The following colorectal cancer research updates extend from Oct 18th, 2018 to Jan 17th, 2019 inclusive and are intended for informational purposes only.

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**DRUGS / SYSTEMIC THERAPIES**

1. No benefit for atezolizumab plus standard of care for maintenance in colorectal cancer subset (Dec 10/18)

The addition of atezolizumab (Tecentriq) to a fluoropyrimidine plus bevacizumab (Avastin) regimen did not demonstrate improved outcomes for patients with BRAF wild-type metastatic colorectal cancer (CRC) in the MODUL trial. Atezolizumab is a monoclonal antibody which binds to the programmed cell death ligand 1 (PD-L1) receptor, blocking its function to suppress the immune system. Many cancer cells may overexpress PD-L1 on their surface, therefore minimizing the immune system’s attack against them. While atezolizumab has shown positive activity in other immune-responsive tumour types, there were no improvements to progression-free survival or overall survival when it was included in CRC maintenance therapy.

The basis of the phase II MODUL study was to identify and evaluate molecular screening approaches and biomarkers for their ability to characterize tumours and identify which patients with metastatic CRC are most likely to benefit from targeted therapies. In the study, patients with unresectable, previously untreated metastatic CRC received 16 weeks of induction treatment with FOLFOX (fluoropyrimidine, leucovorin, oxaliplatin) plus bevacizumab followed by maintenance therapy with fluoropyrimidine plus bevacizumab (control arm) or the experimental treatment which added atezolizumab. Atezolizumab promotes T-cell (a type of white blood cell that recognizes antigens/foreign molecules and initiates an immune response) activation and restores the immune system’s attack on cancer cells. Bevacizumab promotes the maturation of dendritic cells (immune cells which present antigen material to the T cells), normalizes and limits the tumour blood vessel system, and reduces the activity of immunosuppressive cells. Through a combination of these two agents, the researchers aimed to achieve a synergistic effect to reverse immune suppression and promote T-cell infiltration to the tumour.

In the study, 696 patients received induction treatment. 445 patients with BRAF wild-type tumours were randomly assigned to maintenance treatment: 148 received fluoropyrimidine/bevacizumab, and 297 received fluoropyrimidine/bevacizumab plus atezolizumab until disease progression. No differences were observed between the control and the experimental group, indicating that the addition of atezolizumab to maintenance therapy did not cause any improvements to progression-free survival or overall survival. The researchers noted that one patient with a microsatellite instability-high (MSI-H) tumour had a complete response. They stated that almost all patients in the study had microsatellite stable (MSS) tumours, suggesting that further efforts are necessary to develop new strategies for navigating the complicated immune mechanisms in patients with MSS CRC.

2. FDA approves Vitrakvi (larotrectinib), the first ever TRK inhibitor, for patients with advanced solid tumours harbouring an NTRK gene fusion (1,2) (Nov 26/18)

The FDA has approved the drug Vitrakvi (larotrectinib) which has shown a 75% overall response rate across various solid tumours in adults and children regardless of tumour size or grade. Vitrakvi is the first oral TRK inhibitor, which can be used in the treatment of solid tumours with neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known resistance mutation; tumours that are metastatic or where surgical removal presents severe risks; and in cases without satisfactory alternative treatments/ or those that have progressed following treatment.

NTRK gene fusion is a rare driver of cancer that fuses with genes causing overexpression of the TRK protein. The TRK fusion proteins then act as drivers of malignant growth by promoting cell proliferation and survival, leading to TRK fusion cancer. Overexpression of the protein is involved in mechanisms underlying increased tumour cell survival and proliferation. Vitrakvi, developed by Bayer and Loxo Oncology, Inc, is an active TRK inhibitor that inhibits the production of these proteins. In clinical trials, Vitrakvi showed clinical benefit across numerous tumours types including gastrointestinal cancers (colon, cholangiocarcinoma, pancreatic and appendiceal). While TRK fusions are rare, they do occur across many different tumour types. In firstline settings, Vitrakvi has been well-tolerated by most patients. The drug does have warnings and precautions of neurotoxicity, hepatotoxicity and embryo-fetal toxicity. The most commonly observed adverse events occurring in more than 20% of patients were increased ALT and AST (signs of liver damage), anemia, fatigue, nausea, dizziness, cough, vomiting, constipation, and diarrhea. The majority of adverse events that occurred in 10% or more of patients were grade 1 and 2. Vitrakvi will be available in the US market immediately. For further information about the larotrectinib clinical trials, please refer to:

https://clinicaltrials.gov/ct2/show/NCT02637687


3. FOLFIRI plus Regorafenib in metastatic colorectal cancer (Jan 14/19)

Findings from a study published in Cancer suggest that the addition of second-line regorafenib to folic acid, fluorouracil, and irinotecan (FOLFIRI) treatment “only modestly prolonged” progression-free survival for patients with metastatic colorectal cancer (mCRC) when compared to FOLFIRI alone. When used as a single agent, regorafenib had been shown to prolong survival in patients with refractory CRC. In the study, a total of 181 patients with mCRC were randomly assigned to receive FOLFIRI with either regorafenib or placebo. Of the 181 participants, 117 (65%) received bevacizumab or aflibercept prior to the study. The treatment arm receiving regorafenib/FOLFIRI did experience a longer progression-free survival (6.1 months vs. 5.3 months) as well as a higher response rate (34% vs. 21%) when compared to the placebo group. The regorafenib arm did not experience an increased overall survival rate. The researchers suggested that, “The added toxicity cost from this combination leads to frequent dose reductions, which likely account for the lack of an overall survival benefit.” Diarrhea and neutropenia comprised the grade 3 or 4 adverse events that had a greater than 5% increase in the regorafenib group. The researchers concluded that further study will be necessary to achieve a balance between the benefit, in terms of slowing tumour progression and improving survival, and quality of life.

https://jnccn360.org/colorectal/medical-literature/folfiri-plus-regorafenib-in-metastatic-crc/

4. BAY 1834942 is an immunotherapeutic antibody blocking the novel immune checkpoint regulator CEACAM6 (CD66c) (Dec 20/18)

CEACAM6 is a protein that is strongly expressed at the tumour cell surface in multiple cancer types such as non-small cell-lung adenocarcinoma, colorectal carcinoma (CRC), gastric adenocarcinoma and pancreatic cancer. In general, higher CEACAM6 expression is associated with more advanced tumour stages and poor prognosis. The protein has been previously shown to act as a novel immune checkpoint regulator, suppressing the activity of T cells against tumours. Based on these findings, a German research team aimed to test the effectiveness of antibodies targeting CEACAM6 in order to restore T-cell responses against
CEACAM6-expressing cancers. A human monoclonal antibody, BAY 1834942, was found to selectively block the inhibitory effect of CEACAM6 on human T cells. The researchers found that BAY 1834942 increased secretion of T cell signalling molecules in tumour cell/T cell cultures in vitro, resulting in improved tumour cell destruction. CEACAM6 has no equivalent in rodents, which impeded in vivo testing of the drug during the study. The effect was dose-dependant, and the effects could be reproduced in experiments using tumour cell lines and T-cell preparations from different sources, including T cells derived from immune cells from pancreatic cancer. BAY 1834942 was well-tolerated in monkey toxicology studies. In conclusion, BAY 1834942 is a novel checkpoint inhibitor that has the potential for the treatment of patients with CEACAM6 expressing cancers, as a single agent and in combination with other immune checkpoint inhibitors. The first human clinical trials began in 2018. For more information on the clinical trial, please visit:


Joerg Willuda, Marta Tautweins, Jessica Pinkert, Wolf-Dietrich Doecke, Hans-Honning Boehm, Florian Wessel, Yingzi Ge; Eva Maria Gutierrez, Joerg Weiske, Christoph Fredberg, Uwe Gritzan, Julian Glueck, Oliver von Ahsen, Ruprecht Ziere, Sabine Wittmer-Rump, Heiner Apeler, Ziegelbauer Karl, Rianek Offringa, Bertolt Kraft, Beckhove Philipp. BAY 1834942 is an immunotherapeutic antibody blocking the novel immune checkpoint regulator CEACAM6 (CD66c) [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2018; 2018 Apr 14-18; Chicago, IL. Philadelphia (PA): AACR; Cancer Res 2018;78(13 Suppl):Abstract nr 177.

https://www.researchgate.net/publication/327083541_Abstract_1771_BAY_1834942_is_an_immunotherapeutic_antibody_blocking_the_new_immune_checkpoint_regulator_CEACAM6_CD66c

5. Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Jan.16/19)

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.


6. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Jan.14/19)

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 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

7. Study shows declining efficacy of prophylactic antibiotics to prevent SSIs following colorectal surgery (Nov 15/18)

According to evidence from a systematic review published in *Infection Control & Hospital Epidemiology*, the efficacy of antibiotics in the prevention of surgical site infections (SSIs) after colorectal surgery has declined. In recent years, there has been a growing concern that drug resistance would make surgeries and transplants difficult to perform due to the greater risk of untreatable, drug-resistant infections. The researchers analyzed PubMed and Cochrane databases for randomized controlled trials (RCTs) that examined the efficacy of antibiotic prophylactic measures in preventing postoperative SSIs for three commonly performed surgical procedures – appendectomy, caesarean section and colorectal surgery. They found a significant increase in SSIs over time after colorectal surgery, while no observed statistically significant increases in SSIs over time were found for appendectomy or caesarean section. They noted, however, that the small number of RCTs and low infections rates limited their ability to determine the true effect of antibiotics in the latter procedures. Further evidence will be necessary to better understand how the efficacy of antibiotic prophylaxis is changing over time.


8. Living donor liver transplantation for unresectable colorectal cancer liver metastases (Jun. 1/18)

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

![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

RADIATION THERAPIES/INTERVENTIONAL RADIOLOGY

9. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Jun 1/18)

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

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

SCREENING

10. Opting out of cancer screenings linked to increased overall mortality (Dec 28/18)

Based on research published in *JAMA Internal Medicine*, patients who did not follow recommended cancer screening tests were at a significantly higher risk of dying from other causes. The lead researchers suggest that when patients do not follow chronic disease prevention guidelines, it is a marker for a general behavioural profile of not following medical tests and treatments and that this type of behaviour is associated with increased mortality. In the study, the researchers randomly assigned patients from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening trial aged 55 to 74 at 10 screening centres in the United States to either an intervention or control group from 1993-2001. Participants in the intervention arm received protocol screening tests, including chest radiographs and flexible sigmoidoscopy. Participants were categorized as either fully adherent (received all specific screening tests), partially adherent (received some but not all tests) or nonadherent (received no tests). 85.3% of participants were fully adherent, 3.9% were partially adherent and 10.8% were nonadherent. After excluding deaths from cancers and controlling for age, sex, and race/ethnicity, the researchers found that during the 10 years of follow-up, the hazard ratios of mortality were 1.73 for nonadherent participants (i.e. patients in this group were 1.73 times more likely to die) and 1.36 for partially adherent participants compared to patients who were fully adherent. The researchers concluded that by observing cancer screening adherence status, a statistically significant and clinically important difference in
all-cause mortality was found. Future studies will be aimed at investigating this association in clinical settings beyond the context of a research trial.

https://www.healio.com/internal-medicine/oncology/news/online/%7b7b5c6f46d3-0a1d-4ed7-9a3e-70ecf350d52a%7d/opting-out-of-cancer-screenings-linked-to-increased-overall-mortality

11. Million-strong study supports CRC screening every 10 years (Dec 24/18)

Findings from a recent study supported the efficacy of guideline recommendations to screen for colorectal cancer (CRC) once every 10 years in reducing overall risk of developing the disease compared to unscreened individuals. The researchers evaluated more than 1.2 million Californians between the age of 50 and 75 years who were enrolled in a health plan. They compared unscreened individuals with those who had a negative colonoscopy result over a 10-year period. The study results demonstrated that the relative risk of developing CRC among people with a negative result at 10 years was 46% lower than that for unscreened individuals, while the relative risk of CRC death was 88% lower. Furthermore, the risk of proximal CRC was 20-87% lower and the risk of distal cancer was 50-99% lower in the negative colonoscopy group during follow-up compared to the unscreened group. The researchers commented that these findings suggest that clinicians can feel confident about the guideline-recommended 10-year re-screening interval after a negative colonoscopy in which no CRC or polyps are found. This large study presents solid evidence with a high enough number of average-risk individuals to effectively evaluate cancer risks after colonoscopy compared to no screening. Furthermore, the study findings provide greater certainty regarding the appropriate timing for rescreening after a negative colonoscopy, indicating that a 10-year interval is pretty effective.

https://www.medscape.com/viewarticle/906935#vp_2

https://www.healio.com/internal-medicine/oncology/news/online/%7be81624e1-94d2-42cc-a26a-803794284f7d/negative-colonoscopy-linked-to-lower-colorectal-cancer-risk-after-12-years

12. Multicomponent interventions increase colorectal cancer screening rates (Oct 2018)

According to findings from a study published in *JAMA Internal Medicine*, a combination of interventions, specifically those that include fecal blood test outreach and patient support in navigating screening guidelines, were linked to improvements in completion of colorectal cancer (CRC) screening. Despite being recommended by all major medical organizations in the US, CRC screening remains underused. The researchers conducted a systematic review and meta-analysis of 73 randomized clinical trials included 366,766 patients to identify interventions that improved CRC screening rates. The trials had low or medium risk of bias and evaluated completion of CRC screening, colonoscopy after an abnormal initial screening test result and continued rounds of annual fecal blood tests. The researchers found that improved CRC screening completion rates were linked to the following interventions: fecal blood test outreach, patient navigation, patient education, patient reminders, and clinician reminders. Multicomponent interventions demonstrated greater increases in screening completion than single component interventions. For example, when fecal blood tests with patient navigation were mailed repeatedly, annual fecal blood test completion increased. The researchers concluded that combined interventions can be the foundational tools to meet the national goal of reducing CRC burden and disparities in the country. Future research is necessary to understand how to best implement and scale these strategies at the national level, and to determine their cost-effectiveness.

https://www.healio.com/internal-medicine/oncology/news/online/%7b1ea6f763-b07c-408a-b36c-57cdeb8aad4%7d/multicomponent-interventions-increase-colorectal-cancer-screening-rates
Nearly 100 genetic variants linked to colorectal cancer risk (Dec 28/18)

Researchers from the Fred Hutchinson Cancer Research Center have identified 40 new genetic risk variants bringing the total to nearly 100 variants that influence the risk of colorectal cancer (CRC). While each individual genetic risk variant has a relatively insignificant effect, when these variants are combined into a polygenic risk score, it is possible to identify individuals at high and low risk. Then, those at higher genetic risk can be set up for a personalized early screening program or chemoprevention.

The research team included an international array of more than 200 researchers. The team examined data from 125,000 individuals to explore the catalogue of CRC risk variants and to improve our understanding of rare variants, genes and pathways that influence sporadic CRC risk. 40 new genetic loci (positions on a chromosome
which mark the position of a gene or marker) were characterized. Heritability studies suggest that many rare and common variants have yet to be studied, given that those identified so far explain only about 20% of the variation in susceptibility to CRC. An important implication of the study findings lies in the potential for drug-target discovery. Each of the risk loci identifies specific genes, some of which can be targeted for new drug discovery. Studies have shown that the success rate of new drugs is substantially improved when based on human genetic findings such as these. The researchers noted, however, that the study was predominantly conducted in participants of European descent, which limits the application of the polygenic risk score to non-European populations. Adding more diverse populations to the study will allow for the identification of more genetic risk loci. The researchers concluded that substantial progress in understanding the genetic architecture of CRC has been made, demonstrating that CRC is polygenic and that these findings can be used for personalized medicine. Larger experiments that include whole genome sequencing to discover more genetic risk loci will be necessary in order to provide a more complete picture of the underlying pathways and genes linked to the disease.


14. **FIT could reduce colonoscopies by 70% but may miss 30% of cancers (Dec 12/18)**

The annual fecal immunochemical test (FIT) for colorectal cancer (CRC) surveillance among patients with intermediate risk for the disease could reduce colonoscopies and save on healthcare spending, but researchers have warned that they may come at the cost of missed cancers. A recent study published in *Gut* compared the accuracy of FIT with colonoscopy to weigh the disadvantages and advantages of each test. CRC surveillance with colonoscopy places a great demand on endoscopy services. Furthermore, while colonoscopies are the gold standard in CRC screening and undoubtedly help to reduce incidence of the disease, they can lead to fear, anxiety and discomfort among patients. FIT is a useful strategy for CRC screening among patients with average risk, as it tends to boost compliance rates due to its non-invasive nature and the fact that it can be completed from the comfort of one’s home. The test, however, is not as accurate in identifying pre-cancerous or CRC lesions as colonoscopy.

In the study, researchers recruited patients of average risk for CRC who were recommended to undergo CRC surveillance every 3 years. Researchers offered patients FIT at years 1, 2, and 3. Individuals who tested positive at years 1 or 2 were offered an early colonoscopy. The researchers calculated the cost per additional adenoma and CRC detected by colonoscopy compared with FIT. They found that if annual FIT was implemented instead of colonoscopy every 3 years, numbers of colonoscopies could be reduced by more than 70% with significant cost savings. This would come, however, at the cost of missed advanced colorectal neoplasia, and depending on the threshold, annual FIT could miss 30-40% of CRCs and 40-70% of advanced adenomas. Encouraging a healthy dialogue between patients and their clinicians is an essential factor in boosting CRC screening outcomes. Helping patients navigate screening guidelines to make the most sensible choice with respect to which method is best suited to the individual’s unique needs remains an important step in tailoring screening as efficiently as possible. As such, whether it be through FIT or the most costly colonoscopy, these preventative methods can help to avoid the far greater economic and personal costs to quality of life that arise once the disease has taken hold.

https://www.healio.com/gastroenterology/oncology/news/online/%7bb4be711e-87f4-4d99-a688-1c3a796f9f57d/fit-could-reduce-colonoscopies-by-70-but-may-miss-30-of-cancers

15. **Update on ACS colorectal cancer screening guideline: start screening at age 45 (Oct.19/18)**

Since 1994, there has been a 51% increase in colorectal cancer (CRC) among individuals 50 years old or younger. In response to this rise in earlier-onset CRC, the American Cancer Society (ACS) has updated its colorectal screening guidelines, suggesting that screening should begin at age 45 for people at average risk. For adults of average-risk who are in good health with a life expectancy beyond 10 years, CRC screening should continue until the age of 75, beyond which conversations between the individual and the clinician are necessary to weigh the risks and benefits of screening. The guidelines indicate that adults aged 45 and older with an average risk of CRC should undergo regular screening with either a high-sensitivity stool-based test or a colonoscopy or sigmoidoscopy, depending on patient preference and the availability of tests. The recommended options for CRC screening are:

- Fecal immunochemical test annually;
- High-sensitivity guaiac-based fecal occult blood test annually;
- Multitarget stool DNA test every 3 years;
• Colonoscopy every 10 years;
• Computed tomography colonography every 5 years;
• Flexible sigmoidoscopy every 5 years.

Based on epidemiological trends among individuals as young as those born in 1990, a higher risk of developing CRC will be a lasting concern for the decades to come.


PSYCHOSOCIAL

16. Risk for suicide increased in year after cancer diagnosis (Jan 9/19)

According to a recent study published in Cancer, patients who receive a cancer diagnosis have an increased risk for suicide during the first year after their diagnosis, with higher suicide rates for cancers with a poor prognosis. The researchers examined trends in suicide risk following a cancer diagnosis using data from the Surveillance, Epidemiology, and End Results Program. Data from 4, 671, 989 patients diagnosed with cancer between 2000 and 2014 were included. The researchers discovered that 1,585 patients committed suicide within one year of their diagnosis. The highest suicide risks came after diagnoses of pancreatic, lung and colorectal cancers. The study findings demonstrate the importance of patient access to social and emotional support following a cancer diagnosis. The researchers suggest that it is important that health care providers be vigilant of signs of suicide and refer patients to available support networks as they begin their cancer journey.


17. CanDirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Jan.1/19)

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

OTHER

18. Helicobacter pylori and colorectal cancer risk among diverse populations (Nov 19/18)

Findings from a study published in Gastroenterology found that specific strains of the bacteria Helicobacter pylori were found to be linked to increased risk of developing colorectal cancer (CRC), with risk varying between different races/ethnicities. In the study, H. pylori samples from 4,063 cases of CRC and 4,063 matched controls were analyzed using serologic assays. The majority of the study participants were white (75%), with 10% African American, 8% Asian, and 5% Latino. For both control and CRC groups, 4 in 10 cases of CRC were H. pylori seropositive. In general, H. pylori seropositivity varied substantially by race/ethnicity, being lowest among whites and Asian Americans and higher in African Americans and Latinos. The presence of
four *H. pylori* proteins – VacA, GroEL, Omg, and HcpC – were significantly associated with 10% to 11% increased risk of CRC, but differed between races/ethnicities. When a strong antibody response was produced against *H. pylori* factor VacA, it was significantly associated with increased CRC risk, with those in the highest quartile of antibody response linked to a 25% higher chance of developing the disease. The researchers found that the presence of greater quantities of VacA antibodies increased the risk of CRC in African Americans and Asian Americans, but not significantly among whites and Latinos. The study results point to new questions regarding differences in bacterial composition in the body based on genetic origin or heritage, and how this could impact the way cancer pathways manifest.


19. The impact of bariatric surgery on cancer incidence (Dec 21/18)

A study published in the *British Journal of Surgery* aimed to compare cancer frequency after various types of obesity-related surgery in 8794 obese patients compared to an equal number of unoperated obese patients. After a median follow-up of 55 months, the risk for hormone-related cancers was significantly reduced in the operated group compared with the unoperated group. The risk reduction for hormonally dependant cancers was observed in both males (prostate) and females (breast, endometrium) with the benefits being more pronounced with increasing duration of follow-up. For colorectal cancer following gastric bypass, however, there was an overall increase in the risk of the disease. Gastric bypass is one of the most common procedures performed by general surgeons today, and was found to have more than doubled the risk of developing colorectal cancer. Further studies with longer follow-up and a larger population size will be necessary to confirm the findings which suggest that the age for colorectal cancer screening following bariatric surgery should be lowered.


20. Environmental factors, gut microbiota, and colorectal cancer prevention (Jan 2/19)

The increasing incidence of colorectal cancer (CRC) among young adults highlights the importance of lifestyle modification as a complement to screening in the prevention of CRC. Certain dietary and lifestyle factors, such as the consumption of red and processed meats, have been linked to the development of CRC possibly through intricate metabolic and inflammatory mechanisms. The gut microbiota has been recognized as a key metabolic and immune regulator that has been implicated in colorectal tumorigenesis. An increasing body of evidence supports that environmental factors such as diet play an important role in altering the gut microbial composition and function, which can in turn induce changes in the body’s gene expression, metabolic regulation and local and systemic immune response – all of which may influence cancer development. A study published in *Clinical Gastroenterology and Hepatology* aimed to review the epidemiologic evidence with respect to diet and lifestyle and the gut microbiota in the development of CRC. The researchers focused on factors which have substantial data supporting their role in modifying the gut microbiota and their importance in CRC, such as overweight and obesity, physical activity, dietary patterns, fiber, red and processed meat, omega-3 fatty acid, alcohol and smoking. They found however, that due to limitations in available evidence, further investigations will be necessary to draw conclusions on the relationship between environmental factors, gut microbiota and CRC. Such findings could be important in the development of potential microbiota-based strategies for cancer prevention for the future.

21. Folic acid inhibits colorectal cancer cell migration (Jan 2019)

Folate (vitamin B9, folic acid) is an important nutrient that plays a role in regulating DNA replication and is required for numerous bodily functions. Folate deficiency has been linked to the development of atherosclerosis, neural tube defects and cancers. Effects of folic acid supplements on the risk of colorectal cancer have been studied in depth, but existing data has so far been inconsistent. Growing evidence has demonstrated, however, that folate deficiency can cause breaks in DNA strands, diminished DNA repair, and an increase in DNA mutations. Folic acid has been shown to protect against the development of cancer by reducing the error rate during replication. Furthermore, folic acid has demonstrated antioxidant activity, scavenging free radicals and contributing to its possible anti-tumour properties. A recent study published in *The Journal of Nutritional Biochemistry* aimed to investigate whether folic acid supplementation could affect the migratory capability or metastasis of colorectal cancer cells. Cancer cell proliferation and migration are two key events that occur during cancer development. The research team had previously shown that folic acid supplementation can reduce the proliferation rate of human venous endothelial cells (cells that line the interior of the veins) and decrease angiogenic activity, a crucial factor in tumour proliferation. Results from the study demonstrated that folic acid was able to reduce the metastatic ability of colorectal cancer cells by activating cellular pathways which inhibited the cancer cells’ ability to migrate away from their site of origin. Further evidence will be necessary to confirm the potential role of folic acid as a supplement to reduce one’s risk of colorectal cancer development.


22. Does tailored lifestyle feedback given during colorectal cancer screening improve disease-preventive behaviours? (Dec 14/18)

According to results from a study published in *Cancer Epidemiology, Biomarkers & Prevention*, a program that provides individually tailored lifestyle recommendations for patients who are undergoing screening for colorectal cancer (CRC) helped to encourage healthy behaviour among participants. It is well understood that healthy lifestyle factors such as a balanced, plant-based diet and regular physical exercise decrease the risk of CRC. When someone arrives at a clinic for cancer screening, it is an optimal moment to increase participants’
awareness of health behaviours. The researchers wanted to examine whether providing tailored feedback, delivered within a screening program, could effectively promote lifestyle changes to reduce cancer risk.

In the study, the researchers invited 3,642 men and women aged 50-74 years in southeastern Norway to receive a sigmoidoscopy. In the end, 1,054 patients enrolled in the study. Participants completed two lifestyle questionnaires, one prior to screening and one 1-year after screening. The lifestyle questionnaires included questions on smoking status, weight, physical activity, alcohol consumption, and intake of fruits, vegetables, and red or processed meats. The participants were then randomly assigned to receive either: a standardized, individually tailored, written feedback on their health habits; a standard one-page leaflet about healthy behaviours; or nothing, as part of the control group. The group that received the tailored feedback received a two-to three-page letter from the research team, which commented on the participants’ answers to the lifestyle questionnaire before screening and made specific suggestions to improve cancer-preventive behaviours. For example, someone who wrote that they ate less than the daily recommended intake of fruits and vegetables would be reminded to eat at least five servings per day, with examples and serving sizes. 1 year after the participants completed screening and the questionnaire, participants answered the second questionnaire about cancer-preventive lifestyle behaviours. The researchers found that within that year, those who received the tailored feedback increased their number of cancer-preventive behaviours by 11% compared to the control group. Changes were larger among participants who had not previously adhered to healthy lifestyle behaviours. Those who received tailored recommendations had a significantly larger weight loss of 0.84kg compared to the control group.

While many changes in lifestyle behaviours were small, the study demonstrated the effectiveness of individually tailored advice given in the context of CRC screening. The researchers noted that teaching cancer-preventive behaviour in a population-based cancer screening context could increase the chances of reaching the most relevant age group or demographic. The method is limited, however, in that people willing to complete questionnaires and undergo cancer screening in the first place may not be representative of the greater population, especially the many individuals who do not participate in preventative screening methods at all.

http://www.ascopost.com/News/59574

23. Patients with IBD at greater risk for postcolonoscopy colorectal cancer (Dec 26/18)

According to recent research published in Gut, patients with inflammatory bowel disease (IBD) experience higher rates of postcolonoscopy colorectal cancer (CRC), with higher risk of the disease among young patients with ulcerative colitis and greater risk of developing rectal cancers among those with Crohn’s disease. The researchers noted that while this group of patients normally undergoes many colonoscopies, there is a gap in the understanding of rates of postcolonoscopy CRC among this population. Until this study, previous studies have mainly focused on elderly American patients with IBD showing that an increased risk of CRC was for postcolonoscopy CRC. In the study, the researchers analyzed data from a Swedish cohort study in which patients underwent colonoscopy between 2001 and 2010. They identified patients who were diagnosed with CRC within 36 months after colonoscopy and categorized them into three groups: Crohn’s disease (CD), ulcerative colitis (UC), and non-IBD. The researchers found 13,317 CRCs in the non-IBD group, 133 in the CD group and 281 in the UC group. They discovered that the postcolonoscopy CRC rate was 28.3% among patients with CD and 41% in patients with UC. The risk for postcolonoscopy CRC was greater in CD and UC compared with the non-IBD population. The risk for rectal cancer was highest among patients with CD and among younger patients with UC. The younger the individual in the UC group, the higher the rate of postcolonoscopy CRC. The researchers concluded that the high rates in the more advanced stages could suggest that these postcolonoscopy CRCs truly represent missed lesions during surveillance colonoscopy, highlighting the need
for better screening and surveillance strategies. The high rates of postcolonoscopy CRC among younger patients with UC and for rectal cancers in CD could affect the way surveillance strategies are applied in the IBD group for the future.

https://www.healio.com/gastroenterology/inflammatory-bowel-disease/news/online/%7b7bic5343a-02b3-4065-b50c-391275f638e9%7d/patients-with-ibd-at-greater-risk-for-postcolonoscopy-colorectal-cancer

24. Cancer diagnosis may be preceded by heart attack, stroke (Dec 21/18)

The elderly had a 69% higher risk for heart attack and ischemic stroke in the year prior to cancer diagnosis, according to recent research published in Blood. The significantly elevated risk for the disease began 5 months before the diagnosis of cancer, and reached a peak 1 month before diagnosis, when it increased 5-fold. The researchers suggest that since cancers can take months to years to develop, the cancer was probably there all along and could have, at least in some of those patients, caused their stroke or heart attack. By identifying the highest-risk patients, clinicians can determine the usefulness of screening them to help diagnose their cancers earlier, hopefully leading to better health outcomes.

In the study, the researchers reviewed the SEER-Medicare linked data set to identify 374,331 patients aged 67 years or older, with a primary diagnosis of one of the following cancers between 2005-2013: breast, lung, prostate, colorectal, bladder, uterine, pancreatic, gastric, and non-Hodgkin lymphoma. Researchers matched patients with cancer based on demographics and comorbidities (other simultaneous diseases) to Medicare beneficiaries without cancer as a control. It was found that between 360 and 151 days before cancer diagnosis, Medicare beneficiaries with and without cancer had comparable risk of heart attack/stroke. Between 150 days and 1 day before diagnosis, however, there was a higher risk for heart attack/stroke among patients who eventually would be diagnosed with cancer compared to control patients. Furthermore, this risk progressively increased during the time leading up to diagnosis, reaching a peak during the 30 days preceding the cancer diagnosis. Through an analysis of all 360 days prior to entering the study, researchers found that 6,567 of the patients with cancer had a heart attack/stroke compared to 3,916 of the matched controls, indicating that those who were eventually diagnosed with cancer had a 69% increased risk for a heart attack or stroke. These results stress the need for clinicians to be vigilant of signs of cancer in patients who recently experienced heart attack or stroke, compared to those who have not experienced such cardiovascular events.

https://www.healio.com/hematology-oncology/lymphoma/news/online/%7b3bb95f34-948d-41f7-8580-71a60f9f437d/cancer-diagnosis-may-be-preceded-by-heart-attack-stroke?page=2

25. Young adult colorectal cancer clinic available at Sunnybrook (Jan 16/19)

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

NUTRITION/ HEALTHY LIFESTYLE

26. Healthy diet may reduce risk for death among patients with colorectal cancer (Dec 21/18)

A study published in Journal of Clinical Oncology found that patients with colorectal cancer (CRC) who followed healthy diets before and after diagnosis showed a reduced risk of death from the disease or any cause. These results support the association of a lower risk of death and the adoption of a high quality diet after diagnosis, even when a poor diet was consumed prior to diagnosis. Previous studies have shown that diet quality has a significant influence on disease outcomes and that some dietary components are linked to greater survival among individuals with CRC. In this study, the researchers reviewed data from 2,801 participants from the prospective Cancer Prevention Study-II Nutrition Cohort. All individuals were cancer free at baseline and were subsequently diagnosed with invasive, non-metastatic CRC. Pre-diagnosis data on participants’ diet were available for 2,671 individuals in the cohort, and post-diagnosis data were available for 1,321. The researchers evaluated the diets based on the Dietary Approaches to Stop Hypertension (DASH), American Cancer Society guidelines on nutrition and physical activity for cancer prevention (ACS score), and Western dietary patterns. A pre-diagnosis Western diet, characterized by high amounts of red meat and other animal products, was directly associated with higher all-cause mortality. Among patients with poor diet quality prior to diagnosis, improved DASH between pre-diagnosis and post-diagnosis periods were inversely associated with CRC-specific mortality. Post-diagnosis, patients with the highest ACS score (higher score = healthier diet) showed a 65% lower risk of CRC mortality and 38% lower risk of death from any cause compared to patients with the lowest ACS scores. The researchers concluded that dietary patterns which incorporate a higher intake of plant-based foods and lower intake of animal products before and after CRC diagnosis are associated with longer survival. This stresses the importance of diet quality as a modifiable risk factor to improve disease outcomes pre- and post-diagnosis among individuals with CRC.


27. Growing prevalence of excess body weight increasing global cancer burden (Dec 12/18)

In 2012, the growing epidemic of excess body weight was responsible for approximately 3.9% of all cancers worldwide. Obesity and excess body fatness is driven by various factors, including environmental and socioeconomic pressures that can modify an individual’s health environment to one which favours weight gain and unhealthy lifestyle behaviours. Between 1975 and 2016, the prevalence of excess body weight in adults,
which is defined as a BMI of 25 kg/m² or greater, increased from nearly 21% in men and 24% in women to about 40% in both sexes. The prevalence has quadrupled in men, from 3% to 12%, and doubled in women, from 7% to 16%. Researchers from a report recently published in *CA: A Cancer Journal for Clinicians* examined possible drivers of population-level obesity, noting systemic factors, such as policy and economic systems which encourage high levels of consumption; environmental factors, such as food supply and the marketing of high-calorie, low-nutrient foods; behavioural patterns, such as insufficient physical activity; and genetic predisposition to excess weight.

The obesity epidemic has taken a significant toll on global health, resulting in an estimated 4 million deaths in 2015 and illnesses that resulted in a hefty economic burden of $2 trillion in 2014. Furthermore, about 3.9% of all cancers (544,300 cases) in 2012 were linked to excess body weight, varying from less than 1% in low-income countries to about 7%-8% in high-income Western countries and Middle Eastern and North African countries. The International Agency for Research on Cancer Working Group on Body Fatness published a report stating that there exists sufficient evidence to make a causal association between excess body weight and increased risk for 13 cancers, including colorectal cancer. In 2012, 7% of all colorectal cancers among women (42,300) and 6% among men (42,200) could be attributed to excess body weight. Furthermore, women have been found to have a higher cancer burden that can be linked to excess body weight than men (368,500 vs. 175,800 cases).

Controlling global rates of obesity is currently one of nine key initiatives of the World Health Organization to reduce the global burden of cancer and other non-communicable diseases. The organization is suggesting interventions such as changing legislations to ban trans fats, taxes on sugar-sweetened beverages, limits on food portion sizes and package sizes, and improved access to public transportation and safe spaces for walking and cycling. Support networks that provide appropriate guidance on making lasting healthy lifestyle changes with adequate psychosocial support at each step could make an important difference at the community and individual level. The obesity epidemic is a global issue that is demanding a rejuvenated focus on identifying, implementing and evaluating interventions to prevent and control excess body weight.

https://www.healio.com/hematology-oncology/breast-cancer/news/in-the-journals/%7b454f3c1a-8ca8-4cdf-bf67-03e837ae6b37%7d/growing-prevalence-of-excess-body-weight-increasing-global-cancer-burden

28. Is consumption of dairy products linked to colorectal cancer risk? (Oct 23/18)

According to research published in the *International Journal of Cancer*, a high level of total dairy intake, as well as low-fat milk consumption, was significantly associated with a decreased risk of colorectal cancer (CRC) development in an older Mediterranean population with a high cardiovascular risk. These findings were consistent with previous studies and systematic reviews that showed that milk and total dairy products, but not cheese or other individual dairy products, are associated with a reduction in CRC risk. Adhering to a healthy diet is an essential factor for the primary prevention of CRC, with dietary factors estimated to contribute to nearly 50% of cancer cases. The traditional Mediterranean dietary pattern, comprised of an abundance of plant foods, olive oil and fish, low consumption of red meat and processed meat, and a moderate consumption of dairy products (mainly cheese and yogurt) has been associated with a lower incidence of CRC. A total of 7,216 individuals without CRC participated in the study between 2003 and 2009, with follow-up continuing through December 2012. Researchers assessed the consumption of total and specific dairy products using a food-frequency questionnaire, issued at the start of the program and yearly thereafter. At a median follow-up of 6 years, 101 cases of CRC were documented. The hazard ratios of CRC for the highest levels of total dairy consumption were 0.55 (i.e. the risk of developing CRC was 55% lower) and 0.54 for the highest levels of low-fat milk consumption. No specific associations with any other subgroup of dairy products, including whole fat

Image source: http://insidebusinessonline.com
and low-fat dairy products and yogurts, cheese and sugary dairy products were identified. The researchers concluded that further studies as well as clinical trials would be justified to confirm their findings.


25. 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) (Jan. 16/19)

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 (≥150 minutes of moderate-to-vigorous or ≥75 minutes of vigorous exercise/week). Following registration, and prior to randomization, patients must successfully complete at least two stages of a submaximal exercise test to ensure they are able to safely exercise at a moderate to vigorous intensity.

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

26. High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (Jan.17/19)

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