (leucovorin, fluorouracil, and irinotecan) plus bevacizumab chemotherapy, the median overall survival (OS) was 21.7 months compared to 22.0 months, respectively. The median progression-free survival (PFS) was 9.2 months in the maintenance arm and 8.9 months in the observation arm. The study revealed that bevacizumab monotherapy maintenance did not improve tumour control duration (TCD) or the duration of chemotherapy-free intervals after 12 cycles of FOLFIRI plus bevacizumab. The study results stress the importance of further research to better define subgroups of patients who should receive maintenance chemotherapy after initial chemotherapy or could undergo a chemotherapy-free interval, addressing an important quality of life issue that could spare patients the need to undergo more chemotherapy. Researchers emphasize, however, that the results of the PRODIGE 9 study are limited to the fact that bevacizumab was used alone as maintenance therapy; the preferred maintenance therapy is bevacizumab plus fluorouracil, a combination shown in a previous trial to offer a better PFS outcome.

Whether maintenance chemotherapy offers some PFS benefit among patients with advanced disease remains unclear. Recently, there has been a trend towards cycles of maintenance therapy of shorter duration, normally lasting 6 months, in response to patient-requested treatment breaks to address important quality of life concerns. Among patients with mCRC and low disease burden, clinicians may opt for a treatment break after initial FOLFIRI-bevacizumab therapy with close observation during a chemotherapy-free interval, with the option to use re-induction chemotherapy.


3. **ASCO GI 2018: Unselected patients with right-sided metastatic colorectal tumours experience worse disease-free survival than those with left-sided tumours (Jan 19/18)**

Results from the Short Course Oncology Therapy (SCOT) study were revealed at the 2018 Gastrointestinal Cancer Symposium demonstrating that patients with right-sided colorectal tumours who develop metastatic disease experience a worse prognosis than those with left-sided tumours. The researchers divided the study population into
left- and right-sided tumours to determine whether sidedness impacted 3-year disease-free survival. A total of 6,088 patients with stage III/high-risk stage II cancers of the colon or rectum were randomly selected from 244 centres across the UK, Europe and Australia between 2008 and 2013. After a minimum of 3 years of follow-up, information on the sidedness of 3,219 patients’ cancers was available. Of the 1,207 patients with right-sided tumours, the median age was 66 years, 53% were male, 41% had stage IV disease and 17% had stage II disease. Of the 2,012 patients with left-sided tumours, the median age was 64 years, 66% were male, 24% had stage IV disease, and 21% had stage II disease. Patients with right-sided tumours experienced significantly worse disease-free survival - 73% of patients achieved 3-year disease-free survival - compared to 80% of patients with left-sided tumours. It was found that sidedness of tumours did not impact the effect of chemotherapy duration on 3-year disease-free survival. 3 months of oxaliplatin-containing adjuvant chemotherapy proved to have the same outcomes as 6 months in patients with stage III and high-risk stage II colorectal cancer. Researchers suggest that the worse disease-free survival among patients with right-sided metastatic colorectal tumours is influenced primarily by increased disease recurrence rather than other factors that influence a patient’s overall survival. Indeed, the SCOT study demonstrated that patients with right-sided tumours experience greater recurrence after adjuvant chemotherapy compared to patients with left-sided tumours. Future research will be directed at discovering the reason for this higher recurrence rate among patients with right-sided tumours, and to determine whether a different treatment approach is required for this specific subgroup of patients.

4. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Feb.1/18)

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 is a 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=ileoecol-bowel-haip-chemotherapy

5. Living donor liver transplantation for unresectable colorectal cancer liver metastases (Feb.1/18)

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.
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

6. 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 than 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.


RADIATION THERAPIES/INTERVENTIONAL RADIOLOGY

7. 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
8. ASCO GI 2018: Liquid biopsy that identifies circulating tumour cells is promising in detection of early-stage colorectal cancer (Jan 22/18)

Findings from a large-scale evaluation of a test which identifies circulating tumour cells (CTCs) in the bloodstream report an accuracy rate of 85-88% in detecting colorectal cancer (CRC) at an early stage. These findings were presented at the 2018 Gastrointestinal Cancer Symposium. While most studies of CTCs have been able to detect the presence of late-stage CRC, the present test is one of the first to demonstrate how CTCs can be useful in detecting early-stage disease.

620 participants over 20 years of age who were scheduled for a routine colonoscopy or had been diagnosed with confirmed CRC were enrolled in the study. Colonoscopy and biopsy confirmed the presence of pre-cancerous polyps or early- to late- stage CRC in 438 of the participants. The remaining individuals showed no signs of precancerous growths or CRC. 2ml blood samples were drawn from all 620 participants and were processed using the CMx platform, a test which is able to capture rare CTCs such as those in early-stage cancer. These samples were then compared with colonoscopy in a blinded analysis. The CMx platform was able to detect very small numbers of CTCs, even at the level of one CTC per billion blood cells which is the concentration found in most polyps. Specificity, the ability of the test to correctly identify individuals without the disease, was 97.3%. Sensitivity, the ability of the test to correctly identify individuals with the disease, ranged from 77% detection of CTCs in precancerous lesions, to 87% for stage I-IV cancers. Accuracy was high and ranged from 84-88% between precancerous and cancerous samples.

Accuracy was greater than that of the fecal occult blood testing. According to survey results among patients who are reluctant to undergo colonoscopy, more than 80% would consider a blood test over stool-based tests. Furthermore, the potential cost of this test is less than $100 making it affordable, which is currently the most common barrier to screening.

Researchers note than colonoscopy would still be the gold standard diagnostic test and would be needed for tumour or polyp removal if someone tests positive for CTCs in the blood test. Currently, many screening options are uncomfortable and inconvenient for patients, which stops many people from getting screened. Researchers suggest a blood test may help to boost screening rates and CRC detection at earlier stages when it is more treatable and curable.

http://www.practiceupdate.com/c/63340/32/1?elsca1=emc_conf_ASCOGI2018Post1&elsca2=email&elsca3=practiceupdate Onc&elsca4=201805_ASGCI2018Post1&elsca5=conference&nid=NTU2MjE4MDA1NzQS1&lid=10332481

9. The sugar-attaching enzyme that defines colon cancer (Jan 26/18)

Danish researchers have identified an enzyme that is absent in healthy colon tissue but abundant in colon cancer cells. The enzyme appears to stimulate the appearance of normal colon tissue into cancer by attaching sugar molecules, or glycans, to particular proteins in the cell membrane. The researchers pointed to enzymes known as GalNAc transferases (GalNAc-Ts), in particular GalNAc-T6, to be responsible for initiating the cascade of structural changes in the intestinal lining associated with cancer. When a cancer cell line was grown in the presence of GalNAc-T6, tubular structures with the formation of what appears to be more colon cancer tissue was observed. When the enzyme was removed from the cell line, the tissue formation suddenly changed to look more like the typical healthy intestinal lining. Using mass spectrometry, the team was able to characterize the proteins that GalNAc-T6 acted on in the intestinal cells. The data indicate that the enzyme acts on a subset of proteins that could be involved in how cells adhere to one another. The glycan or sugar modifications changed the patterns in which cells stuck together, causing cells to develop as something more similar to a tumour than healthy tissue. The next step for the researchers is to understand why the addition of sugar molecules to the specific protein sites that are modified by GalNAc-T6 causes colon cells to develop abnormally. In normal cell functioning, sugar modifications can affect protein function in many ways, preventing two proteins from binding to one another or inhibiting the division of large protein units into smaller units. Researchers hope that a more in-depth understanding of the process of sugar modification among cancer cells will lead to better early diagnostic tools and treatment options.

https://www.sciencedaily.com/releases/2018/01/180126110030.htm


10. Detecting and localizing eight cancer types with one multianalyte blood test (Jan 29/18)

Researchers from the Johns Hopkins Kimmel Cancer Center have developed a single blood test that screens for eight common cancer types and also helps to identify the location of the cancer. The test is called cancerSEEK and detects circulating DNA in the blood to identify gene mutations and the presence of cancer. Circulating tumour DNA mutations
can be highly specific markers for cancer. The researchers took advantage of this specificity by developing a small yet robust mutation panel that aimed to minimize false-positive results and keep the screening test affordable. In this study, the test resulted in greater than 99% specificity for cancer. Very high specificity was a key demand for the test as false-positive results can cause patients to undergo unnecessary invasive follow-up tests and procedures to confirm the presence of cancer. The test was administered to 1,005 patients with nonmetastatic stage I-III cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung, or breast. CancerSEEK is non-invasive and could be administered by primary care providers at the time of routine blood work. For a test to be used routinely for cancer screening, the developers felt that it must have a cost that is in line with or less than other currently available screening tests for single cancers, such as colonoscopy. They envision the cancerSEEK test to eventually cost less than $500. Larger scale studies of the test are currently in progress.

http://www.ascopost.com/News/58480

PSYCHOSOCIAL

11. Candirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Feb.1/18)

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/NCT02890615

OTHER

12. 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
- Geneticists
- Nurse navigator
Remodeling and Cholesterol Availability Regulate Intestinal Stemness and Tumorigenesis
Bo Wang, Xin Rong, Elisa N.D. Palladino, Jiafang Wang, Alan M. Fogelman, Martín G. Martín, Waddah A. Alrefai, David A. Ford, Peter Tontonoz.

A study from the University of California discovered that when cholesterol levels were amped up in mice, intestinal stem cells were encouraged to divide more rapidly and enabled tumours to form 100 times faster. The research has identified a molecular pathway that could serve as a new drug target for colon cancer treatment. While previous evidence has supported the link between dietary cholesterol and colon cancer risk, the underlying mechanism has never been well understood. In the study, mice were administered a high-cholesterol diet to increase the cholesterol in the intestinal stem cells. Other mice received an altered gene that regulates phospholipids, the principal fats in cellular membranes, which stimulated the cells that produce more cholesterol on their own. In both mouse groups, the ability of intestinal stem cells to multiply increased. It was observed that as the animals’ cholesterol levels rose, their intestinal cells divided more rapidly which caused the lining of their guts to expand and their intestine to lengthen. These changes significantly increased the rate of tumour formation in the colon. Future research will be directed towards whether the molecular pathway they discovered plays a similar role in augmenting the rate of other cancers as well.

https://www.sciencedaily.com/releases/2018/01/180125135551.htm


13. Genetic markers can help predict CRC outcomes (Jan 27/18)

A recent study presented at the 2018 Gastrointestinal Cancers Symposium examined the impact of identifying microsatellite status, tumour mutational burden and protein expression in colorectal cancer (CRC) tumours on disease outcomes among patients with microsatellite instability (MSI). In-depth molecular profiling of CRC can help to better inform treatment decisions by identifying patient subgroups at varying risks of death. For example, the presence of the p16 protein is prognostic in many tumour types, high tumour mutational burden (TMB) suggests genomic instability, and patients with MSI are more likely to respond to immunotherapy treatment.

In the study, the researchers used proteomic (i.e. relating to proteins) and genomic profiling to gather 145 clinical samples of CRC to identify which measures from molecular profiling could be associated with survival. Patients were grouped by microsatellite status (MSI vs. microsatellite stable), TMB (high vs. low), and p16 protein expression level. 27% of samples had high TMB, suggesting that their cancer tumour cells had a high number of genetic mutations. 20% of samples had MSI status, which occurs when mismatch repair (MMR) of DNA fails to repair errors as proteins are being created during DNA replication. The mistake remains uncorrected, and thus continues to be reproduced leading to MSI-high (MSI-H). While MSI and MSI-H can increase a person’s risk for CRC, this mutation may actually expand their options for treatment and their chances of better responses. Opdivo (nivolumab) and Keytruda (pembrolizumab) are two immunotherapy agents approved by the Food and Drug Administration (FDA) to treat patients with MSI-H or MMR deficiency who have already been treated on standard chemotherapy regimens. The study findings demonstrated that patients with MSI tumours had longer overall survival (OS) than those with microsatellite stable tumours. Patients with high TMB had longer OS than those with low TMB. Patients with high p16 expression had poorer prognoses compared to those with low p16 expression. It was found that a combination of microsatellite stability, low TMB and low p16 expression characterized a subset of patients with longer survival. These results demonstrate a potential benefit among this subgroup of patients that they can obtain when treated with personalized therapy. These findings are important for patients with microsatellite stable tumours as they have limited treatment options but may respond to specific pathway inhibitors due to their low p16 expression. Molecular profiling of CRC can therefore be very important in identifying patient subgroups that normally have poor prognoses and could benefit from personalized therapy.


14. Study could explain link between high-cholesterol diet and colon cancer (Jan 25/18)

A study from the University of California discovered that when cholesterol levels were amped up in mice, intestinal stem cells were encouraged to divide more rapidly and enabled tumours to form 100 times faster. The research has identified a molecular pathway that could serve as a new drug target for colon cancer treatment. While previous evidence has supported the link between dietary cholesterol and colon cancer risk, the underlying mechanism has never been well understood. In the study, mice were administered a high-cholesterol diet to increase the cholesterol in the intestinal stem cells. Other mice received an altered gene that regulates phospholipids, the principal fats in cellular membranes, which stimulated the cells that produce more cholesterol on their own. In both mouse groups, the ability of intestinal stem cells to multiply increased. It was observed that as the animals’ cholesterol levels rose, their intestinal cells divided more rapidly which caused the lining of their guts to expand and their intestine to lengthen. These changes significantly increased the rate of tumour formation in the colon. Future research will be directed towards whether the molecular pathway they discovered plays a similar role in augmenting the rate of other cancers as well.

https://www.sciencedaily.com/releases/2018/01/180125135551.htm
15. “Inflammatory” diet linked to higher risk of colorectal cancer (Jan 22/18)

An analysis of more than two decades of US survey data on eating habits and cancer diagnoses suggest that individuals who eat lots of foods linked to chronic inflammation, such as red meat and refined grains, may be more likely to develop colorectal cancer (CRC). Data from 74,246 female nurses and 46,804 male health professionals were examined and sorted into five groups based on how likely their daily diets could contribute to chronic inflammation. Compared to people with diets with the least potential to cause inflammation, individuals with pro-inflammatory diets were 32% more likely to develop CRC during the study. A pro-inflammatory dietary pattern consists of a high intake of red meat, processed meat, organ meat, refined grains, and sugary beverages and a low intake of tea, coffee, dark, yellow and leafy green vegetables. Such a diet will cause the bowels to be chronically stimulated, producing a constantly higher level of inflammatory mediators that may contribute to the development of cancer. In the study, it was found that men with the most pro-inflammatory diets were 44% more likely to develop CRC than men with diets least likely to cause inflammation. Women with the most pro-inflammatory diets were 22% more likely to get colorectal tumours. In both men and women, this association between diet and CRC risk held true across all anatomical sites where these tumours can develop, except for the rectum in women. The risk of CRC was even higher among overweight or obese men and lean women, and among men and women who didn’t consume alcohol. Despite study limitations (i.e. relying on accurate patient recall and report of daily food consumption), the findings offer fresh evidence that a typical Western diet full of pro-inflammatory foods like meat and processed grains and low in fruits and vegetables can lead to serious health problems. Furthermore, the study adds to previous evidence that a pro-inflammatory diet is linked to several types of diseases beyond cancer, including type 2 diabetes and cardiovascular diseases.


16. 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?x_cmd=trial_info&g_trial_cd=CO21](https://scooby.ctg.queensu.ca/tum_bank/tum.php?x_cmd=trial_info&g_trial_cd=CO21)

17. **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 randomized into 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_Ontario: 613-792-1222, toll free 1-855-546-1244 or research@oicc.ca](https://scooby.ctg.queensu.ca/tum_bank/tum.php?x_cmd=trial_info&g_trial_cd=CO21)

18. **Do high blood glucose levels increase colorectal cancer risk? (Jan 27/18)**

To date, there is an increasing body of evidence to support the link between colorectal cancer (CRC) and lifestyle-related diseases such as diabetes and obesity. A Swedish research team aimed to better understand the association between high blood glucose and insulin levels and the incidence of CRC. In the study, the participants had their first measurements taken in the 1990s and were followed-up until a diagnosis of CRC, death, migration, or the end of the study in 2010. Blood tests were administered to measure blood glucose levels, insulin levels, and insulin resistance. Patient’s sex and cancer site were also recorded to determine if the relationships were related to one sex or a particular part of the colon. Out of 4,910 participants in the study, 145 developed CRC. Those who developed CRC had a larger waist and higher insulin levels at baseline in the 1990s. The researchers observed a stronger association between high blood sugar levels and CRC in men compared to women. Insulin levels and insulin resistance, however, did not appear to have a correlation with the incidence of CRC.

Preclinical studies have described the relationship between high glucose and insulin on inflammation, which is linked to the development of cancers. The researchers hypothesize that the stronger association seen in men and not women may be partially explained by hormonal differences between the sexes. Further research is necessary to better understand the underlying mechanisms of this association and how this can be translated to better prevention and screening for CRC and lifestyle diseases like diabetes.
