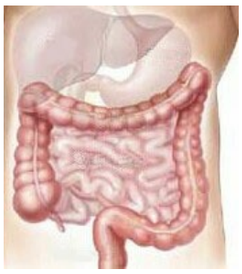
COLORECTAL CANCER CANADA

COLORECTAL CANCER RESEARCH UPDATES

Month Ending August 31st, 2019



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

Table of Contents

DRUGS/SYSTEMIC THERAPIES

Survival and chemotherapy success rates for colorectal cancer (Aug 13/19)

The following table presents the percentages of individuals with colon cancer who undergo treatment involving chemotherapy:

	Colon cancer stage		
Treatment choice	**Stage 1 & 2**	**Stage 3**	**Stage 4**
Colectomy (removal of part or all of the colon) and chemotherapy	10%	67%	40%
Chemotherapy alone	Less than 1%	Less than 1%	26%
Total	Approx. 11%	Approx. 68%	66%

The following table presents the percentages of individuals with rectal cancer who undergo treatment involving chemotherapy:

	Rectal cancer stage		
Treatment choice	**Stage 1**	**Stage 2& 3**	**Stage 4**
Tumour removal/destruction plus chemotherapy and/or radiotherapy	4%	2%	1%
Removal of rectum and/or part of the colon plus chemotherapy and/or radiotherapy	28%	67%	31%
Chemotherapy and/or radiotherapy without surgery	4%	13%	49%
Total	46%	82%	80%

Colorectal cancer survival

The following table presents information about survival rates for people with colorectal cancer, according to its stage at diagnosis:

	Colon cancer stage		
	Localized	**Regional**	**Distant**
% of people with this stage of cancer at diagnosis	39%	36%	20%
5-year relative survival rate	90%	71%	13%

https://www.medicalnewstoday.com/articles/326031.php

Regorafenib dose-escalation strategy vs. standard dosing in colorectal cancer (Aug 10/19)

The phase II ReDOS trial found that a regorafenib dose-escalation strategy compared well with the standard dosing with respect to toxicity and activity in patients with previously treated advanced colorectal cancer (CRC). Regorafenib is an oral kinase inhibitor that is used to treat refractory metastatic cancer, targeting proteins on some normal and cancer cells which are involved in promoting cellular proliferation. Despite its effectiveness, it causes side effects that serve as a barrier to many patients to continue treatment. The ReDOS trial employed a dose-escalation strategy beginning with an 80mg/day dose with a weekly escalation of 40mg increments until 160mg/day, as long as no significant drug-related adverse events occurred. Median overall survival was prolonged by 3.6 months in the dose-escalation group compared to the standard-dose group. The frequency of grade 3 adverse events typically seen with regorafenib was generally lower in the dose-escalation group. A regorafenib dose-escalation strategy provides a potential alternative to optimizing the drug's effectiveness, with comparable activity to standard dosing and a lower incidence of adverse events.

https://www.ascopost.com/issues/august-10-2019/regorafenib-dose-escalation-strategy-vs-standard-dosing-in-colorectal-cancer/

BEACON CRC: Encorafenib/Binimetinib/Cetuximab improves survival in BRAF V600E-mutated metastatic colorectal cancer (Aug 10/19)

Based on findings from the phase III BEACON CRC clinical trial, the combination of three drugs encorafenib (a BRAF inhibitor), binimetinib (a MEK inhibitor) and cetuximab (an EGFR inhibitor) was found to significantly improve overall survival among patients with BRAF-mutated metastatic colorectal cancer (mCRC). Detection of the BRAF V600E mutation via genetic testing has very important prognostic and therapeutic implications for patients with mCRC, as it helps to identify the subgroup of patients who will not receive much benefit from standard treatments and have very poor disease outcomes. In August of 2018, the US food and Drug Administration allowed "Breakthrough Therapy" designation to encorafenib in combination with binimetinib and cetuximab for the treatment of patients with BRAF-mutated mCRC after previous treatment on one or two previous lines of therapy. BEACON CRC is an international study and a multi-institutional collaboration of more than 200 cancer centres. Overall, the researchers found that the triplet combination was well-tolerated by patients without any unexpected toxicities. The triplet therapy increased the median overall survival of patients by 3.6 months, and boosted the objective response rate to 26%, compared to 2% in the control group. Based on the promising outcome of the therapy, the researchers suggest that the triple targeted therapy should be considered as a new standard therapy among this difficult-to-treat patient group. Future studies will be aimed at determining whether this triplet therapy also may benefit patients with less advanced disease or as a first-line treatment.

https://www.ascopost.com/issues/august-10-2019/beacon-crc/

SCREENING

Text instructions and reminders may improve colonoscopy adherence rates (Aug 28/19)

A recent study found that simple text messaging with patients one week prior to a scheduled colonoscopy decreased no-show rates. Using text messaging, the research team found that the rate of colonoscopy adherence increased to 90%, vs. the 62% adherence rate among patients who did not receive any text message reminder. Texting is an appealing tool in

health systems because it can be scaled to large population sizes and it offers opportunities to effectively engage with patients before important health prevention activities. In the study, patients were sent automated messages that included reminders with the office's address, prompts for any questions about the procedure, a nudge to pick up prep materials such as sports drinks and laxatives, and messages to prompt each step of the prep sequence the night before the appointment. If patients responded with questions (75% responded), their questions were forwarded to gastroenterology staff that answered within 24 hours. The researchers commented that texting as a tool to boost screening adherence was so successful because it is a patient-centered strategy. While texting did dramatically increase rates of adherence and was popular among users, the study found that it did not change the quality of the patients' preparation for their colonoscopy compared to those who only received a reminder phone call and paper instructions. Further research will be aimed at evaluating the effectiveness of texting among a larger population.

CRC rates low after negative FIT regardless of cut-off (Aug 22/19)

Data from a population-based screening program demonstrated that incidence of colorectal cancer (CRC) after a negative result from a fecal immunochemical test (FIT) is low, independent of what test threshold is used. The FIT threshold indicates the minimum amount of blood in the fecal sample necessary to qualify for a positive test result, suggesting the presence of CRC or advanced adenomas. While FIT has demonstrated effectiveness in detecting CRC at low positivity cut-offs or at short screening intervals, screening programs will often use higher cut-offs to find a balance between true and false positives (the lower the positivity threshold, the likelihood of false positives increases). In the study, the research team examined data from a Dutch nationwide screening program that started out with a positivity cut-off of 15 micrograms haemoglobin/g feces (Hg/g), and increased the cut-off to 47 micrograms (Hg/g) as the program continued. They found that the incidence of CRC after a negative result was 9.5 per 10,000 in the low cut-off group compared to 13.8 per 10,000 persons in the high cut-off group. The age-adjusted sensitivity of FIT for CRC was 90.5% in the low cut-off group compared to 82.9% in the high cut-off group. The team concluded that their findings demonstrate a high overall sensitivity for FIT to detect CRC, with a low incidence of subsequent CRC after a negative result from FIT. Despite a decline in FIT sensitivity as the test threshold increased, it still remained above 80%.

https://www.healio.com/gastroenterology/oncology/news/online/%7Bfcb8d683-3b40-44a6-a405-0a830447bfd8%7D/crc-rates-low-after-negative-fit-regardless-of-cutoff

Lower FIT threshold increases sensitivity for colorectal cancers (Aug 28/19)

A recent meta-analysis found that by changing the positivity threshold of a fecal immunochemical test (FIT) to 10 micrograms haemoglobin/g feces (Hg/g) or less, rather than the standard 10-20 micrograms Hg/g, could increase the sensitivity for detecting colorectal cancers (CRC) by more than 10%. The Swiss research team behind the study found that the optimal FIT positivity cut-off is not known and is subject to change based on many factors, such as age and sex. This threshold can be adjusted to maximize CRC detection while taking local colonoscopy resources into consideration. In the United States, there are experts that favour a threshold of 20 micrograms Hg/g or less, but this cut-off lacks sufficient evidence to be the standard threshold across the board. The team used data from existing literature that included results from FIT for CRC screening in asymptomatic adults. They were able to observe any changes in CRC detection and quantify them at different positivity cut-offs, as well as by age and sex. They found that sensitivity, or the ability of the test to correctly identify those with CRC or advanced adenomas, increased from 69% to 80% for CRC and from 21% to 31% for advanced adenomas at the lower positivity threshold. Their findings suggest that FIT positivity threshold as low as 10 micrograms Hg/g or less could be considered preferable in settings that have sufficient resources for follow-up colonoscopies.

https://www.healio.com/gastroenterology/oncology/news/online/%7B4c6f91a5-a87b-4ac8-b1bc-e61b6cbd70a1%7D/lower-fit-threshold-increases-sensitivity-for-colorectal-cancers

Intervention improves colorectal cancer screening in rural areas (Aug 12/19)

Results from a recent trial found that a low-cost intervention tailored to the health literacy of the population increased colorectal cancer (CRC) screening among an underserved, rural population. Nationwide screening goals have been set to between 70-80% of eligible adults being up to date with CRC screening. In order to achieve these goals, better strategies will be necessary to improve CRC screening in underserved populations. In the study, 41% of participants were of limited health literacy. Participants received literacy-appropriate CRC education materials as well as patient-friendly screening guidelines, instructions on use of a simplified fecal immunochemical test (FIT), and a FIT kit. Follow-up phone calls were used to prompt participants to complete and mail their FIT kits. Results demonstrated an overall FIT completion rate of 68%. The intervention demonstrated an important step towards the improvement of healthcare among disadvantaged patient populations, and the importance of tailoring screening guidelines based on factors such as socioeconomic status, sex, or health literacy in order to reach the most vulnerable and high-risk populations.

https://www.healio.com/hematology-oncology/gastrointestinal-cancer/news/online/%7B54fe0eab-74fa-4256-a2ce-9f22176110a3%7D/intervention-improves-colorectal-cancer-screening-in-rural-areas?page=2

Cancer screening rates "unexpectedly high" among adults aged 85 years and older (Aug 7/19)

A recent report found that individuals aged 85 years and older participated in cancer screening at "unexpectedly high" rates, despite screening generally not being recommended for this age group. The number of adults aged 85 years and older is projected to nearly triple from 2016 to 2060, as less smoking, better screening and treatment reduce all-cause mortality. Screening is not typically recommended for those above the age of 85 years due to decreased life expectancy, higher rates of complications and limited evidence to support any survival benefit. Despite the limited probable benefit of screening, more than one third of women aged 85 years and older reported that they underwent some form of cancer screening during the last few years. To date, there exists very little data on how to treat this age group, since clinical trials make it very difficult for people in this group to enrol. One of the main challenges with older adults is that they tend to either be over-treated or undertreated, making physician-patient communication a crucial factor when deciding screening and treatment strategies for this group. Depending on the person's current health status and ultimately, what *they* want to do in this particular moment in their life will determine next steps after screening.

Cell-free DNA may aid in early detection, monitoring of various cancer types (Aug 8/19)

Testing for cell-free DNA in the blood is a non-invasive diagnostic tool for patients with cancer. Existing methods of screening, such as colonoscopy, are crucial in the early detection of the disease but compliance is not as high as it could be. A blood-based test could make early screening easier to perform in a real-world setting, potentially reaching more individuals as it requires no preparation and is non-invasive. In studies examining the effectiveness of blood-based screening tests, anywhere from 57% to 99% of cancers could be detected and clinicians were also able to identify where the cancer was coming from. In 75% of cases, the origin of the cancer was correctly identified. By accurately detecting the cancer in the early stages of the disease and identifying where it is coming from, clinicians are better able to determine the most effective treatment strategy. Given the simplicity of administering the test and the use of inexpensive lab methods for analysis, it may be a cost-effective screening option with the potential to reach a much wider population.

https://www.healio.com/hematology-oncology/gastrointestinal-cancer/news/online/%7B74763e1e-00e2-471c-a552-c57ecb8beeab%7D/cell-free-dna-may-aid-in-early-detection-monitoring-of-various-cancer-types?page=2

Implications of different guidelines for surveillance after serrated polyp resection in the US and Europe (Aug 9/19)

Since individuals with serrated polyps and adenomas are at an increased risk of developing new polyps and colorectal cancer (CRC), surveillance (i.e. colonoscopy at specified intervals) after surgery is justified. To date, international guidelines on surveillance after resection of serrated polyps are inconsistent. While the United States Multi-Society Taskforce on CRC base their surveillance guidelines on the specific subtype of serrated polyp that is resected (traditional serrated adenoma, sessile serrated polyp, hyperplastic polyps), the European Society of Gastrointestinal Endoscopy guidelines do not take polyp subtype into consideration. A recent study aimed to examine the implications of this difference. It was found that despite the different criteria used to determine surveillance strategies after serrated polyp resection, most individuals are recommended the same colonoscopy surveillance intervals. This suggests that considering polyp subtype is not a necessary factor in determining appropriate surveillance recommendations.

Long-term risk of colorectal cancer after removal of conventional adenomas and serrated polyps (Aug 7/19)

Individuals who have undergone screening and removal of precursor colorectal cancer (CRC) lesions, such as conventional adenomas or serrated polyps, are advised to follow-up with colonoscopy surveillance to prevent CRC. Guidelines for surveillance intervals after diagnosis of a precursor lesion, especially for individuals who have removed serrated polyps, vary widely and the evidence remains inconsistent. As a result, some high-risk patients may not receive sufficient surveillance, while lower-risk patients may receive surveillance in excess. A recent study examined the association between the first sigmoidoscopy or colonoscopy and subsequent CRC risk. Using data from three large cohort studies, the findings support guidelines that recommend **a repeat of a sigmoidoscopy/colonoscopy within 3 years of a diagnosis of advanced adenoma and large serrated polyps.** In contrast, patients with non-advanced adenoma or small-serrated polyps may not require much more intensive surveillance compared to patients for whom no polyps were found.

Temporal trends and risk factors for postcolonoscopy colorectal cancer (Aug 30/19)

While colonoscopy remains the gold standard in colorectal cancer (CRC) prevention, patients may still develop CRC despite following screening and/or surveillance intervals. Currently, there is limited evidence on how to predict postcolonoscopy CRC, which is defined as any CRC that is diagnosed in between guideline-recommended screening/surveillance intervals. A recent study aimed to compare patients with postcolonoscopy CRC to those with spontaneous CRC to measure postcolonoscopy CRC rates and identify any risk factors. The findings from the study found that postcolonoscopy CRC rates have been on the rise in recent years. Postcolonoscopy CRC was found to be more common among older patients and those identified to have proximal, early-stage tumours. Furthermore, it was found that a large proportion of postcolonoscopy CRCs are diagnosed by a different physician from the physician who did the first colonoscopy, suggesting that many physicians are unaware of their own patients' postcolonoscopy CRC. Further research will be needed to better understand how to predict and prevent postcolonoscopy CRC.

ctDNA testing now valuable tool in CRC, next steps underway (Aug 19/19)

Detecting circulating tumour DNA (ctDNA) via liquid biopsy (blood test) can be used during all phases of a patient's journey with cancer, serving as a non-invasive screening tool for colorectal cancer (CRC) as well a means to monitor patients

diagnosed with the disease. Current research on the role of ctDNA in CRC treatment is showing increasing promise in the advanced metastatic disease setting. More tests are being developed for early-stage disease that are more sensitive, enabling physicians to better characterize the cancer and employ a more tailored treatment strategy. The vast majority of current clinical trials and data on the role of ctDNA are examining the role of liquid biopsy tests in the early-stage and adjuvant settings where patients who may need to be put on a more aggressive treatment regimen can be identified as soon as possible. Furthermore, ctDNA and liquid biopsy testing can serve as a dynamic marker of patient response to treatment, and then as a means of surveilling patient response after they have been offered therapy. ctDNA testing for cancer prevention and surveillance is a promising new tool which has the potential to reach a greater patient population thanks to its applicability throughout one's cancer journey and its relative simplicity and non-invasiveness compared to other screening tests.

https://www.onclive.com/web-exclusives/ctdna-testing-now-valuable-tool-in-crc-next-steps-underway?p=2

OTHER

Antibiotics and bowel cancer: study finds a link (Aug 21/19)

Despite the development of increased antibiotic resistance worldwide, the use of oral antibiotics continues to grow. From 2000-2010, consumption increased by 35%. Over recent years, the significant role that gut bacteria play in maintaining overall health has become more established. When antibiotics kill off colonies of beneficial bacteria, it makes room for other bacteria including pathogenic or harmful bacteria to colonize. Currently, there is a growing body of evidence that link the use of oral antibiotics to the risk of developing colorectal cancer. A recent study aimed to better examine the relationship between antibiotic use and cancer risk. Using extensive data from large health databases from the United Kingdom, the researchers found that participants who eventually developed colon cancers were slightly more likely to have been exposed to antibiotics compared to the no antibiotic exposure (71.3% vs. 69.1%). It was found that taking even a single course of antibiotics might boost- albeit slightly – the risk of developing colon cancer, but not rectal cancer, a decade later. There was approximately 8% increased risk of colon cancer with 15 to 30 days of total antibiotic exposure and approximately 15% increased risk of colon cancer with 30 or more days of total antibiotic exposure. The relationship between antibiotic use and rectal cancer risk was found to be inversely related – the more total antibiotic exposure – specifically, total exposures of 60 days or more – the less likely the person was to develop rectal cancer. These findings shed more light on the significant role that the gut microbiome may play in the development colorectal cancer.

Abdominal fat and mortality in patients with colorectal cancer (Aug 1/19)

Among patients with colorectal cancer, new research suggests a stronger link than previously known between abdominal fat deposits and higher rates of death from all causes within 7 years of cancer diagnosis. The researchers highlight that patients with colorectal cancer and their oncologists need to know how obesity and body composition can predict clinical outcomes of their disease. A better understanding of this correlation can help patients answer simple questions such as whether or not losing weight will actually influence their disease outcome. In the study, researchers found that the accumulation of abdominal and subcutaneous fat tissue increased the risk of mortality among patients with colorectal cancer. Female patients with colorectal cancer with a high amount of abdominal or visceral fat were more than twice as likely to die within 7 years of diagnosis compared to female patients with very little visceral fat. Among men with colorectal cancer, those with a high amount of subcutaneous fat (fat localized just below the skin) were more than twice as likely to die within 7 years of diagnosis compared to male patients with very little subcutaneous fat. These results demonstrate the differences in fat distribution and colorectal cancer risk as they vary by sex, offering insight into the potential biological mechanisms behind obesity and clinical outcomes among patients with colorectal cancer.

https://www.ascopost.com/News/60297

NUTRITION/ HEALTHY LIFESTYLE

Frying oil consumption worsened colon cancer and colitis in mice, study shows (Aug 23/19)

A recent study from the University of Massachusetts at Amherst found that feeding frying oil to mice exaggerated colonic inflammation, enhanced tumour growth and worsened gut leakage, spreading bacteria and/or toxic bacterial products into the bloodstream. The findings do not imply that frying oil can *cause* cancer, but rather that it may exacerbate and advance existing conditions of the colon. In their experiments, the researchers used samples of canola oil which had been used to fry falafel at the standard 325 F in a commercial fryer. Canola oil is a widely used vegetable oil for frying in North America. The mice that were fed on a diet combining frying oil and fresh oil, in addition to the standard diet, experienced worsened colonic inflammation, colon tumour growth and gut leakage compared to the control group which was fed only the standard diet plus fresh oil. The tumours doubled in size from the control group to the experimental group.

To test a hypothesis that it is the high level of oxidation of polyunsaturated fatty acids which occurs when the oil is heated to high temperatures that is instrumental in the inflammatory effects, the researchers isolated oxidized fat compounds from the frying oil and fed them to the mice. The resulting health effects were very similar to those from the previous

experiment where mice were fed frying oil, suggesting that the oxidized compounds may mediate the inflammatory effects. Further research will be needed to consolidate the findings, though among individuals with or prone to inflammatory bowel disease, the researchers suggest that is probably a good idea to avoid eating fried foods whenever possible.

Chemicals found in vegetables prevent colon cancer in mice (Aug 14/19)

A new study shows that chemicals produced by vegetables such as kale, cabbage, and broccoli could help to maintain a healthy gut and prevent colon cancer. In the study, mice were fed on a diet rich in indole-3-carbinol (I3C), a chemical that is produced when we digest vegetables from the Brassica genus. These mice developed protection from gut inflammation and colon cancer. While the health benefits of vegetables are widely accepted, many of the mechanisms underlying their protective effect remain unknown. In the study, the researchers found that the chemical I3C activates another protein which effectively "turns on" an immune response in the gut lining to protect the organism from inflammatory responses. Using mouse models, it was found that mice that lacked this specific protein readily developed gut inflammation which progressed to colon cancer. Furthermore, when mice that already had cancer were switched to an I3C-enriched diet, they ended up which significantly fewer tumours, many of which were found to be benign. The study findings suggest that it is not just the fibre content of vegetables that help to reduce the risk of colorectal cancer, but also the specific health-promoting molecules found in these foods. Further research will be aimed at investigating whether the molecules in these vegetables have the same effect in humans, but in the meantime there are many good reasons to be eating more vegetables.

Does exercise improve outcomes in patients with metastatic colorectal cancer? (Aug 19/19)

A new study found that patients with metastatic colorectal cancer who participated in moderate exercise while undergoing chemotherapy tended to have delayed progression of their disease and fewer severe side effects from treatment. Engaging in even low-intensity exercise, such as walking 4 or more hours a week, was associated with a nearly 20% reduction in cancer progression or death throughout the course of the 6-year study. Total physical activity equivalent to 30 or more minutes of moderate daily activity was associated with a 27% reduction in severe treatment-related toxicities. Physically active patients in the study also seemed to tolerate chemotherapy better. Progression-free survival was almost 20% greater among those who exercised more during treatment. Such findings help to justify encouraging patients to exercise and referring patients to physical therapists or small-group training directed at patients living with cancer.

EARLY ONSET COLORECTAL CANCER

Colorectal cancer on the rise among younger Canadians (Aug 3/19)

Findings from a recent study identified a growing incidence of colorectal cancer (CRC) diagnoses among Canadian men and women below the age of 50. While overall rates among younger adults are still lower than older adults, the findings suggest that younger individuals are experiencing the highest rates of CRC incidence ever recorded in Canada. The research team found that when men in the youngest cohort were compared to men from the older cohort, the younger men had more than double the risk of developing CRC. Among women, the difference in incidence rates were not significant, but did increase in successively younger age groups. Given that these changes are occurring in such short timeframes, it is unlikely that they can be explained by genetic changes occurring in the population. The likely causes are modifiable risk factors such as lifestyle influences, including overweight and obesity being observed at much younger ages than in previous generations. Poor diet consisting of an increased consumption of processed foods and a decreased consumption of fibre and key nutrients may also be an important contributing factor.

Younger CRC patients more likely to present with abdominal pain (Aug 13/19)

According to a recent study, younger patients with CRC are more likely to present with abdominal pain and via an emergency. The research team compared the interval before diagnosis, presenting symptoms, and likelihood of an emergency diagnosis for those under age 50 and older patients. Not only were younger patients more likely to present with abdominal pain and via an emergency, they also had the lowest percentage of early-stage cancer. Compared to older patients aged 60-69 years, younger patients tended to undergo a longer period between referral and diagnosis of CRC, indicating a higher proportion of non-urgent referrals. If the symptom identified was nonspecific (i.e. not indicative of CRC in and of itself), the likelihood for an emergency diagnosis increased significantly for young patients. In a time when the incidence of CRC among younger adults is on the rise, primary care physicians should be increasingly attentive to any warning symptoms to help reduce missed signs that could prevent emergency and late-stage diagnoses.

Trends in the age at diagnosis of colorectal cancer (Aug 8/19)

In the United States, the incidence of colorectal cancer (CRC) in adults younger than 50 years has increased over the past decades. A retrospective study examined data from the National Cancer Data Base from 2004 to 2015. It was found that the number of cases of CRC among individuals younger than 50 increased from 2004 and 2015, and the increase was seen in both white men and women, but not among African Americans or Asians. Individuals of all socioeconomic backgrounds

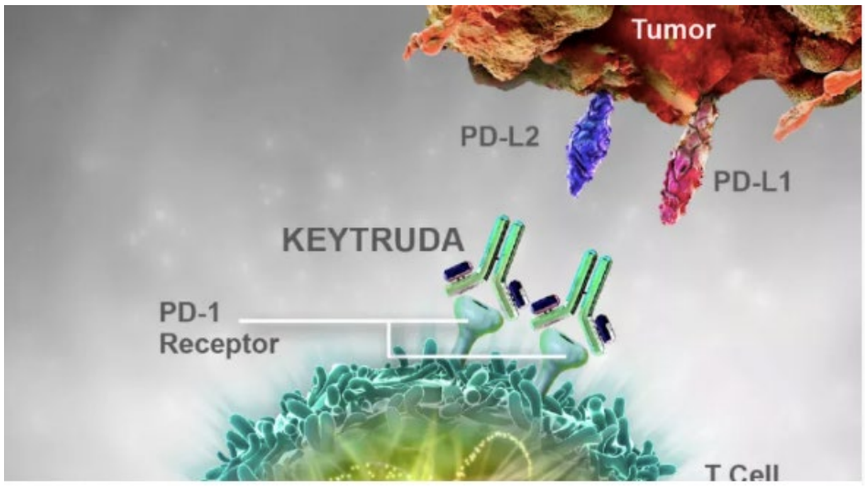
had a proportional increase in younger adult cases over time. It was also found that the proportion of younger onset disease increased in urban areas but not in rural ones. Such early-onset CRC accounted for 12% of all CRC cases. Early-onset CRC were more likely to be found in the rectum and also more likely to be diagnosed at more advanced stages. These data add to the growing body of evidence that warrant further discussion of potential changes to national screening guidelines to begin CRC screening at an earlier age.

ONGOING PROGRAMS AND CLINICAL TRIALS

Keytruda – approved by Health Canada for the treatment of MSI-H and dMMR colorectal cancer (August 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 (August 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 (August 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 (August 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.

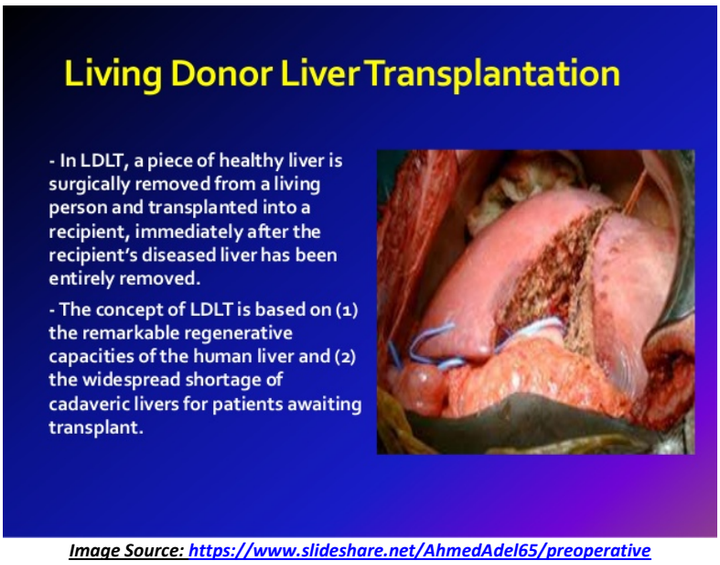


Image Source: https://www.slideshare.net/AhmedAdel65/preoperative

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 (August 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 (August 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 (August 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 (August 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 (August 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