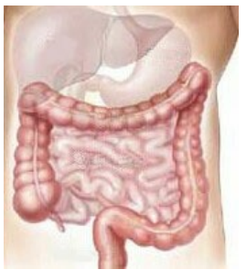
COLORECTAL CANCER CANADA

COLORECTAL CANCER RESEARCH UPDATES

Month Ending July 31st, 2019



The following colorectal cancer research updates extend from July 1st, 2019 to July 31st, 2019 inclusive and are intended for informational purposes only.

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DRUGS/SYSTEMIC THERAPIES

ReDOS: Regorafenib dose-escalation strategy in refractory advanced colorectal cancer (July 11/19)

In the phase II ReDOS trial reported in *The Lancet Oncology,* a regorafenib dose-escalation strategy compared well with the standard dosing with respect to activity and toxicity among patients with previously treated advanced colorectal cancer (CRC). Regorafenib (Stivarga) is an oral drug that binds to tyrosine kinase receptors and inhibits important receptors on the cell surface which are crucial to cell division. While regorafenib has been shown to improve survival in previously treated mCRC, the high rate of severe adverse events has limited its use in clinical practice. 116 patients with advanced disease were randomly assigned to a regorafenib dose-escalation strategy (beginning with 80mg/day and increasing in an 40mg increment weekly until 160mg/day if no significant drug-related adverse events occurred) or a standard-dose strategy (160mg/day) for 21 days in a 28-day cycle.

Median overall survival was 9.8 months in the dose-escalation group compared to 6 months in the standard-dose group. Initiation of three cycles of treatment was achieved by 23 patients in the dose-escalation group compared to 16 patents in the standard-dose group; more patients were therefore able to undergo a third cycle of treatment with the more "flexible" regorafenib dosing compared to the standard treatment group. The frequency of grade 3 adverse events commonly associated with regorafenib – fatigue, hand-foot skin reaction, hypertension, and diarrhea – was generally lower in the dose-escalation group in the first two cycles of treatment. Findings from the ReDOS trial were confirmed by another study, REARRANGE, which also examined a more flexible dosing of the drug and found a reduction in adverse events without jeopardizing efficacy. The research team concluded that the dose-escalation strategy may be an alternative approach for optimizing regorafenib dosing with comparable activity and lower incidence of adverse events, providing a promising therapeutic strategy in clinical practice.

https://www.ascopost.com/News/60234
https://www.medscape.com/viewarticle/915446

Maintenance panitumumab vs. panitumumab/fluorouracil/leucovorin in RAS wild-type metastatic colorectal cancer (July 18/19)

Results from an Italian phase II trial published in *JAMA Oncology* found that maintenance therapy with panitumumab alone had worse progression-free survival (PFS) compared to maintenance therapy with panitumumab plus fluorouracil/leucovorin in RAS wild-type metastatic colorectal cancer (mCRC).

In the trial, patients with previously untreated metastatic disease were randomly assigned to receive maintenance therapy with panitumumab alone or panitumumab plus fluorouracil/leucovorin. Maintenance treatment was continued until the disease progressed or the patient experienced unacceptable toxicity.

PFS at 10 months was significantly better in the combination group (49% for panitumumab alone vs. 59.9% for the combination). Median PFS was 9.9 compared to 12 months in the combination group. Grade 3 or higher adverse events occurred in 20.3% of the panitumumab group compared to 42.4% of the combination group. The combination group experienced higher rates of diarrhea, and stomatitis. While the panitumumab combination therapy prolonged PFS among RAS wild-type mCRC patients compared to panitumumab alone, patients did experience an increase in treatment toxicity.

https://www.ascopost.com/News/60262

Bowel cancer: 3-drug combo may offer alternative to chemo (Jul 14/19)

Up to 15% of metastatic colorectal cancer (mCRC) patients have a mutation in the BRAF V600E gene. This genetic change can accelerate the spread and growth of certain cancer cells and causes this form of mCRC to be more difficult to treat, as it can be aggressive and tends not to respond to combination treatments involving chemotherapy. The BEACON CRC phase III trial tested a combination of targeted therapies without chemotherapy to treat BRAF V600E mCRC. A mixture of three drugs - two of which target the cancer cells and one which inhibits the BRAF gene – was analyzed on a number of individuals who had shown no response to one or two previous treatments. The researchers highlight that CRC does not respond to BRAF therapy alone because tumour cells are able to adapt through other mechanisms to continue their survival. Using a triple targeted therapy, the researchers intend to inhibit BRAF at the same time as other possible survival mechanisms of the tumour cells.

While standard therapy was associated with a general survival rate of 5.4 months, the triple-drug combination provided a median survival rate of 9 months. The response rate was 26% for the triple therapy, compared to just 2% for the standard regime. The results are promising and will hopefully lead to increased access to this treatment among patients where there is currently a large unmet need. Future studies will be focused on determining whether double or triple therapy is best; researchers believe, however, that the three-drug treatment should replace chemotherapy among this patient subset. The advantages of chemotherapy do not seem to outweigh the disadvantages, and the possibility of avoiding the side effects that are typically experienced with chemotherapy is an important consideration. The research team highlight the important of routine testing of patients with CRC for BRAF mutations in order to triage them to the most efficient targeted therapies.

https://www.medicalnewstoday.com/articles/325730.php

Targeting FOLFOXIRI plus bevacizumab to a metastatic colorectal cancer subset (July 10/19)

Metastatic colorectal cancer (mCRC) patients are considered to be "high risk" in the presence of an elevated number of circulating tumour cells (CTCs). The Phase III VISNU-1 trial evaluated the first-line treatment of patients with metastatic colorectal cancer deemed to be high risk due to the presence of CTCs. Patients were randomly assigned to FOLFOXIRI or FOLFOX, both with bevacizumab. Results demonstrated that the FOLFOXIRI/bevacizumab regimen improved progression-free survival by about 3 months, though it was associated with significantly more grade ≥3 toxicities (78% vs. 67% in the control arm), especially diarrhea. The median progression-free survival was significantly longer with FOLFOXIRI/bevacizumab – 12.4 months vs. 9.3 months with FOLFOX/bevacizumab. The benefit was shown to be greatest for patients with left-sided primary tumours and wild-type RAS/BRAF tumours. Results from the VISNU-1 trial suggest that

FOLFOXIRI plus bevacizumab could be considered an adequate treatment option among high-risk mCRC patients with three or more CTCs.

https://www.ascopost.com/issues/july-10-2019/targeting-folfoxiri-plus-bevacizumab-to-a-metastatic-colorectal-cancer-subset/

SURGICAL THERAPIES

Precutting endoscopic mucosal resection effective for difficult colorectal lesions (July 28/19)

A multi-center retrospective study from Japan examined the use of pre-cutting endoscopic mucosal resection (EMR) to achieve en bloc resection (removal of the affected tissues as a whole) of colorectal lesions that are 20mm or larger in size. An alternate technique, endoscopic submucosal dissection, enables en bloc resection of more difficult lesions that cannot be removed by standard EMR, though it is far more time-consuming and associated with a high rate of adverse events. Pre-cutting EMR involves making an incision along the full or partial circumference of the colon mucosa around a colorectal lesion to achieve en bloc resection. Although pre-cutting EMR was a longer procedure compared to standard EMR, it had a significantly higher en bloc resection rate (88.6% compared to 42.5%) and histologic complete resection rate, where the apparently non-tumour tissue around the tumour is excised and later confirmed histologically to be free of tumour cells (71.4% compared to 42.9%). Pre-cutting EMR may be an important technique to achieve en bloc resection when standard EMR or endoscopic submucosal dissection is not indicated or easily performed.

Cryotherapy for liver metastases (July 10/19)

A July Cochrane review aimed to determine whether cryotherapy was beneficial or harmful for the local destruction of colorectal cancer tumours that have spread to the liver. When cancer spreads in the body via metastasis, one of the most common sites is to the liver. After cancer of the liver (primary liver cancer), metastases that originate from colorectal cancer are the most common cancer affecting the liver. Over half of patients with liver metastases die from complications. Cryotherapy, or the use of extreme cold to destroy affected tissue, is one method to treat liver metastases. The method requires the placement of a special probe near the cancer site. The probe delivers extreme cold to the site, produced by liquid nitrogen or argon gas. The rapid freezing process kills cancerous cells, reducing the size of the tumours.

A review of existing evidence was conducted to determine whether cryotherapy prolongs life or increases quality of life among patients with liver metastases. Based on evidence from one trial conducted in Ukraine, mortality at 10 years was 81% (51/63 patients) in the cryotherapy group and 92% (55/60 patients) in the conventional surgery group. No significant difference in recurrence of the liver malignancy was found between the cryotherapy and conventional surgery groups. The evidence to support the effectiveness of cryotherapy compared to conventional therapy was found overall to be of low certainty. No evidence for the benefits or harms of cryotherapy compared to no intervention, or compared to systemic treatment was found.

The effect of having nutrition within the first 24 hours after bowel surgery on length of hospital stay and postoperative complications (July 22/19)

A July Cochrane review reviewed the evidence to support whether feeding patients soon after surgery (orally or through a tube) can help them to leave the hospital sooner with few complications. Traditionally, after gastrointestinal surgery, it was normal for patients to not eat until their bowel regained some function (e.g. bowel sounds, passing wind, bowel motion). Some studies have examined whether feeding patients sooner after surgery can help reduce complications (e.g. pneumonia), though results have been unclear.

The review examined 17 relevant studies on early nutrition after bowel surgery. Some evidence demonstrated that patients who received nutrition within the first 24 hours after their surgery were able to leave the hospital almost two days sooner than patients who were not given any nutrition until their bowel activity returned. All relevant studies that were included in the review, however, were determined to be of low quality. This suggests that the study results may be less reliable. To better determine whether early feeding after surgery is truly beneficial, more studies are needed which are larger and of better quality and design. Future trials should address quality issues and focus on clearly defining and measuring postoperative complications to allow for better comparison between studies.

SCREENING

Financial incentives to increase colorectal cancer screening uptake and decrease disparities (July 16/19)

A recent study aimed to evaluate three different approaches to increase uptake of colorectal cancer screening. 838 participants were randomized to receive either only mailed information on the importance of screening and available tests, mailed information plus a guaranteed monetary incentive, or mailed information plus the incentive of winning a monetary lottery. While the monetary incentives did not increase colorectal cancer screening uptake overall, they did increase the rate of fecal immunochemical test completion. Such incentives could help minimize screening disparities in the future particularly among individuals with socioeconomic disadvantages.

OTHER

Transfer of oncogene in colon cancer cells demonstrated (July 19/19)

New research from the University of Minnesota Medical School proposes that there is a cellular and molecular cause to why colon cancer patients can receive drugs successfully for months or even years, before developing a drug resistance. Their findings have potential application to other similarly aggressive cancers as well. The research team found that proteins derived from the cancer gene KRAS have the ability to be transferred between colon cancer cells via long cellular extensions called "tunnelling nanotubes". KRAS is an important gene involved in driving cancer development, and is involved in 30% of all cancers as well as in the processes that take place as cancer becomes resistant to drugs. The researchers found that the transfer of KRAS proteins causes the surrounding cells to behave in a more cancerous, invasive manner that is more likely to be resistant to standard drug regimens.

The more aggressive the metastatic colon tumours are, the more likely the patient will develop drug resistance. The research team suggests that by cutting off this line of communication for the transfer of signals between cells could present itself as a novel therapeutic strategy in addition to the standard-of-care chemotherapy. Their findings provide a new perspective on how KRAS can influence the development of colon cancer and other cancers driven by this gene. Future research will be directed at figuring out how to cut off the communication of vital signals between cancerous and normal cells.

Does the association between diet and colonic-mucosa-associated microbiota affect cancer risk? (July 18/19)

Findings published in *The American Journal of Clinical Nutrition* demonstrated an association between diet quality and microbiome composition in the human colon. The researchers found that a good-quality diet such as the one recommended by the Dietary Guidelines for Americans which is high in fruits, vegetables, and whole grains and low in added sugar, alcoholic beverages and solid fats, was associated with an abundance of beneficial bacteria in the gut, such as those that produce an anti-inflammatory effect. A poor-quality diet was linked to a higher number of potentially pathogenic bacteria, such as those of the genus *Fusobacteria,* which have been linked to the development of colorectal cancer. The researchers suggest that the effect that diet has on the structure of bacterial communities in the human colonic mucosa can lead to changes in our immunity, inflammation, and our risk of chronic diseases.

Diet is a principal factor that influences the structure of the microbial community in the gut, affecting the ability of beneficial or harmful microorganisms to colonize it. The composition of the human gut microbiome also influences nutrient uptake, synthesis of vitamins, how energy is extracted from our diet, chronic inflammation, carcinogen metabolism, and the body's immune and metabolic response, all of which are factors that can impact disease risk.

Future research will examine these findings in a larger population. While other factors such as aging, genetics, or certain medications also influence the risk of disease, we cannot change them. Diet is modifiable and provides a strategy to develop a microbiome that promotes good health.

https://www.ascopost.com/News/60263

Common blood pressure drug may harm gut health (July 12/19)

High blood pressure is an increasingly common condition that increases the risk of heart attack, stroke, chronic heart failure, and kidney disease. From national, regional, and community population-based studies, worldwide trends in blood pressure were analyzed from 1975-2015, demonstrating that the prevalence of high blood pressure had almost doubled over the past 40 years. Treatment includes changes in lifestyle factors such as diet and exercise, and medications. The most commonly prescribed medications include inhibitors, which help to relax the blood vessels, and channel blockers, which prevent the narrowing of the blood vessels.

A research team from Imperial College London and Ludwig Maximilian University in Germany investigated the efficacy and potential side effects of three common blood pressure medications: ACE inhibitors, beta-blockers, and calcium channel blockers.

The team found an association between calcium channel blockers and a lower risk of cardiovascular disease, but they also found that some components in these drugs might increase the risk of **diverticulosis**. This condition includes the formation of small pouches in the lining of the digestive system. The bulges tend to appear in the lower part of the large intestine, and are not harmful unless they become inflamed or infected - a condition known as **diverticulitis** –or if the pouches burst. The researchers found that the association was found between a specific type of calcium channel blocker called the "nondihydropyridine class". While the underlying mechanism remains unknown, the researchers suggest that it might relate to effects on the function of the intestinal muscles, which perform the rhythmic contractions known as peristalsis to transport food through the intestinal tract.

https://www.medicalnewstoday.com/articles/325722.php

NUTRITION/ HEALTHY LIFESTYLE

Consumption of fish and long-chain n-3 polyunsaturated fatty acids and reduced risk of colorectal cancer (July 18/19)

A recent study examined the relationship between the consumption of fish and long-chain n-3 polyunsaturated fatty acids and the development of colorectal cancer. Long-chain n-3 polyunsaturated fatty acids are present in foods such as flaxseeds, chia seeds and fish, and play important roles in the body in the formation the structure of cell membranes. In addition to their structure role, omega-3s provide energy for the body and are used to form signalling molecules that have wide-ranging functions in the body's cardiovascular, pulmonary, immune, and endocrine systems. Using data from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, the researchers found that total intake of fish, intake of fatty fish, intake of lean fish and intake of long-chain n-3 polyunsaturated fatty acids were all significantly correlated with a reduced incidence of colorectal cancer. The regular consumption of fish is associated with a lower risk of colorectal cancer, a relationship that may be directly mediated by one's dietary exposure to n-3 long-chain polyunsaturated fatty acids.

Sugary drink consumption and risk of cancer (July 25/19)

The consumption of sugary drinks such as soda has increased worldwide in recent decade. These beverages are strongly associated with the risk of obesity, which is an important risk factor for many types of cancer and chronic illnesses. It is believed that sugary drinks with their high glycemic index promote a pro-inflammatory state by stimulating an excess of insulin and creating insulin resistance. A recent study assessed the associations between the consumption of sugary drinks and the risk of developing cancer among 101,257 French adults who were followed for a median of 5.1 years. There was a significant association between the consumption of sugary drinks including 100% fruit juice and an increased risk of overall cancer and breast cancer.

Weight in adolescence may affect colorectal cancer risk (Jul 24/19)

A new study has found a link between being overweight or obese in adolescence and an increased risk of developing colon cancer in later life. Obesity was also associated with an elevated risk of developing rectal cancer. Published online in *CANCER*, a peer-reviewed journal of the American Cancer Society, the study findings come at a time of growing concern regarding the impact of being overweight and obese as a teen on chronic disease later in life.

An inflammatory diet correlates with colorectal cancer risk (July 15/19)

Results from a multi-center European study published in *Nutrients* reveal a correlation between inflammatory and antioxidant diets and the risk of developing colorectal cancer. Individuals who followed an inflammatory diet - characterized by the consistent consumption of refined carbohydrates, red and processed meat, and saturated or trans fats - had almost twice the risk of developing colorectal cancer compared to those who followed an antioxidant diet rich in vegetables, legumes, fruits and nuts. While a pro-inflammatory and pro-oxidant diet is an important risk factor for colorectal cancer development, it is a modifiable risk factor that can be changed. Increased efforts on the part of official agencies and international agencies to reorient the general population towards an anti-inflammatory, anti-oxidant diet will be needed to better help individuals follow dietary recommendations and change poor eating habits for good.

Colon cancer: could yogurt prevent precancerous growths? (July 1/19)

Many factors can lead to the development of colorectal cancer (CRC), though among the most prominent is a poor diet. New studies have begun to investigate the association between different foods and the risk of tumours or precancerous growths. These precancerous growths, or adenomas, are usually benign; some of them do have the potential to develop into cancerous tumours given the right circumstances. Researchers from the Harvard T.H. Chan School of Public Health alongside many collaborating institutions have found an association between a reduced risk of adenomas in men and a high consumption of yogurt.

Some researchers suggest that high yogurt intake may reduce the risk of CRC, an effect that is potentially mediated by the gut microbiome. It was found that men who reported consuming two or more servings of yogurt per week were 19% less likely to develop precancerous growths in the colon compared to men who reported eating no yogurt at all. Furthermore, men who ate two or more servings of yogurt per week were 26% less likely to develop abnormal growths in the colon (but not the rectum) that had a high likelihood of becoming cancerous. The research team found no associations between yogurt consumption and the risk of adenomas in women.

The researchers suggest that yogurt consumption could help to prevent the formation of abnormal growths in the colon in several ways. Two common probiotics used in yogurt, *Lactobacillus bulgaricus* and *Streptococcus thermophilus,* produce enzymes and other substances that may reduce levels of carcinogens such as nitroreductase, fecal activated bacterial

enzymes, and soluble fecal bile acids. The team also linked yogurt consumption to lower levels of inflammation, with yogurt exerting anti-inflammatory effects on the colon mucosa and improving gut barrier dysfunction.

https://www.medicalnewstoday.com/articles/325516.php

EARLY ONSET COLORECTAL CANCER

Colorectal cancer distribution different in young populations (July 28/19)

The incidence of colorectal cancer has had a marked increase among younger adults (<50 years of age) over the past decade. A recent study aimed to better understand the anatomical distribution of colorectal tumours among colorectal cancer patients <50 years of age. It is known that left-sided colorectal tumours differ from those that arise in the right colon in terms of their molecular biology, symptoms and most effective therapies. Through a retrospective review of data from the National Cancer Data Base, it was found that 74.4% of patients <50 years had left-sided colorectal tumours compared to 56.1% of patients >50 years of age. The study demonstrates the changing biology, histology and distribution of colorectal cancer in different patient populations, differences that should be considered in screening and treatment strategies.

Colonoscopy rates increased in those aged 45-54 years (July 17/19)

According to results published in the *Journal of Medical Screening,* though colonoscopy rates increased among those aged 45 to 54 years from 2000-2015, colorectal cancer incidence has **increased** among those aged 40 to 54 years. Future studies will be aimed at better understanding the rising colorectal cancer incidence rates among young adults and monitoring colonoscopy rates among adults aged 45-49 to assess the impact of recent American Cancer Society guidelines lowering the age of recommended screening.

Proportion of CRC diagnoses increased in adults younger than 50 (July 24/19)

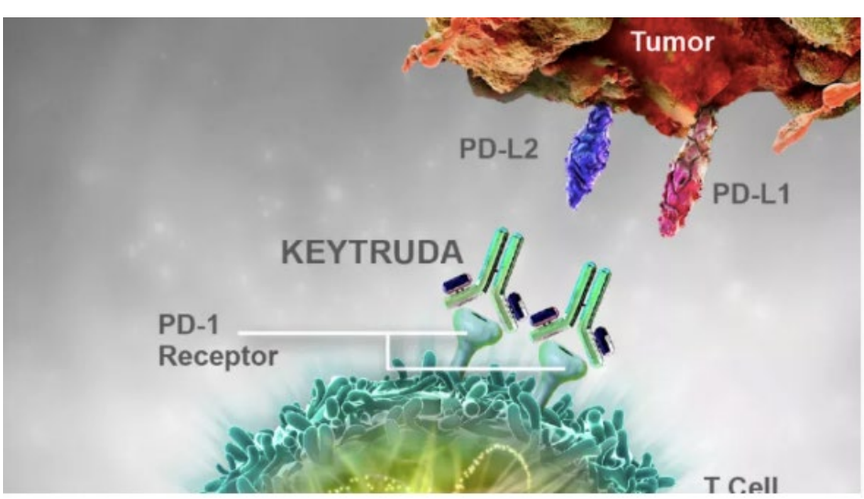
From 2004 to 2015, there was in increased in the proportion of individuals diagnosed with colorectal cancer at an earlier age (<50 years). A study published in *Cancer* found that there was an increase in the proportion of the total number of patients diagnosed with colorectal cancer at a younger age from 10.0% in 2004 to 12.2% in 2015. Furthermore, younger adults presented with more advanced disease than those who were diagnosed at a later age (stage III/IV, 51.6% vs. 40%). Due to the lack of screening, younger adults are more likely to present with and die of advanced disease, a fact that should be considered to keep screening guidelines relevant and up to date.

ONGOING PROGRAMS AND CLINICAL TRIALS

Keytruda – approved by Health Canada for the treatment of MSI-H and dMMR colorectal cancer (July 31/19)

Keytruda (pembrolizumab) is a monoclonal antibody or targeted cancer therapy that is directed against the PD-1 receptor on the cell surface. The drug blocks the PD-1 receptor, preventing the binding and activation by its ligands PD-L1 and PD-L2. By blocking this interaction, T-cell mediated immune responses are activated against tumour cells.

As of April 18, 2019, Keytruda has been issued a marketing authorization with conditions in Canada, pending the results of studies to verify its clinical benefit. The drug is indicated for adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC), whose tumours have progressed following treatment with a fluoropyrimidine, oxaliplatin and irinotecan regimen. For more information on Keytruda: www.keytruda.com, and for Health Canada's Notice of Compliance with conditions – drug products website: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html#k.



Keytruda blocking the PD-1 receptor to prevent interaction with the PD-L1 and PD-L2 ligands, thereby activating T-cell mediated immune responses against tumour cells.

Image source: http://www.pharmaceuticaldaily.com/torque-merck-to-test-keytruda-with-deep-il-15-primed-t-cells/

Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (July 31/19)

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.

http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal-cancer-phase-1-study-cobimetinib-treatment-risk-trial/article/702469/

Clinicaltrials.gov. Study of cobimetinib in combination with atezolizumab and bevacizumab in participants with gastrointestinal and other tumours. NCT02876224. https://clinicaltrials.gov/ct2/show/NCT02876224. Accessed October 24, 2017

Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (July 31/19)

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 Oc :ancer 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

Living donor liver transplantation for unresectable colorectal cancer liver metastases (July 31/19)

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.

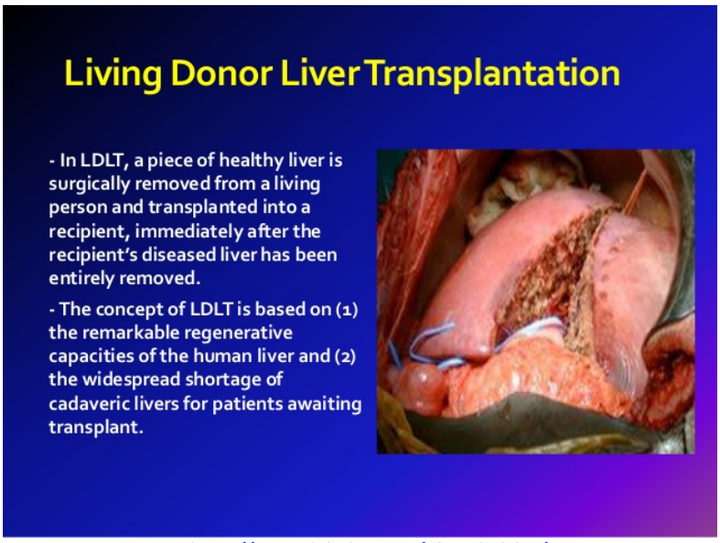


Image Source: ***https://www.slideshare.net/AhmedAdel65/preoperative***

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

Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (July 31/19)

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
A Cancer Care Ontario Partner

CanDirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (July 2019)

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 access the following link:

https://clinicaltrials.gov/show/NCT02890615

Young adult colorectal cancer clinic available at Sunnybrook (July 31/19)

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 consists 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

Exercise for adults diagnosed with rectal cancer: a feasibility study (July 2019)

The purpose of the study is to examine the safety and feasibility of a supervised 12-week exercise intervention for adults diagnosed with rectal cancer. The exercise program will take place at the Behavioural and Metabolic Laboratory (200 Lees Ave., Ottawa) 3x a week and will be tailored to each individual.

Below is the inclusion criteria for the study:

1. Men and women 18 to 85 years of age;
2. Diagnosed with stage I-III rectal cancer and currently undergoing treatment or have completed treatments with the last 5 years;
3. Able to read/understand English or French;
4. Ambulatory;
5. Live <50km of the University of Ottawa;
6. Approval of healthcare provider to participate in the intervention.

Individuals will be asked to complete a brief questionnaire and physical assessments (e.g., resting blood pressure) before and after the 12-week intervention.

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) (July 31/19)

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 ($\geq$150 minutes of moderate-to-vigorous or $\geq$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

High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (July 31/19)

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