COLORECTAL CANCER TREATMENT & CLINICAL RESEARCH UPDATES

Month Ending October 12th, 2023

The following colorectal cancer treatment and research updates extend from September 14th, 2023, to October 12th, 2023, inclusive and are intended for informational purposes only.

This content is not intended to be a substitute for professional medical advice. Always consult your treating physician or guidance of a qualified health professional with any questions you may have regarding your health or a medical condition. Never disregard the advice of a medical professional or delay in seeking it because of something you have read on this website.
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1. TRK Fusion Cancer and How to Test for It (Sept.13/23)

**What is TRK fusion cancer?**

- TRK (pronounced track) fusion cancer is a term used to describe cancers that are caused by a change to the neurotrophic tyrosine receptor kinase (NTRK) gene called a fusion.
- During this fusion, an NTRK (pronounced on-track) gene joins together, or fuses, with a different gene.
- This joining causes the body to make TRK fusion proteins, which can cause cancer cells to multiply and form a tumour.
- The presence of TRK fusion proteins may be associated with more aggressive cancer.

Having TRK fusion cancer doesn’t change your original diagnosis, it just means that your tumour is driven by an NTRK gene fusion.

Testing is the only way to find out if NTRK gene fusion is driving your cancer.

**Who should be tested for NTRK gene fusions?**

Your doctor may consider testing in people:

- with solid tumours that are metastatic, and
- who are likely to experience severe complications from surgical resection, and
- when there are no satisfactory treatments options available.

It’s important to know what’s driving your cancer to help your doctor take action.

**FastTRK**

FastTRK is a clinical testing program for diagnosing NTRK gene fusions.

Sponsored by Bayer, this is a complimentary service for healthcare professionals to find out if their patients’ cancer has an NTRK gene fusion.

Talk to your doctor about which tests are recommended for you.
INTRODUCING

Tumour-Agnostic Therapies

Advances in precision medicine have brought therapies that specifically target what is driving a patient’s cancer.

Treatment with more traditional cancer therapies is based on where the tumour is located in the body.

Tumour agnostic therapies target a specific genomic change in the cancer cells regardless of where the tumour is located in the body.

Genomic changes in cancer cells are identified through diagnostic testing of the cancer cells. The results help clinicians decide on a treatment for each patient.

Advantages of tumour agnostic therapies:
- Targets the genomic change that is the root cause of the cancer to suppress tumour growth
- Harnesses our growing understanding of cancer biology
- Offers an innovative, new and effective approach to treating cancer

Change required to adopt tumour agnostic therapies in Canada:
- A shift in mindset: this is a new concept that differs from the traditional approach of treating cancer based on tumour location
- Access to genomic testing: identifying patients who would benefit from treatments requires a robust testing infrastructure
- An evolved, more adaptive assessment of treatments for public coverage is required that includes recognition of smaller patient populations, new clinical trial methods, and ability to examine new data over time

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https://www.bayer.ca/en/media/news/?dt=TmpBPQ==&st=1
2. Immunotherapy Combined with Targeted Therapy in Patients with BRAF V600E–Mutated CRC (Sept.15/23)

In one of the first clinical trials combining immunotherapy and targeted therapy for patients with BRAF V600E–mutated colorectal cancer (CRC), researchers discovered that a combination regimen of dabrafenib, trametinib, and spartalizumab resulted in long-lasting responses. The study successfully met its primary endpoint and achieved a confirmed response rate of 24.3%, compared with a response rate of 7% in a prior trial where patients were treated with each of the same targeted therapies individually. The researchers also reported improved outcomes in one of the trial’s secondary endpoints: durability. Previously, patients with BRAF V600E–mutated CRC have seen only a short-lived clinical benefit after treatment with BRAF or MEK inhibitors. But the combination therapy resulted in an increased durability of response, with a median progression-free survival of 5 months compared with 3.5 months with BRAF or MEK inhibitors alone. The researchers noted that 57% of the patients continued with the treatment for more than 6 months and 18% continued for more than 1 year.

The findings suggested how targeted therapies in combination with immunotherapies may drive a greater immune response and improve treatment overall. This merits further clinical investigation and preclinical experiments to determine the best targeted approach to increase immune reactivity against [BRAF-mutated] CRC. The researchers acknowledged that the implications of their research may go well beyond CRC.


3. VITRAKVI (Larotrectinib) is Now Covered in Ontario, Quebec, Saskatchewan, Manitoba and New Brunswick (Sept.15/23)

Please find information below regarding public funding for VITRAKVI (Larotrectinib) in Ontario, Quebec, Saskatchewan, Manitoba and New Brunswick.

4. Skincare Tips while on Cetuximab or Panitumumab Treatment for CRC (Aug.28/23)

Amgen has collaborated with FUSE Health and Dr. Nathan Lamond (Medical Oncologist, Dalhousie University) to produce a 5-minute video on the importance of good skin hygiene for patients on EGFRi therapy. During this talk, Dr. Lamond discusses the importance of good skin care to help prevent or lessen skin side effects caused by certain cancer treatments such as cetuximab and panitumumab used to treat colorectal cancer (CRC). Dr. Lamond provides tips for protecting the skin and using appropriate soaps, cleansers, moisturizers, sunscreens, and lip balms.

To download and view the video: https://fusehealth.sharefile.com/d-s2d0a0747b8154e368ed5219e5654421c

5. Could Cetuximab Maintenance Play a Role in RAS Wild-Type Metastatic CRC? (Sept.18/23)

Maintenance therapy with cetuximab after FOLFIRI plus cetuximab induction therapy led to better outcomes for patients with RAS wild-type metastatic colorectal cancer (mCRC) in a phase II randomized trial, yet it failed to reach the study’s prespecified threshold for success.

At 6 months after randomization, more patients assigned to maintenance therapy with the EGFR inhibitor were alive and without progressive disease compared with an observation group (39% vs 6%), falling short of the primary endpoint goal of 50%. The trial wasn’t powered for comparisons between groups, but over a median follow-up of 40.5 months, numerically higher median progression-free survival (PFS) and overall survival (OS) were observed in the cetuximab arm:

- PFS: 5.3 months and 2.0 months
- OS: 24.8 months and 19.7 months

During the maintenance phase, 30 of 67 patients in the cetuximab group (44.8%) experienced at least one grade 3 or higher adverse event related or unrelated to study medication, with rash (11.9%) and diarrhea (6%) reported most
frequently. Although this randomized clinical trial did not meet its primary endpoint, maintenance cetuximab after induction FOLFIRI plus cetuximab appeared feasible and was associated with longer PFS, OS, and chemotherapy-free intervals than observation.

In explaining the rationale behind the study, the investigators pointed out that the optimal maintenance strategy after induction chemotherapy with EGFR inhibition for patients with RAS wild-type, mCRC remains uncertain. In a commentary accompanying the study, Federica Morano, MD, and Filippo Pietrantonio, MD, both of the Fondazione IRCCS Istituto Nazionale dei Tumori in Milan, called the study results "disappointing." They suggested that a "thorough understanding of the biology underlying anti-EGFR resistance is of paramount importance, especially when it comes to identifying the best strategy (i.e., continuation, treatment break, or drug de-escalation) after achieving maximum response in the first-line setting."

https://www.medpagetoday.com/hematologyoncology/coloncancer/106389

6. Postoperative ctDNA-Based Molecular Residual Disease in Patients with BRAF V600E and MSI-H CRC (Aug.3/23)

Postoperative circulating tumor DNA (ctDNA)-based molecular residual disease (MRD) is reported to be associated with a high risk of recurrence. The authors of this article present an updated analysis of MRD detection and correlations with BRAF and MSI status in radically resected, stage II-IV colorectal cancer (CRC) from the observational GALAXY study.

Among 3,615 CRC patients who were enrolled between May 2020 and April 2022 in GALAXY study, 2,083 patients that met the inclusion criteria were analyzed. Of 2,083 patients, 60 (2.9%) had BRAF V600E mutant and microsatellite stable (MSS) tumors, 100 (4.8%) had BRAF wild type (wt) and high level micro satellite instability (MSI-H) tumors, and 115 (5.5%) had BRAF V600E mutant and MSI-H tumors.

In the overall population, 286 (14%) were ctDNA-positive at the 4-week MRD time point and 1,797 (86%) were ctDNA-negative. Those with ctDNA-positivity at the 4-week demonstrated inferior disease-free survival (DFS) and were 12x more likely to recur, compared to ctDNA-negative patients. Patients with BRAF wt and MSI-H tumors had significantly better DFS compared to patients with BRAF wt and MSS tumors. Finally, patients with BRAF V600E mutant and MSI-H tumors had significantly better DFS compared to patients with BRAF wt and MSS tumors.

On the other hand, ctDNA-positivity was associated with significantly shorter DFS in patients with BRAF V600E mutant and MSS tumors and BRAF V600E mutant and MSI-H tumors compared to patients with BRAF wt and MSS tumors. Multivariate analysis in DFS showed that ctDNA positivity was significantly associated with poor prognosis, outperforming other clinicopathologic factors such as BRAF and MSI status.

Thus, ctDNA status at the postoperative MRD time point is the most prognostic risk factor of DFS regardless of BRAF V600E or MSI-H status. Those with positive postoperative ctDNA should be examined carefully due to a high risk of recurrence. ctDNA-guided adjuvant strategies will further be established by the ongoing randomized VEGA and ALT AIR studies in CIRCULATE-Japan.


7. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Oct.1/23)

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 Michael Raphael are the program leads and happy to see patients who may be eligible for the therapy.
Presently at Sunnybrook Odette Cancer Centre, HAIP is being used in patients with colorectal cancer that has spread to the liver that cannot be removed surgically and has not spread to anywhere else in the body. Patients who have few (1-5) and very small tumors in the lungs may be considered if the lung disease is deemed treatable prior to HAIP. If you believe you may benefit from this therapy and/or would like to learn more about the clinical trial, your medical oncologist or surgeon may fax a referral to 416-480-6179. For more information on the HAIP clinical trial, please click on the link provided below.

http://sunnybrook.ca/content/?page=colorectal-colon-bowel-haip-chemotherapy

8. Living Donor Liver Transplantation for Unresectable CRC Liver Metastases (Oct.2/23)

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 5-year survival after liver resection for LM of 40-50%, compared to 10-20% 5-year survival for chemotherapy alone. Liver transplantation (LT) would remove all evident disease in cases where the colorectal metastases are isolated to the liver but considered unresectable.

While CRC LM is considered a contraindication for LT at most cancer centers, a single center in Oslo, Norway demonstrated a 5-year survival of 56%. A clinical trial sponsored by the University Health Network in Toronto will offer live donor liver transplantation (LDLT) to select patients with unresectable metastases limited to the liver and are non-progressing on standard chemotherapy. Patients will be screened for liver transplant suitability and must also have a healthy living donor come forward for evaluation. Patients who undergo LDLT will be followed for survival, disease-free survival, and quality of life for 5 years and compared to a control group who discontinue the study before transplantation due to reasons other than cancer progression.

https://clinicaltrials.gov/ct2/show/NCT02864485

9. In Vivo Lung Perfusion (IVLP) for CRC Metastatic to Lung (Oct.9/23)

A new study is investigating a technique called In Vivo Lung Perfusion (IVLP) for delivering chemotherapy directly into the lungs at the time of surgery. Delivering chemotherapy directly to the lungs could potentially kill any microscopic cancer cells that are present in the lungs at the time of surgery, while sparing other major organs in the body from the side effects of chemotherapy.

At the University Health Network, this IVLP technique has been used recently in a Phase I study in patients with sarcoma, and they are now expanding on that experience to include patients with colorectal metastases. The purpose of this study is to test the safety of the IVLP technique and find the dose that seems right in humans. Participants are given oxaliplatin into one lung via IVLP and are watched very closely to see what side effects they have and to make sure the side effects are not severe. If the side effects are not severe, then more participants are asked to join the study and are given a higher dose of oxaliplatin. Participants joining the study later on will get higher doses of oxaliplatin than participants who join earlier. This will continue until a dose is found that causes severe but temporary side effects. The other lung will not be infused with anything, so that researchers can limit unforeseen toxicity to a single lung and see if one lung does better than the other.
The estimated enrolment is 10 participants, each with a diagnosis of colorectal carcinoma. The primary outcome is safety as measured by acute lung injury findings and the estimated primary completion date is January 1, 2027.

In Vivo Lung Perfusion Model

https://clinicaltrials.gov/ct2/show/NCT05611034?term=ivlp&draw=2&rank=1
Image Source: https://pie.med.utoronto.ca/TVASurg/project/in-vivo-lung-perfusion/

Radiation Therapies / Interventional Radiation

10. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Oct.9/23)

Magnetic resonance-guided focused ultrasound (MRg-FU) is a less 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 a real-time thermal mapping to ensure accurate heating of the designated target with minimal affect 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

11. Trends in the Incidence of Young-Onset CRC with a Focus on Years Approaching Screening Age (Oct.10/23)

With recent evidence for the increasing risk of young-onset colorectal cancer (yCRC), the objective of this population-based longitudinal study was to evaluate the incidence of yCRC in one-year age increments, particularly focusing on the screening age of 50 years. The study was conducted using linked administrative health databases in British Columbia, Canada including a provincial cancer registry, inpatient/outpatient visits, and vital statistics from January 1, 1986 to December 31, 2016. Researchers calculated the incidence rates per 100,000 at every age from 20 to 60 years and estimated annual percent change in incidence (APCI) of yCRC using joinpoint regression analysis. 3,614 individuals were identified with yCRC (49.9% women). The incidence of CRC steadily rose from 20 to 60 years, with a marked increase from 49 to 50 years. Furthermore, there was a trend of increased incidence of yCRC among
women. Analyses stratified by age yielded APCi’s of 2.49% and 0.12% for women aged 30-39 years and 40-49 years, respectively and 2.97% and 1.86% for men. These findings indicate a steady increase over one-year age increments in the risk of yCRC during the years approaching and beyond screening age. These findings highlight the need to raise awareness as well as continue discussions regarding considerations of lowering the screening age.


For more information, please visit the OncoHelix website.

13. LifeLabs Launches Signatera, Offering Canadians an Innovative and Personalized Approach to Managing Cancer (Oct.1/23)

LifeLabs is pleased to share the launch of Signatera, a highly sensitive, personalized molecular residual disease assay (MRD) test developed by Natera for treatment monitoring and molecular residual disease (MRD) assessment in patients previously diagnosed with cancer. This innovative test uses circulating tumor DNA (ctDNA) and is personalized for each patient to help assess recurrence risk and identify relapse up to two years earlier than the current standard of care tools. The clinical utility of Signatera across cancer types has been validated by multiple studies. In those trials, Signatera demonstrated predictive values such as:

- 88% sensitivity to relapse
- 89% sensitivity to relapse
- 92% sensitivity to relapse
- 100% sensitivity to relapse

Signatera testing involves two phases with pre-supplied collection kits. The first phase is an initial test that analyzes both a tumor tissue and blood sample, and the second phase involves subsequent blood tests on an as-needed basis. It is a safe, non-invasive way to monitor ctDNA levels to help physicians understand treatment efficacy and detect relapse without the inconvenience of repeated tissue biopsies or/and imaging.


14. Natera Announces Publication of Prospective, Multi-Site CIRCULATE Study in Nature Medicine Demonstrating Signatera’s Ability to Predict Chemotherapy Benefit in CRC (Aug.1/23)

Natera, Inc., a global leader in cell-free DNA testing, announced the publication of a new study in Nature Medicine, which demonstrates the ability of the Signatera molecular residual disease (MRD) test to identify patients with stage II-IV colorectal cancer (CRC) who are at an increased risk of recurrence and predict who is likely to benefit from adjuvant chemotherapy (ACT).
The paper describes results from the GALAXY arm of the ongoing CIRCULATE-Japan trial, which is one of the largest and most comprehensive prospective studies of MRD testing in resectable CRC. The data builds on results previously presented at the 2022 ASCO Gastrointestinal Cancers Symposium (ASCO GI), now with median clinical follow-up extended to 16.74 months and DFS assessment at 18 months.

In the study, 1,039 patients with stage II-IV resectable CRC were monitored prospectively using the Signatera MRD test. Key takeaways include:

- **Post-surgical MRD status was predictive of chemotherapy benefit**
- **Post-surgical MRD status was the most significant prognostic risk factor for recurrence**, in a multivariate analysis that accounted for all clinicopathological risk factors currently used for prognostication (HR 10.82, p-value <0.001).
- **Pre-surgical detection rate of 95.9%** in patients with pathologic stage II-III disease and 93.1% in patients with stage II-IV disease.
- **Signatera dynamics are indicative of treatment response**

This study provides strong evidence that Signatera MRD-positive patients will benefit significantly from adjuvant therapy, while MRD-negative patients may be safely observed, regardless of clinical or pathological stage.


15. Young Adult CRC Clinic Available at Sunnybrook (Oct.5/23)

A recent study led by the University of Toronto doctors has observed a rise in colorectal cancer (CRC) rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing CRC rates in young people come after decades of declining rates in people over 50, which have occurred most likely due to increased use of CRC 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), along with **Dr. Petra Wildgoose** (Hepatobiliary and Colorectal Oncology Surgical Assistant), and their team at the Sunnybrook Health Sciences Centre understand the needs of this patient population.

Dr. Shady Ashamalla, Head Young Adult Colorectal Cancer Program
Dr. Petra Wildgoose, Lead Young Adult Colorectal Cancer Program

Both belong to a multidisciplinary team of experts in the **Young Adult Colorectal Cancer Clinic** who work with young CRC patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Patients’ 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

16. CCRAN’s Partnership with “Count Me In” (Oct.1/23)

CCRAN is proud to partner with Count Me In, a nonprofit research initiative, on The Colorectal Cancer Project. This new project is open to anyone in the United States or Canada who has ever been diagnosed with colorectal cancer (CRC). Patients can find out more and join at JoinCountMeln.org/Colorectal.

Through the project, patients are asked to complete surveys to share information about their experience with CRC, to share biological sample(s), and to allow for the research team to request copies of their medical records. The project team then de-identifies and shares data from these with the entire research community.

Every patient’s story holds a piece of the puzzle that can help us better understand CRC. By discovering more about what drives cancer and sharing this data, CCRAN and the Colorectal Cancer Project believe insights can be gained to develop more effective therapies. One of the aims of the project is to reach populations that have been understudied, including individuals who are diagnosed with CRC at a young age, individuals from marginalized communities who have historically been excluded from research, and patients with metastatic CRC. Together, we can accelerate our understanding of CRC. To learn more or sign up to participate, visit JoinCountMeln.org/Colorectal.

“Count Me In”, a nonprofit cancer research initiative, is inviting all patients across the United States and Canada who have ever been diagnosed with colorectal cancer (CRC) to participate in research and help drive new discoveries related to this disease. The Colorectal Cancer Project will enable patients to easily share their samples, health information and personal lived experiences directly with researchers in order to accelerate the pace of research. Patients who have been diagnosed with CRC at any point in their lives can join the project by visiting JoinCountMeln.org/colorectal. From there, patients will be invited to share information about their experience through surveys and to provide access to medical records as well as saliva samples and optional blood, stool, and/or stored tissue samples for study and analysis. Researchers from the Broad Institute of MIT and Harvard and Dana-Farber Cancer Institute use this information to generate databases of clinical, genomic, molecular, and patient-reported data that is then de-identified and shared with researchers everywhere. To date, more than 9,000 patients with different cancers have joined Count Me In and shared their data. “We still do not know why there is an alarming rise in CRC in young adults”, said Andrea Cercek, MD Co-Director, Center for Young Onset Colorectal and Gastrointestinal Cancers Memorial Sloan Kettering Cancer Center and co-scientific leader of the Colorectal Cancer Project. “What we do know is that this is a global phenomenon that affects otherwise healthy individuals with no known risk factors. The Colorectal Cancer Project will provide researchers important information that will lead to a better understanding of this disease.”
Over 250 patients have joined the Colorectal Cancer Project since the launch in fall 2021. Every patient that joins the Colorectal Cancer Project enables us to learn more about colorectal cancer. Pts diagnosed at any age, whether newly diagnosed or years from their diagnosis, can enroll. If you have ever been diagnosed with colorectal cancer, you can visit JoinCountMeIn.org/Colorectal to enroll and have a direct impact on research and future treatment strategies.


17. CCRAN Announces the Launch of 4 New Information/Support Groups (Oct.2/23)

CCRAN is pleased to announce a new format for monthly information / support group meetings. To ensure peer support is relevant, meaningful and timely for each participant, CCRAN has stratified the groups according to disease stage and early vs average onset colorectal cancer:
Meetings will begin with a brief treatment update. Following the presentation, patients and caregivers will be assigned to the support group of relevance to them. Please RSVP to Cassandra Macaulay: Cassandra.m@ccran.org. We look forward to hosting you at our monthly information/support group meetings.

18. Changing Epidemiology of CRC — Birth Cohort Effects and Emerging Risk Factors (Sept.18/23)

In this review article, the authors discuss the changes in the epidemiology of colorectal cancer (CRC) that are becoming evident, including trends in CRC incidence and mortality by age and birth cohort, and consider the contributions of early-life exposures and emerging risk factors to these changes. Additionally, they examine the causes and potential consequences of these changes.

Key points from the article include:

- Incidence and mortality of CRC are increasing worldwide, suggesting broad changes in the epidemiology of CRC.
- The incidence of CRC has increased among people born since the early 1950s in nearly all regions of the world; so-called birth cohort effects.
- Birth cohort effects implicate factors that influence the earliest stages of carcinogenesis and have effects across the life course.
- Accumulating evidence supports the idea that early-life exposures, including those during fetal development, childhood, adolescence and young adulthood, are important risk factors for CRC.
- Environmental chemicals could have a role in birth cohort effects because the introduction of many in the 1950s and 1960s coincides with increasing incidence of CRC among people born during those years.
- To prevent expected increases in the global burden of CRC, participation in average-risk screening programs needs to be increased, and emerging risk factors responsible for the increases need to be identified.

https://www.nature.com/articles/s41575-023-00841-9

Early-onset colorectal cancer (age under 50 years) (EOCRC) is an entity of undeniable importance, both because of its growing incidence, and the population it affects. Other current reviews emphasize the essential points regarding the clinical management and knowledge of its molecular basis. With the increased significance of patient participation and disease experience in mind, the authors have integrated the voice of the patient to show the weaknesses and the needs, and next steps in the advancement of knowledge and management of EOCRC.

Key points from the review include:

- Although most EOCRC cases seem to be sporadic, there is still an important proportion belonging to families with well-defined CRC predisposition syndromes.
- Excluding hereditary syndromes, general population screening strategies don’t cover most cases in the majority of countries, except in some defined ones with first-degree relatives with CRC.
- At present, the management of EOCRC should be considered a lifelong process: from the early care of symptoms to avoiding delays in diagnosis; through a multidisciplinary treatment in both the present and future; and with considerations for the possible consequences in the short and long term.
- The participation of patients in each step of the process, as well as in the awareness of the problem is especially critical in EOCRC.

The specific needs of EOCRC patients should be considered and addressed in the comprehensive management by all clinicians. Recent approaches, as multi-omics analyses; the definition of exposome and its application in exploring lifestyles, habits, and exposures; microbiome interactions; or the construction of international multidisciplinary comparative cohort studies are steps in the right direction to solve the EOCRC problem. Active participation of patients along all the phases of the process should be a priority. EOCRC is one of the best examples in which multidisciplinary practice including patients and advocates, should reach an integrative needs assessment.


20. Sona’s ‘THT’ Cancer Therapy to be Assessed for Efficacy and Ability to Act as a Catalyst to Generate Immune Responses in Research Study (Sept.11/23)

Sona Nanotech Inc., recently announced an innovative research initiative to be undertaken with The Giacomantonio Immuno-Oncology Research Group. This study aims to evaluate the efficacy of Sona’s Targeted Hyperthermia Therapy ("THT") technology in not only attenuating the development of colorectal, breast, and melanoma tumor models in mice but also in facilitating systemic immune responses.

Sona CEO, David Regan, commented, “This innovative study will go significantly beyond our current plans for THT applications to explore the potentially synergistic effect of its use with certain immunotherapy treatments for cancer. In it, we aim to harness the tremendous potential of immunotherapy, leveraging Sona’s biocompatible gold nanorods as a pivotal, catalytic element. This effort marks the beginning of Sona delivering on the ‘mountain of data’ we committed to developing in support of our planned regulatory submissions for human clinical trial approvals.”

Dr. Carman Giacomantonio, principal investigator of the Research Group, commented: “We are committed to exploring two distinct yet interrelated biological processes with the potential to unlock the elusive Holy Grail of intra-tumoral cancer immunotherapies, known as the Abscopal Effect. The first avenue capitalizes on the kinetic excitation of gold nanorods, capable of inducing localized tumor destruction. This process exposes potent tumor neo-antigens, which can then be strategically mobilized to immune-responsive sites. This strategy holds the potential of profoundly reshaping and amplifying the efficacy of the immune response against cancer. Concurrently, the second dimension of our research delves into the profound impact of intralesional immunomodulation in the context of both local and systemic Targeted Hyperthermia Therapy. Together, these objectives, if successful, may establish a strategic framework to illuminate the path towards groundbreaking, innovative, and potent immunotherapeutic interventions for colorectal cancer, breast cancer, and melanoma.”
The research group is exploring two distinct yet interrelated biological processes with the potential to unlock the “elusive Holy Grail of intra-tumoral cancer immunotherapies, known as the Abscopal Effect”. The first process involves the kinetic excitation of gold nanorods, capable of inducing localized tumor destruction. This exposes potent tumor neo-antigens, which can then be strategically mobilized to immune-responsive sites. This strategy holds the potential of profoundly reshaping and amplifying the efficacy of the immune response against cancer. The second avenue examines the profound impact of intralesional immunomodulation in the context of both local and systemic THT. Together, these objectives, if successful, may establish a strategic framework to illuminate the path towards groundbreaking, innovative, and potent immunotherapeutic interventions for colorectal cancer, breast cancer, and melanoma. The findings of this study will aid in informing and improving Sona’s planned first-in-human studies as that important milestone is approached.

https://www.sonanano.com/tht-cancer-therapy-to-be-accessed-for-efficacy/
Image Source: https://www.sonanano.com/therapies/tht/

21. EXercise for Cancer to Enhance Living Well (EXCEL) Study (Oct.11/23)

Exercise for Cancer to Enhance Living Well (EXCEL) is a 5-year Canada-wide project, which offers free, 12-week exercise classes designed specifically for individuals undergoing or recovering from cancer treatment. Classes are online through a secure video-conferencing platform, and where possible, in-person (post-COVID). Physical activity can help overcome treatment-related side effects such as fatigue and pain, improve mental health by reducing anxiety and depression, and improve overall quality of life for individuals living with and beyond cancer. Studies show that physical activity may even reduce the risk of recurrence for some cancers. Many urban centres in Canada offer cancer-specific exercise programs, however, rural and remote areas tend to lack exercise resources to support cancer survivors, resulting in lower activity levels, poorer health, and diminished quality of life. Thus, EXCEL targets cancer survivors living in rural and remote regions across Canada, empowering them to move more and providing opportunities to benefit from physical activity.

To learn more about the EXCEL study: https://kinesiology.ucalgary.ca/labs/health-and-wellness/research/research-studies/exercise-cancer-enhance-living-well-excel
To hear about participant experiences: https://www.youtube.com/watch?v=c01oo4Yd3oA

22. Vitamin C Intake and CRC Survival According to KRAS and BRAF Mutation: A Prospective Study in Two US Cohorts (Sept.30/23)

The associations of vitamin C intake with colorectal cancer (CRC) survival according to tumour KRAS or BRAF mutation status remain unclear. Therefore, researchers conducted the first prospective study to examine the association of post-diagnostic vitamin C intake with CRC-specific and all-cause mortality according to KRAS or BRAF mutation status in two large U.S.-wide cohort studies. They also assessed SLC2A1 mRNA expression according to KRAS or BRAF mutation in the TCGA database.

During an average of 12.0 years of follow-up, researchers documented 2,096 CRC cases, of which 703 cases had KRAS and BRAF mutation data. The association between total vitamin C intake and CRC-specific mortality suggestively differed according to KRAS or BRAF mutation status, with the multivariable hazard ratio (HR) per 400 mg/day increase in vitamin C intake for CRC-specific mortality of 1.07 in cases with both wild type and 0.74 in cases with either KRAS or BRAF mutant type. TCGA analysis showed a higher mRNA SLC2A1 expression in KRAS or BRAF-mutated tumours than in wild-type tumours.

These findings support the laboratory evidence for a potential benefit of vitamin C for CRC patients with KRAS and BRAF mutated tumours. Further studies are needed before making any clinical recommendations for vitamin C use in CRC patients with KRAS/BRAF mutations.

https://www.nature.com/articles/s41416-023-02452-2
Image Source: https://plantura.garden/uk/green-living/nutrition/vitamin-c-fruits
23. Pan-Cancer Analysis of Postdiagnosis Exercise and Mortality (Aug.31/23)

Despite the data, the impact of postdiagnosis exercise on cause-specific mortality in cancer survivors and whether this differs on the basis of cancer site is unclear. Therefore, researchers performed an analysis of 11,480 patients with cancer enrolled in the Prostate, Lung, Colorectal, and Ovarian cancer screening trial. After a median follow-up of 16 years from diagnosis, 4,665 deaths were documented (1,940 due to cancer and 2,725 due to other causes).

In multivariable analyses, exercise consistent with exercise guidelines was associated with a 25% reduced risk of ACM compared with non-exercise. Compared with non-exercise, exercise consistent with guidelines was associated with a significant reduction in cancer mortality and mortality from other causes. The inverse relationship between exercise and cause-specific mortality varied by exercise dose. Exercise consistent with guidelines was associated with a reduced hazard of ACM for multiple cancer sites. Reduction in cancer mortality for exercisers was only observed in head and neck and renal cancer.


24. Frequently Asked Questions for COVID-19

Q: What is COVID-19 (or novel Coronavirus Disease - 19)?

A: Coronaviruses are a large family of viruses that can cause illnesses in humans and animals. Coronaviruses can cause illnesses that range in severity from the common cold to more severe diseases such as Severe Acute Respiratory Syndrome (SARS) and most recently, COVID-19. COVID-19 or novel coronavirus originated from an outbreak in Wuhan, China in December 2019. The most common symptoms associated with COVID-19 can include fever, fatigue, and a dry cough. Though additional symptoms have now been linked with the disease, which may include aches and pains, nasal congestion, runny nose, sore throat, diarrhea, skin rash and vomiting. It is also possible to become infected with COVID-19 and not experience any symptoms or feeling ill. The spread of COVID-19 is mainly through the transmission of droplets from the nose or mouth when a person coughs, exhales or sneezes. These droplets land on surfaces around a nearby person. COVID-19 can be transmitted to that nearby person who may end up touching the surface contaminated with COVID-19 and then end up touching their nose, mouth, or eyes. A person can also contract COVID-19 through inhaling these droplets from someone with COVID-19. Although research is still ongoing, it is important to note that older populations (over the age of 65), those with a compromised immune system and those with pre-existing conditions including heart disease, high blood pressure, lung disease, diabetes or cancer may be at a higher risk of severe illness due to COVID-19.

https://www.who.int/news-room/q-a-detail/q-a-coronaviruses

Q: What can I do to avoid getting Coronavirus?

A: There are various ways in which we can reduce our risk of contracting COVID-19. Below are some measures suggested by the World Health Organization
1. Keep at least 2 metres (or 6 feet) between yourself and other people. This will reduce the risk of inhaling droplets from those infected with COVID-19.
2. Regularly clean your hands for at least 20 seconds with warm water and soap, or an alcohol-based hand rub. This will kill any viruses on your hands.
3. Avoid touching your eyes, nose and mouth. If the virus is on your hands, it can enter the body through these areas.
4. Follow good respiratory hygiene by covering your mouth and nose with a tissue or elbow when you cough and sneeze. This prevents the droplets from settling on surfaces or being released into the air around you.
5. Stay home as much as possible, especially if you are feeling unwell. If you think you may have the Coronavirus, please see “What should I do if I think I have Coronavirus?” section.
6. Please wear a face covering or mask in public when physical distancing is not possible.

https://www.who.int/news-room/q-adetail/q-a-coronaviruses

Q: Are there special precautions that people with cancer can take?

A: People with cancer (and other chronic ailments such as heart disease, diabetes, high blood pressure and lung disease) are at a higher risk of severe illness due to COVID-19 as cancer is considered a pre-existing health issue. Some cancer treatments including chemotherapy, radiation and surgery can weaken the immune system, making it harder for the body to fight infections and viruses, such as Coronavirus. It is important to diligently follow the World Health
Organization’s recommendations above to reduce the risk of contracting COVID-19. If you have any concerns about your risk, it is best to contact your doctor or healthcare team.

Q. Will anything change with regards to my cancer related medical visits?

As each patient and treatment plan is unique, it is always best to contact your health care provider for updated information about your treatment plan. In some cases, it is safe to delay cancer treatment until after the pandemic risk has decreased. In other cases, it may be safe to attend a clinic that is separate from where COVID-19 patients are being treated. Oral treatment options could be prescribed by your care provider virtually, without the need to attend the clinic. Finally, some follow-up appointments or discussions could be held virtually (via skype or zoom for example) or over the phone to minimize your risk. As we know, conditions and protocols are changing daily due to the nature of the COVID-19 outbreak, and vary based on location, therefore, the best first step is to reach out to your care provider for guidance.

https://www.cancer.gov/contact/emergencypreparedness/coronavirus

Should you wish to contact your local public health agency, please see below.

**Alberta**
COVID-19 info for Albertans
Social media: Instagram @albertahealthservices, Facebook @albertahealthservices, Twitter @GoAHealth
Phone number: 811

**British Columbia**
British Columbia COVID-19
Social media: Facebook @ImmunizeBC, Twitter @CDCofBC
Phone number: 811

**Manitoba**
Manitoba COVID-19
Social media: Facebook @manitobagovernment, Twitter @mbgov
Phone number: 1-888-315-9257

**New Brunswick**
New Brunswick Coronavirus
Social media: Facebook @GovNB, Twitter @Gov_NB, Instagram @gnbca
Phone number: 811

**Newfoundland and Labrador**
Newfoundland and Labrador COVID-19 information
Social media: Facebook @GovNL, Twitter @Gov_NL, Instagram @govnlsocial
Phone number: 811 or 1-888-709-2929

**Northwest Territories**
Northwest Territories coronavirus disease (COVID-19)
Social media: Facebook @NTHSSA
Phone number: 811

**Nova Scotia**
Nova Scotia novel coronavirus (COVID-19)
Social media: Facebook @NovaScotiaHealthAuthority, Twitter @healthns, Instagram @novascotiahealthauthority
Phone number: 811

**Nunavut**
Nunavut COVID-19 (novel coronavirus)
Social media: Facebook @GovofNunavut, Twitter @GovofNunavut, Instagram @governmentofnunavut
Phone number: 1-888-975-8601

**Ontario**
Ontario: The 2019 Novel Coronavirus (COVID-19)
Social media: Facebook @ONThealth, Twitter @ONThealth, Instagram @ongov
Phone number: 1-866-797-0000

**Prince Edward Island**
Prince Edward Island COVID-19
Social media: Facebook @GovPe, Twitter @InfoPEI,
Quebec
Coronavirus disease (COVID-19) in Québec
Social media: Facebook @GouvQc, Twitter @sante_qc
Phone number: 1-877-644-4545

Saskatchewan
Saskatchewan COVID-19
Social media: Facebook @SKGov, Twitter @SKGov
Phone number: 811

Yukon
Yukon: Find information about coronavirus (COVID-19)
Social media: Facebook @yukonhss, Twitter @hssyukon
Phone number: 811