The following colorectal cancer research updates extend from March 15th, 2018 to April 12th, 2018 inclusive and are intended for informational purposes only.

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**DRUGS / SYSTEMIC THERAPIES**

1. **Opdivo combination granted priority review to treat metastatic colorectal cancer (Mar 27/18)**

The Food and Drug Administration (FDA) has recently granted a priority review to the combination use of Opdivo (nivolumab) and Yervoy (ipilimumab) to treat metastatic colorectal cancer (mCRC) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) mCRC who have not responded to previous fluoropyrimidine, oxaliplatin and irinotecan regimens. This subgroup of patients currently represents 4-5% of mCRC patients. The FDA priority review is based on data from the ongoing phase II CheckMate-142 study published in the *Journal of Clinical Oncology* and recently presented at the 2018 Gastrointestinal Cancers Symposium. The study demonstrated that the combination appeared to be safe and effective while providing lasting responses and disease control among mCRC patients defined by MSI-H or dMMR biomarkers. The eventual approval of this drug combination could provide better options to individuals with MSI-H or dMMR-positive mCRC, as these patients are less likely to respond to traditional chemotherapy regimens. The researchers stress the importance of genetic testing in cancer diagnoses. As more drug therapies become available, genetic testing can help to improve patients’ prognoses by creating more personalized drug regimens.


2. **Duration of adjuvant chemotherapy for stage III colon cancer (Mar 29/18)**

Among patients with stage III colon cancer, the standard treatment since 2004 has been a regimen of 6 months of treatment with oxaliplatin plus fluoropyrimidine. Since oxaliplatin is linked to cumulative neurotoxicity, a shorter duration of therapy could spare toxic effects and healthcare costs. An analysis of six randomized phase III trials were conducted at the same time to evaluate whether adjuvant therapy with either FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CAPOX (capecitabine and oxaliplatin) produced any significant difference in disease-free survival at three years when given for 3 months compared with 6 months. Overall, the analysis was unable to prove that 3 months on either regimen was as effective as 6 months. *The 3-month regimen was found to be non-inferior (i.e. just as effective as) compared to the 6-month regimen in the CAPOX arm, but not the FOLFOX arm.* Researchers found that among patients with early stage tumours (T1, T2, T3 and N1), 3 months of the combined therapy produced the same results as 6 months of treatment, with a 3-year rate of disease-free survival of 83.1% and 83.3%, respectively. Among patients with more advanced stage tumours (T4, N2), the disease-free survival rate for a 6-month treatment regimen proved to be superior to that of a 3-month regimen. In conclusion, 3 months of adjuvant therapy with FOLFOX or CAPOX was not proven to be as effective as the standard 6 months of treatment. Patients treated with CAPOX for 3 months, however, had similar 3-year disease-free survival compared to 6 months, specifically in the lower-risk subgroup.


3. **Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Mar 30/18)**

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.


4. **Comparing Regorafenib to TAS-102 in metastatic colorectal cancer (Apr 11/18)**

Regorafenib and TAS-102 have shown to be superior to placebo in refractory metastatic colorectal
cancer. However, no studies have directly compared these two drugs. Given the lack of standard options in this scenario, a systematic review to compare the efficacy and safety of regorafenib and TAS-102 was performed. A systematic review for randomized controlled trials for patients with metastatic colorectal cancer, involving regorafenib or TAS-102, was performed. Data including overall survival, progression-free survival, and toxicity were extracted. Three randomized controlled trials fulfilled eligibility criteria:

1. The CORRECT trial
2. The CONCUR trial
3. The RECURSE trials

According to the results, there were no statistically significant differences observed between regorafenib and TAS-102 in overall survival or progression-free survival. Regorafenib had statistically more all grade any toxicity compared with TAS-102. Subgroup analysis of adverse events showed a different toxicity profile between both drugs. Investigators concluded that in this indirect comparison, regorafenib and TAS-102 appeared to have similar efficacy. However, regorafenib was associated with more toxicity compared with TAS-102.

NB: TAS-102 is currently under a funding review in Canada by pCODR and INESSS. A funding recommendation will be issued shortly. In the meantime, TAS 102 is being made available to eligible mCRC patients by the manufacturer (TAIHO).


5. **Immunoediting processes help colorectal cancer escape immune attack (Mar 26/18)**

In an online report by Cancer Discovery, researchers indicated that among microsatellite-instability-high (MSI-H) or immune-infiltrated tumours (tumours that have already been attacked by the body’s immune system), mutations have evolved that may promote resistance to recognition by the immune system. Such “immunoediting” phenomena help MSI-H colorectal tumours evade destruction by the body’s immune system. Researchers point out that other mechanisms are at play besides mutation load which impact the ability of the immune system’s T cells to infiltrate tumours that are both MSI-H and microsatellite stable (MSS). The researchers’ findings are based on an analysis of more than 1,200 colorectal cancer cases. MSI-H colorectal cancer comprised 15% of the samples and has been shown to respond to the use of immunotherapy agents which lift inhibition on the immune system causing the activation of T-cell mediated immune responses against tumour cells. MSS usually does not respond to such therapies. Analysis of the MSI-H samples demonstrated a high incidence of highly mutated genes involved in important immune regulating pathways such as antigen presentation. If a tumour cell can evolve to stop presenting certain antigens or targets on its surface, the body’s immune system will not be able to recognize the tumour cell as an invader that must be destroyed. Essentially, the cancer cell is able to outwit the immune system and continue proliferating without being “seen”. It was found that most MSI-H cases had at least one mutation believed to be important in decreasing antigen presentation. The analysis suggests that immune editing can happen as soon as the immune system begins attacking the cancer cells from the start, even before immunotherapies are administered to the patient. Beyond mutations involved in antigen presentation, the researchers were able to identify 11 mutated immune-related genes in MSI-H cases which may present novel therapeutic targets in the future.


6. **Modified XELIRI vs. FOLFIRI as second line treatment for metastatic colorectal cancer (Apr 2/18)**

A phase III trial (AXEPT) from Asia found that modified XELIRI (capecitabine plus irinotecan) was non-inferior (i.e. not worse than) with respect to overall survival when compared to standard FOLFIRI (leucovorin, fluorouracil, and irinotecan), both given with or without bevacizumab (Avastin), as second-line treatment of metastatic colorectal cancer (mCRC). In the trial, 650 patients from China, Japan and South Korea were randomly assigned to receive modified XELIRI with or without bevacizumab, or FOLFIRI with or without bevacizumab. Median follow-up was 15.8 months. Median overall survival was 16.8 months in the modified XELIRI group compared to 15.4 months in the FOLFIRI group. Median progression-free survival was 8.4 months vs. 7.2 months. Grade 3 or higher adverse events occurred in 54% of the modified XELIRI group compared to 72% of the FOLFIRI group, with the most common side effect being neutropenia (17% vs. 43%). Serious adverse events occurred in 15% of the modified XELIRI group compared to 20% of the FOLFIRI group. Treatment-related death occurred in two patients in the XELIRI group (as a result of pneumonitis and lung infection) and one patient from the FOLFIRI group (lung infection). In conclusion, it was observed that modified XELIRI with or without bevacizumab is well-tolerated and non-inferior to FOLFIRI with or without bevacizumab in terms of overall survival. Modified XELIRI could be a potential alternative to the standard FOLFIRI second-line treatment for mCRC.

http://www.ascopost.com/News/58680

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**SURGICAL THERAPIES**

7. **Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Mar 20/18)**
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 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=colorectal-colon-bowel-haip-chemotherapy

8. Living donor liver transplantation for unresectable colorectal cancer liver metastases (Mar 30/18)

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

9. Minimalist movement: preventing ostomies in colorectal cancer (Mar 17/18)
An ostomy is a surgically created opening in the body used for the discharge of body wastes such as stool. Patients with colorectal cancer (CRC) who undergo surgery may have a colostomy, an opening where the remaining large intestine (colon) is brought through the abdominal wall, or an ileostomy, an opening where the small intestine (ileum) is brought through the abdominal wall. While efforts are made to preserve the intestines during surgery, for some patients with CRC, a permanent ostomy may be the only life-saving option. For many people living with ostomies, issues concerning body image and depression, odor control and sexual activity can negatively impact quality of life. In recent years, however, with the use of neoadjuvant radiation and chemotherapy which are given prior to surgery, as well as improved surgical techniques, there has been an increase in the proportion of sphincter-saving procedures which minimize the need for ostomies. Currently, surgical resection is the most common treatment for CRC and normally involves the removal of the tumour, some surrounding healthy tissue as well as nearby lymph nodes. Many patients with locally advanced disease will undergo chemoradiation treatment before surgery to try to lessen the size of the tumour, thereby minimizing the amount of intestinal tissue that needs to be removed. These pre-surgical treatments also lower the long-term risk of disease recurrence and mortality. Furthermore, studies have demonstrated that the rates of patients needing abdominoperineal resection (APR) are reduced using neoadjuvant chemoradiation compared with treatments that are given after surgery. APR is a surgical procedure that completely removes the lower portion of the colon, the rectum and the anal sphincter resulting in the need for a permanent colostomy.

The watch-and-wait management approach is being studied in patients with CRC that achieve complete clinical response after neoadjuvant chemoradiation. 25-30% of patients treated with chemoradiation will achieve a complete response and are candidates for the watch-and-wait approach. Colleagues from the Memorial Sloan Kettering Cancer Center have been using this approach for years among patients with complete clinical response. They have found that in cases where the tumour does grow back, it usually grows slowly. Since this approach requires the patient to be seen at frequent intervals, the tumour can be detected in time to do the same surgery that would have been done in the beginning. The Memorial Sloan Kettering Centre is currently conducting the only prospective, multi-institutional study on the watch-and-wait approach, but data will likely remain unavailable for the next three years. Until there is more evidence, patients are still recommended to undergo surgical resection as the standard of care for CRC.


10. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Mar 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

Sunnybrook Odette Cancer Centre

11. iPad-based intervention doubles CRC screening rates (Mar 12/18)

A recent trial demonstrated that a technological health intervention that enabled patients to order colorectal cancer (CRC) screening tests themselves doubled the proportion of patients who underwent screening. There are two components of the Mobile Patient Technology for Health-CRC (mPATH-CRC) that directly encourage screening orders: the decision aid, which increases patients’ intention to receive screening; and the ability to self-order tests, which decreases barriers to completing the orders. In the trial, 450 patients who were due for routine CRC screening and were scheduled for a visit with their primary care provider were randomly assigned to receive either the iPad-based mPATH-CRC intervention or a control intervention. The mPATH-CRC intervention is comprised of an 8.6-minute
decision aid with information about fecal testing and colonoscopy, which the patient could self-order. Afterward, the program set up automated follow-up message tailored to the chosen test to assist the patient in completing the screening procedure. The control intervention was only comprised of a 4.3 minute video on diet and exercise. All participants completed a phone survey 24 weeks after receiving the intervention. It was observed that those who received the mPATH-CRC intervention were twice as likely as those in the control group to complete a chart-verified screening test within 24 weeks of enrolment (30% vs. 15%), which was the primary outcome for the trial. Colorectal adenoma detection rates were 2.6% in the control groups and 7.2% in the intervention group. More participants in the intervention group ordered screening tests (69% vs. 32%). Completion of an ordered colonoscopy was higher than completion of an ordered fecal test among all participants (mPATH-CRC, 61% vs. 26%; control, 53% vs. 32%). The researchers note that although screening increased substantially among study participants, among which were many low-income individuals with limited health literacy, about 50% of patients did not actually complete the tests that they ordered. Further strategies are necessary to help stimulate patients to complete the screening process from start to finish.


12. Novel scope in development to improve imaging in colonoscopy (Mar 23/18)

A $500,000 grant was awarded by the National Science Foundation to an engineering professor to continue his work on developing a new endoscopic probe to improve the imaging of living tissue. The device uses a fiber optic bundle to illuminate the gastrointestinal tract and produce high-resolution images in real time. The probe could help to improve colorectal cancer (CRC) screening and expand what we currently know about the relationship between abnormal cell progression and blood and oxygen delivery in primary tumours of the colon. The probe generates tissue maps which can quantify haemoglobin (the iron-containing molecule in blood) concentrations and detect any abnormal blood vessels. Abnormal amounts of blood and oxygen in the tissue may be important signs of tumour development and proliferation. The probe is an interesting new technology which could help to advance the ways in which we are currently able to observe the gastrointestinal tract.


13. Every patient who has a GI cancer should be tested for MSI-High status (Apr 5/18)
Numerous well-conducted clinical trials have demonstrated that immunotherapies can help to treat a subset of gastrointestinal (GI) and other cancers that are considered microsatellite instability-high (MSI-H) or mismatch repair-deficient, which indicates that cancer cells have a mutation which leaves them unable to repair their own DNA when it is damaged. In MSI-H cancers, the mutation causes the cancer cells to develop a variety of additional mutations, making the tumours more susceptible to recognition by the body’s immune system. As a result, immunotherapies such as checkpoint inhibitors which lift the brake on the immune system’s inhibitory mechanisms may be more effective at controlling the growth of MSI-H tumours. Based on evidence supporting the effectiveness of immunotherapies in this subset of cancers, the Food and Drug Administration (FDA) approved two immunotherapies for the treatment of MSI-H colorectal and gastric cancers. Keytuda (pembrolizumab) was approved in May 2017 to treat MSI-H advanced cancer, and a few months later Opdivo (nivolumab) was approved by the FDA to treat metastatic MSI-H colorectal cancer that is unresponsive to previous chemotherapy. Recent studies have suggested that a combined treatment using two types of checkpoint inhibitors can further improve the effectiveness in advanced cancer patients. While these drugs provide more options for this subset of GI cancer patients, only 1 in 7 colorectal cancers is MSI-H. Since immunotherapies may provide a significant benefit to these patients, it is important that those who are diagnosed with a GI cancer that is MSI-H undergo genetic testing if possible. In this way, the most personalized treatment can be delivered, minimizing undesirable side effects and improving quality of life. For a rare number of patients, genetic testing could reveal the presence of Lynch Syndrome, a genetic condition linked to the development of some MSI-H GI cancers. Not only will patients who undergo genetic testing benefit from immunotherapy, but in doing so they may stimulate their family members to get tested for any inherited conditions, enabling them to take preventative measures or have any cancers detected at an earlier stage.


14. Adequate bowel prep key to colon cancer prevention via colonoscopy (Mar 28/18)

According to specialists, adequate cleansing of the bowel in preparation for a colonoscopy is very important for the effective detection and removal of suspicious polyps in the prevention of colorectal cancer (CRC). Sometimes polyps can be easy to identify – they have a long stalk and are mushroom-shaped (pedunculated polyps). These polyps do not provide a great deal of difficulty for the endoscopist conducting the colonoscopy to detect. Some polyps, however, are sessile polyps, meaning that they are flat and more or less blend in with the wall of the intestine. Without adequate bowel prep that properly cleans off the mucosal wall as best as possible, it can be easy to miss sessile polyps. Sometimes, patients may not strictly adhere to the instructions of the bowel prep. Often, not enough fluid is consumed, or sometimes the entire prep solution is not consumed because the individual finds it unpleasant. Patients at greatest risk for inadequate bowel prep are the elderly, diabetics, those who have trouble swallowing, those who have impaired intestinal motility, and those who are chronically constipated. Currently, many different preps exist on the market and they are not all the same. They may be composed of different chemicals and active ingredients, with some preps safer and more efficient than others. The dosing of the prep solutions may vary as well. In conclusion, the approach to best ensure adequate bowel prep is to personalize the prep choice depending on the patient’s age, their ability to follow directions, their home situation and their preferences.

https://www.healio.com/gastroenterology/interventional-endoscopy/news/online/%7ba559226f-3ece-4b19-84cd-6180e2967d71%7d/adecuate-bowel-prep-key-to-colon-cancer-prevention-via-colonoscopy/hvc/4

A large study published in the *European Journal of Internal Medicine* suggests that the use of cannabis may be a safe and effective palliative treatment for patients with cancer. The study was conducted across Israeli Tikun-Olam clinics and demonstrated that 95.9% of participants reported an improvement in their cancer-related symptoms such as sleep problems, pain, nausea, and decreased appetite. Tikun-Olam is the first and largest medical cannabis supplier in Israel. Treatment with medical cannabis is becoming more common and the rates of clinical use are increasing across the globe. Currently, there is a severe lack of research and evidence that supports the safety and efficacy of medical cannabis use for the treatment of specific conditions such as cancer, characterized by a vast array of symptoms and accompanied by a wide variety of pharmaceutical drugs. The growing use of cannabis in the treatment of various medical conditions is mainly patient-driven, based on the subjective feeling of the patients and their own evaluation of the impact of the plant on their condition.

In the study, the researchers examined data from 2,970 patients with cancer who were treated with medical cannabis between 2015 and 2017. All patients were prescribed one or more of Tikun Olam’s own cannabis strains, which were developed to address specific cancer-related symptoms. The participants in the study were on average 60 years of age, and the majority were women (54.6%). Only 26.7% of patients reported having previously used cannabis. 20.7% of patients had breast cancer, 13.6% lung cancer, 8.1% pancreatic cancer, 7.9% colorectal cancer, and 51.2% of patients had stage IV disease. Patients were treated with medical cannabis to address cancer treatment-related symptoms such as sleep problems (78.4%), pain with median intensity 8/10 (77.7%), weakness (72.7%), nausea (64.6%) and lack of appetite (48.9%). After six months of follow-up, 902 patients died and 682 stopped treatment. Of the remaining 1,211 patients, 95.9% reported an improvement in the condition they were being treated for with medical cannabis. Certain symptoms showed greater improvement than others, with the greatest improvement seen with nausea and vomiting (91% improvement), sleep disorders (87.5%), restlessness (87.5%), anxiety and depression (84.2%), pruritus or severe skin itching (82.1%), and headaches (81.4%). After six months of treatment, only 4.6% of patients reported a pain intensity of 8/10. With respect to self-reported quality of life (QoL), less than 20% of patients reported a good QoL before they began treatment with cannabis. After six months of treatment, 70% reported good QoL.

Side effects linked to cannabis use were reported by 362 patients, and included 8% reporting dizziness, 7.3% dry mouth, 3.6% increased appetite, 3.3% sleepiness, and 2.8% reporting a psychoactive effect. 3.7% of patients reported no change in their symptoms and 0.3% reported deterioration in their medical condition. The researchers are hoping that this evidence will help to address the pharmaceutical opioid epidemic. The study found that opioids were the most commonly used pharmaceutical drug consumed by 33.9% of participants when they enrolled in the study. By the end of 6 months, 36% of opioid users stopped taking opioids at all and 9.9% asked for a decreased dose. The study demonstrated that cannabis treatment among cancer patients appeared to be well-tolerated, safe and effective at helping patients cope with their symptoms. Today, where each symptom that a patient experiences may be treated with a different pharmaceutical drug, each with their own range of side effects, cannabis therapy may be a comprehensive alternative that addresses multiple symptoms at once with minimal to no side effects.


16. Candirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Apr 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:
17. Survivorship planning should start at diagnosis (Mar 27/18)

According to Nancy Corbitt, an oncology nurse from the University of Maryland Medical Center, a survivor is a person who was just diagnosed with cancer – whether they’re stage I or stage IV. In the majority of survivorship literature, survivors are people who cured their disease and moved on. According to Nancy, sharing the available tools and resources for people in all stages of their cancer journey is important in contributing to a happier and healthier quality of life. One aspect of survivorship is empowering patients to take charge of their own care, starting with educating themselves early on through resources such as books, the internet, or support groups. Online technology shapes many patients’ cancer journeys offering a way to reach out to others, as well as facilitating easy access to information regarding their treatment and potential side effects. These online technologies may also help to bridge uncomfortable conversations, such as sexual dysfunction, that are a part of many cancer diagnoses.

While resources and support are essential to the survivor, it is just as important to care for and empower their caregivers as well. The burden that caregivers feel as they witness their loved one go through cancer is a real issue that must be addressed. Many caregivers may feel guilty for taking time for their own self-care, or feel that they cannot leave the person they are caring for. In reality, neglecting their own well-being only takes away from their capacity to care for another. The National Cancer Institute offers a booklet titled, “Caring for the Caregiver”, which offers tips and guidance about caregivers asking for help, caring for themselves, accompanying their loved ones at their medical visits and more.

Even after their last treatment, the stress does not end for many survivors. The transition to post-cancer survivorship has its own particular circumstances, such as patients seeing the doctor less frequently and transitioning from an oncologist back to a primary care physician. End of treatment summaries describe what medications and treatment a patient has received. These summaries are not only being sent to the survivors, but to their primary care providers so that everyone is aware of the unique details of a patient’s care. A survivorship care plan which patients also receive at the end of their treatment provides support on living well after cancer. It can help to guide patients through healthy habits as well as surveillance plans for any recurrences - a very real fear that many survivors experience. Through a well-organized survivorship care plan, survivors and their caregivers can be empowered to continue along their cancer journey with more confidence and peace of mind.

https://www.curetoday.com/articles/survivorship-planning-should-start-at-diagnosis

18. Colon cancer formation linked to two interacting bacteria strains (Apr 10/18)
According to two new studies, two species of bacteria appear to work together to promote the formation of colon cancer among patients with a hereditary form of the disease. *Bacteroides fragilis* and *Escherichia coli* produce substances that stimulate cancerous growths in patients with familial adenomatous polyposis (FAP), which is a hereditary condition that is the cause of about 5% of colon cancers. The combination of these conditions creates the “perfect storm” to drive colon cancer development. Past research has examined how different strains of bacteria can invade the colon mucosal layer in about 50% of patients who develop colon cancers. The bacteria are able to penetrate the protective mucosal layer and form a sticky film next to the colon epithelial cells where colon cancers generally originate. The researchers removed colon tissue from six patients with FAP and found portions of the sticky bacterial film along the length of the colon in about 70% of the patients. The bacterial film was found to be mainly composed of *B. fragilis* and *E. coli* bacteria. *B. fragilis* secreted a toxin that stimulated cancer-causing pathways among colon epithelial cells and upregulated inflammation. *E. coli* secreted another toxin that causes DNA mutations in the cells. Based on the researchers’ findings, the two bacteria must be present together to promote cancer development. Using mouse models, the researchers found that animals whose guts were colonized with both species of bacteria developed more tumours than those which were colonized with only one type. These findings are important as they could lead to new screening techniques to help identify patients with FAP as early as possible and could even be applied to other non-hereditary forms of colon cancers.


**19. Calcium supplements linked to precancerous colon polyps (Mar 15/18)**

According to a recently completed trial, calcium supplements with or without vitamin D seemed to increase the risk for premalignant serrated polyps – more specifically, sessile serrated adenomas and polyps – among patients with a history of colorectal adenomas. The researchers found that women and active smokers who regularly took calcium supplements were at particular risk for developing serrated polyps, and the effects appeared to arise 6-10 years after supplementation began. While the study findings will require further evidence to make more conclusive statements, it appears that patients with a history of precancerous serrated polyps should consider weighing the possible risks with the benefits of calcium and vitamin D supplementation.

Some past studies have shown that people with calcium-rich diets are at a lower risk of colon polyps including serrated polyps, so researchers were surprised to find that calcium supplementation did not have beneficial effects in preventing colon cancer or polyp formation. The researchers reviewed data from the “treatment phase” of a randomized controlled trial in which 2,058 participants with at least one adenoma when they entered the trial were randomly assigned to receive daily supplementation with calcium, vitamin D, both, or neither for 3 to 5 years, after which they underwent a colonoscopy. Then, data was assessed from the “observational phase” or follow-up portion of the study. The study focused on the risk of developing a particular class of colon polyps called sessile serrated polyps. These polyps have only recently been recognized as important precursors to colon cancer, giving rise to about 20-30% of colon cancer cases. Sessile serrated polyps are an important target in colon cancer screening, but they also happen to be more difficult to detect through colonoscopy because of their flat shape that blends in with the intestinal wall compared to the more obvious mushroom-shaped adenomatous polyps. In the study, the researchers found that calcium or vitamin D supplementation did not have any effect on the incidence of sessile serrated polyps during the treatment phase, but the risk of developing these polyps significantly correlated with calcium supplementation and calcium + vitamin D supplementation during the observational follow-up phase. Vitamin D alone was not associated with an increased risk of developing these polyps. When the researchers analyzed different patient subgroups, active smokers and women demonstrated a significantly higher risk for any serrated polyp when taking calcium. The researchers stress that these findings are not any reason to suddenly stop taking calcium supplements as many people do take low doses in multivitamins. This possible association, however, does put the spotlight on patients who have a history of serrated polyps and/or are smokers, and may be reason to more closely examine the risks and benefits of calcium supplementation among these subgroups.
20. Young adult colorectal cancer clinic available at Sunnybrook (Mar 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

Should a patient wish to be referred to Sunnybrook, they may have their primary care physician or their specialist refer them to Sunnybrook via the e-referral form which can be accessed through the link appearing below. Once the referral is received, the Young Adult Colorectal Cancer Clinic will be notified if the patient is under the age of 50. An appointment will then be issued wherein the patient will meet with various members of the team to address their specific set of concerns.

http://sunnybrook.ca/content/?page=young-adult-colorectal-cancer-clinic

21. Links between eating red meat and distal colon cancer in women (Apr 2/18)

An international study conducted by researchers at the University of Leeds in the United Kingdom assessed whether red meat, poultry, fish or vegetarian diets are linked to risk of colon and rectal cancer. In the study, the effect of these diets on cancer development in specific sub-sites of the colon was examined. For the study, researchers conducted an analysis of data from the United Kingdom Women’s Cohort Study. The study included data from 32,147 women across the UK who were tracked for an average of 17 years. The women’s dietary habits were reported, and a total of 462 colorectal cases were documented and of the 335 colon cancers, 119 cases were cancers found in the distal colon. It was found that individuals that regularly ate red meat compared to a completely plant-based diet had higher rates of distal (or left sided) colon cancer, or cancer found on the descending portion of the colon where feces are stored.

More than 2.2 million new cases of colorectal cancer are expected to be diagnosed across the globe by 2030. Currently, colorectal cancer is the third most commonly diagnosed cancer in women worldwide. Previous research has suggested that eating a diet rich in red and processed meat increases the risk of colorectal cancer but to date, there is limited research on the effect of specific dietary patterns and where the cancer develops along the colon. This study
sheds light on how regular meat consumption may affect the sections of the colorectum differently, and further reinforces the existing evidence which supports a plant-based diet for reducing colorectal cancer risk.


22. 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) (Mar 15/18)

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_tri

23. High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (Mar 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-week 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 vtdstudy@inspirehealth.ca Ontario: 613-792-1222, toll free 1-855-546-1244 or research@oicc.ca