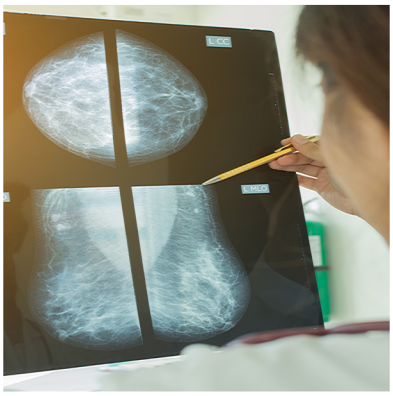
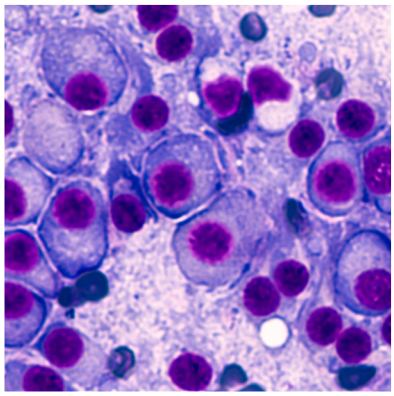
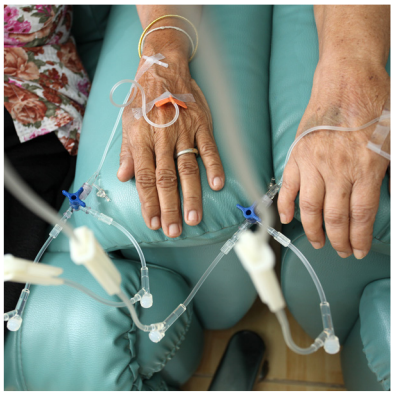
Canadian Cancer Trials Group

Groupe canadien des essais sur le cancer

2024 Annual Report







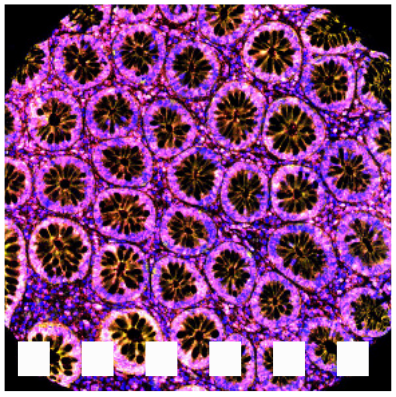


Table of Contents

CCTG Year in Review

2024 Highlights & Achievements

Dr Janet Dancey, CCTG Chair and Director

2024 was another landmark year for CCTG, marked by significant achievements, new challenges, and important progress for patients and cancer research.

Advancing Clinical Trials
We exceeded expectations in trial activation, launching 18 new trials across both early- and late-phase programs and diverse cancer settings—surpassing group targets. We also completed six final analyses, advancing knowledge across multiple cancer types.

A significant highlight was the IND.227 trial. Based on its findings, both the FDA and Health Canada approved pembrolizumab in combination with chemotherapy for mesothelioma—an advancement that brings new options to patients facing this difficult-to-treat disease.

Research Funding & Productivity
In 2024, there were 11 successful grants securing $13.7M to support our research. Our scientific productivity remained robust with 71 peer-reviewed publications in leading journals.

Several landmark trials were highlighted in the highest impact journals, including:

- The Lancet HE1 – Demonstrated that palliative radiotherapy provides better pain control and quality of life compared to best supportive care in liver cancer.
- New England Journal of Medicine CX5 – Showed that simple hysterectomy offers equivalent cancer control with improved quality of life compared to radical hysterectomy in cervical cancer.
- New England Journal of Medicine HDC1 – Established nivolumab plus AVD as a new standard of care in Hodgkin's lymphoma, providing better long-term survival.
- Annals of Oncology PR13 RADICALS – The follow up study reported that adding six months of androgen deprivation therapy to postoperative radiotherapy did not improve metastasis-free survival, giving clinicians and patients valuable evidence to guide shared decision-making.

Partnerships & Collaboration
Our partnerships grew stronger in 2024. We expanded collaborations with international peers and with industry, accelerating the advancement of cancer clinical trials worldwide.

Looking Ahead
In 2025, our focus will turn to the NCTN grant renewal application and the launch of our next five-year Strategic Planning process. These efforts will allow us to reflect on lessons learned, strengthen our operations, and chart the vision for the next era of CCTG cancer clinical trials research. We remain committed to our core mission to support the development and conduct of clinical trials across all cancer settings, for all cancer patients

Closing Reflection
As we reflect on the past year, it is clear that none of these achievements would be possible without the dedication of every person in our group and across our network. Together, we are shaping the future of cancer research. This is how trials are conducted, and—most importantly—how lives are saved.

CCTG BY THE NUMBERS 2024

Accrual

Since 1980 **111,074** patients have been accrued to CCTG trials and **80,896** were Canadians.

In 2024:

3,304 Patients Accrued Globally

3,053 Patients Accrued in Canada

Trials

74 trials open in communities across Canada with clinical research in over **30** different cancer types

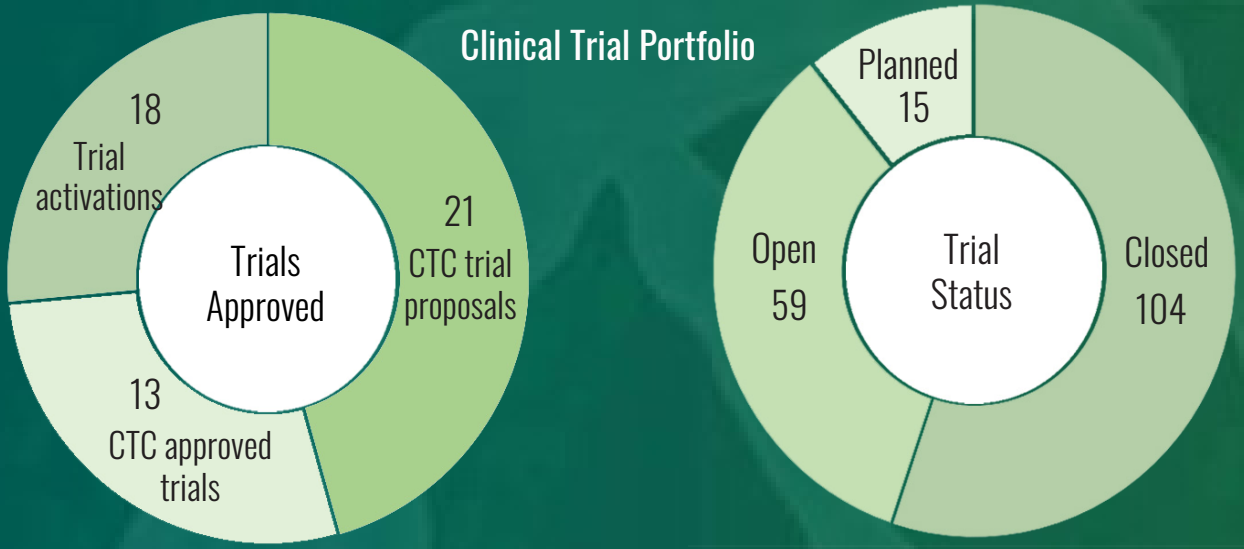
72 CCTG led clinical trials

71 NCTN Intergroup led trials

9 NCTN CCTG led trials

26 International Intergroup Led

178 total number of clinical trials



CCTG NETWORK AT A GLANCE

The CCTG network includes **87** Canadian centres working with **563** international centres in **19** countries.

Canadian Members
7,235

Total Network
22,232

International Members
14,997

2,313
Canadian Investigators

4,571
International Investigators

4,922
Canadian Clinical Trial Personnel

10,426
International Clinical Trial Personnel

Publications

11 successful grant applications securing $13.7M to support CCTG research with 71 peer-reviewed publications

Abstracts	Publications	IND Trial Analyses	Phase III Analyses
71	71	8	10

Patient Representative Committee

2024 Overview

2024 was a milestone year for the Patient Representative Committee, marked by the Patient Priorities in Cancer Research Report, which outlines six key research priorities that matter most to patients to guide strategic planning and future clinical trial development.

The committee continued their focus on investigator awareness with Patient Engagement training sessions at the fall New Investigator Training Course and at the Spring Meeting. This continued outreach has improved Patient Representative engagement during new proposal development, ensuring patient-centered trial design and endpoints from the onset. There was also Patient Representative participation in all of the EDIIA Working Groups, with a focus on incorporating diversity and cultural perspectives into the ongoing work for members.

This was a year of transition for the committee, with several long-serving members completing their terms and many new members joining. A key priority was effective on-boarding, with an emphasis on encouraging committee chairs and senior investigators to actively participate in the Patient Representative orientation sessions. This collaborative approach supported stronger integration of patient voices from the earliest stages of trial development from the development and reinforced the value of patient partnership across all CCTG activities

Another important initiative for the committee was led by the Patient-Facing Communications for Trial Outcomes Working Group. They completed a comprehensive review of the information letters provided to trial participants at the end of a study or when results become available. The result was an updated communication template that emphasizes plain language with content review by a Patient Representative—ensuring that messages are clear, accessible, and meaningful to clinical trial participants.

2025 Priorities

- Encourage patient research priorities consideration at disease site committees
- 100% Patient rep review new proposals, protocol and consent, plain-language summaries
- Implement the plain-language summaries at trial closure
- Transition to a new Chair and continue and recruitment for PRC members
- Continue investigator engagement: Practicum and Spring Meeting sessions
- Assist in identifying and addressing barriers to accrual
- Ongoing support of 100% of grant applications
- Continue embedding EDIIA in everything the committee does
- Continue sharing patient engagement best practices

Patient Representatives

Judy Needham
Chair Emeritus

Michelle Audoin
Incoming Chair

> "Everything you do, so passionately and selflessly, is with the aim of making things better for others. Your unwavering commitment to improve the lives of others has been a guiding force for me, and I am deeply grateful to have had the opportunity to contribute my visions and ideas to this meaningful work. - Judy Needham"

Ruth Ackerman

Dawn Barker

Hayden Bechthold

Louise Bird

Emi Bossio

Deb Clark

Lindsay Clarke

Carol Gordon

Jasmine Heuring

Carol Hill

Janice Hodgson

Hilary Horlock

Marie-Térèse Little

Sally Nystrom

Joan Petrie

Bill Richardson

Bob Taylor

Erwin Wanderer

Catherine Wreford

Martina Wood

4 Patient Rep interview videos

6 quotes for trial opening stories

16 new Patient Rep interviews

8 new Patient reps welcomed

7 new Patient Rep orientation sessions

CCTG Patient Representative Committee

CANCER RESEARCH PRIORITIES

In the spring of 2024 the CCTG Patient Representatives participated in a facilitated session to identify the research topics that they view as being most important to cancer patients and caregivers. The top six identified priorities, in order of importance, are intended to help guide the development of the CCTG trial portfolio based on the views of those with lived experience.

OVERARCHING PRINCIPLES

The working group identified principles that they believe should be regarded as paramount when considering the Cancer Research Priorities:

All clinical trials should ensure outcomes are focused on having a direct positive impact on patients and include robust quality of life patient surveys and reporting.

Every effort should be made to include patients from historically under represented groups. Trial designs should specifically outline how researchers intend to recruit from these groups, including success criteria and reporting requirements around diversity goals and metrics.

It is critically important that access to clinical trials be expanded and that the time from ideation to operationalization of clinical trials be significantly shortened so that patients can have more ready access to potentially life-saving or life-improving treatments.

Cancer Research Priorities are disease site agnostic and are intended to encompass all cancers, including those considered "rare".

1. Innovative treatments

Focus on innovative therapies, to find treatments to completely cure cancers by killing both growth and stem cells while sparing normal cells. Some novel treatments available in other countries are not available yet in Canada, prioritize these as study options.

- Antibodies, nanoparticles or oncolytic viruses in targeted therapies.
- Treatments using oncogenomic analysis.
- CRISPR in vitro gene editing.
- CAR T-cell, TIL, mRNA, and therapeutic vaccine therapies (dendritic cell).
- Other leading edge research areas.

2. Biomarkers

Biomarkers and ctDNA investigation is a vital path towards defeating cancer. Encourage cancer research and treatment options based on biomarkers rather than location of occurrence, where one or more biomarkers are common to several sites.

- Identification of an individual's predisposition to cancer.
- Preventative vaccines and early detection.
- Personalized treatments, like therapeutic vaccines.
- Surveillance for progression and recurrence during and post treatment.

3. Use of Technology

Exploration of how artificial intelligence (AI) can be used to enhance the identification of research opportunities, as well as the analysis of clinical trial results.

- Clinical data that could be used to better patient outcomes or identify patterns for further research.
- Conduct trials with AI objectives (i.e. AI study to see if is can improve treatment decisions, progression or recurrence predictions).
- Support efforts underway to digitize patient samples and results to optimize their utility.

4. Psychological Holistic Oncology

A patient's mental state and physical well-being can impact their ability to cope with a cancer diagnosis, adhere to treatments, and improve outcomes. Holistic cancer treatments can equip patients to develop wellness habits that enhance long-term quality of life.

- Examine if the use of holistic approaches, including exercise, nutrition, appearance, and mental well-being can augment healing and overall wellness.
- Explore existing web-based tools that have been developed for these purposes.

5. Early Detection

Research in minimally invasive, cost-effective screening tools to detect cancer early in all populations including individuals under age 40. With the goal of quick transitions to active treatment.

- Includes bio-marker based screening.
- Other less-invasive screening methods.
- Enhanced stool based tests for colorectal cancer.
- Detection through blood, saliva or breath.
- Enhanced imaging, such as low-dose CT scanning.

6. Treatment Optimization

Trials that aim to optimize treatment dosages and time periods, with the goals of minimizing side effects, patient burden, improving long-term quality of life, while maintaining effective tumour control.

- New, innovative agents that directly target cancer cells while sparing healthy cells.
- Improve long-term quality of life, replacing damaging treatments with less invasive treatments.
- De-escalation and dose optimization.




The Patient Representatives Research Priorities

A focus on CCTG's work and current trials

1. Innovative treatments

CCTG's Chimeric Antigen Receptor (CAR) T-cell therapy studies will be a new treatment option for Canadians. T-cells from the patient are genetically modified to target the cancer cell, then infused back to attack cancer harnessing the immune system.

- **GCAR 1** a phase I feasibility safety study of a CAR-T therapy for patients with relapsed refractory GPNMB-Expressing solid tumors.
- **TACTful** researchers have developed a next generation cell therapy that offers the potential for reduced toxicity and improved duration of response - a much needed therapy option.

2. Biomarkers

Exploring treatment options based on biomarkers and ctDNA of the cancer rather than the location of occurrence.

- **EN.10** molecular testing to identify endometrial cancer patients at low risk of cancer recurrence based on the molecular features of their tumours - can they safely receive less, or no radiotherapy or chemotherapy after surgery.
- **EN.11** molecular testing to identify endometrial cancer patients who may benefit from immunotherapy - also evaluating if immunotherapy prevents tumour recurrence or spread and comparing the effects of combining a new drug with radiation therapy.

3. Use of Technology

Exploration of how AI and new technology can enhance research opportunities, and analysis of clinical trial results.

- **PR.21** investigating new advanced imaging (177Lu-PSMA) designed to deliver high doses of radiation directly to prostate cancer sites - to find out if it can slow the growth of prostate cancer compared to standard chemotherapy.
- **IND.227** substudy using AI to predicate outcomes in IND.227 mesothelioma patients with based on their CT imaging analysis.

4. Psychological Holistic Oncology

Addressing a patient's mental state and physical well-being to improve outcomes enhancing long-term quality of life.

- **SC.26** a palliative care intervention delivered by social workers or psychologists to reduce physical and emotional suffering of the patient undergoing acute leukemia induction chemotherapy.
- **SC.28** evaluating the use of a smartphone app-based mindfulness and meditation intervention for cancer survivors to help improve stress and well being after treatment is completed.

5. Early Detection

Research in minimally invasive, cost-effective screening tools to detect cancer early.

- **IND.241** - Using ctDNA to evaluate the role of early progression detection in metastatic breast cancer patients and using biomarkers to assign treatment with innovative therapies.
- **MAC.22** an early detection screening study for breast cancer comparing digital mammography to tomosynthesis (3D)

6. Treatment Optimization

Optimize treatment to minimize side effects, patient burden and improve quality life.

- **MA.39** Using biomarkers to safely reduce radiation and preserve the breast in low-risk, hormone receptor–positive breast cancer patients.
- **CO.32** using an intense combination chemotherapy treatment to improve the supporting data for surgical sparing in rectal cancer avoiding surgical complications and QoL for patients.

Equity, Diversity, Inclusivity, Indigenization, and Accessibility

2024 Overview

CCTG remains committed to fostering a culture of equity, diversity, inclusivity, indigenization, and accessibility (EDIIA) across all facets of our research, network, and workplace. In 2024 we advanced this commitment through the implementation of its EDIIA Action Plan, placing particular emphasis on expanding EDIIA training and learning opportunities for both central office staff and network members. These activities are part of a broader and ongoing effort to build meaningful relationships with equity-deserving communities and researchers, ensuring that diverse voices are included in all aspects of cancer clinical research.

Over the past year, significant progress was made in integrating EDIIA into its core operations and scientific work. The recommendations of three EDIIA Working Groups are being finalized, helping to inform how EDIIA principles will be embedded in our scientific priorities, trial designs, and research activities. The CCTG network leadership formally endorsed the creation of a Health Equity Standing Committee to provide strategic oversight to ensure that equity considerations are integrated across CCTG's clinical trials and organizational practices in a sustainable and systematic manner.

Integrating Equity Diversity and Inclusion into CCTG Clinical Trials

Spotlight on the PR.25 and HN.13 trials

To align scientific priorities with EDIIA principles, CCTG hosted a focused workshop during the 2024 Annual Spring Meeting. The workshop explored ways to improve equity and access in two pilot trials: HN.13, a phase III study comparing stereotactic body radiation therapy with standard palliative radiation for head and neck cancer; and PR.25, a phase III trial investigating platinum and taxane chemotherapy in advanced prostate cancer patients with DNA damage response gene alterations.

The workshop convened trial committee members, senior investigators, central office staff, patient representatives, and external experts in cancer care equity and inclusive clinical research. Participants applied an equity lens to the trial protocols and discussed evidence-based strategies for improving diversity and inclusion in trial design and implementation. The aim was to identify practical, scalable actions that could improve participant access and representation in these studies and potentially be adopted across future CCTG trials.

Several initiatives emerged from these discussions and will be piloted in the PR.25 and HN.13 trials. These include integrating EDIIA training into trial start-up webinars; developing a reimbursement policy to offset trial-related expenses for participants; creating Diversity Action Plans tailored to each study; translating patient-facing materials into additional languages; and developing culturally safe, trauma-informed clinical trial resources in collaboration with Indigenous and equity-deserving communities. These efforts mark an important step toward embedding EDIIA principles into the operationalization of clinical trial research, with the ultimate goal of ensuring that all patients, regardless of background, can access and benefit from cutting-edge cancer treatments.

Investigational New Drug Program

2024 Overview

The CCTG Investigational New Drug (IND) Program continued to access new anticancer drugs for testing in trials with innovative designs. The program also worked to facilitate patient access to early clinical trials and to identify promising treatments for pivotal randomized studies. Other key strategic initiatives included patient-focused research, optimizing genomic and radiomic data collection, increasing academic partnerships nationally and internationally and building relationships with companies with promising new drugs.

IND.227 was reported, showing statistically significant overall survival benefits (The Lancet 2023) and supported multiple regulatory approvals in Canada, USA, Europe and Japan for pembrolizumab in combination with first line pemetrexed and platinum chemotherapy for pleural mesothelioma. Ongoing secondary analyses will be presented at meetings in 2025.

A major initiative (2023-2024) was development of a national team to support CCTG's Cell Therapy Platform. The GCAR1 trial studying solid tumours including a rare cancer cohort with young adults (planned 2025) and the TACtful myeloma trial involve multiple pan-Canadian collaborations and have been awarded Canadian Institutes of Health Research, BioCanRx, Leukemia and Lymphoma Society of Canada and Myeloma Canada peer reviewed grant funding. IND.245 is a third trial being developed under this platform investigating induction therapy prior to CART therapy (mantle cell lymphoma; planned 2025).

Platform trials and personalized medicine trials, especially in high unmet need areas including rare cancers remain a high priority. IND.243 was a master protocol of lunresertib in patients with advanced usually refractory cancers in combination with gemcitabine or camonsertib. Interesting anti-cancer activity was seen in primary platinum refractory ovarian cancer and a sub-study was added for these patients. IND.244, a phase II study of ibrutinib combination therapy in transplant ineligible individuals with newly diagnosed primary central nervous system lymphoma, opened for accrual.

IND.238, a phase II study of durvalumab for patients who discontinued prior checkpoint therapy due to immune-related toxicity, also allows continued protocol therapy for responding patients previously enrolled to completed CCTG studies.

IND.240 is an immunotherapy platform study in patients with high grade serous ovarian cancer and includes multiple sub-studies testing investigational drugs and drug combinations. The first 2 sub-studies were completed and a new sub-study, toripalimab-tpzi and ENB-003 (endothelin B receptor inhibitor), will start enrollment in 2025.

Final and correlative analyses were completed for multiple trials including: IND.242 a neoadjuvant platform trial in patients with surgically resectable NSCLC; IND.223/IND.234 a prostate cancer biomarker selected platform trial including 7 sub-studies; and the IND.236, IND.237 and IND.239 trials, testing Canadian developed therapeutics in patients with advanced breast cancer.

Ensuring patient and collaborator engagement is a high priority. A retreat was held summer 2024 to discuss strategies for inclusion of Patient Reported Outcomes (PRO) in IND trials as well as improving access to early clinical trials (collaboration with Australian investigators). Engagement in PRO international initiatives continues.

2025 Priorities

- Open and accrue to 6 new IND trials, including 2 new cell therapy-based trials
- Enhance national and international partnerships and opportunities
- Ensure CCTG EDIIA strategies are implemented for all IND trials; consider, and develop through engagement with CCTG EDIIA leadership, any early clinical trial specific activities that may be appropriate
- Test and pilot the incorporation of PROs in selected IND trials and ensure cost effective
- Continue with initiatives to increase efficiency and quality in IND trial conduct including activation activities at sites, as well as ongoing educational and communication activities

Trial Spotlight

IND.241 is a liquid-biopsy informed platform trial to evaluate treatment in CDK4/6-inhibitor resistant ER+/HER2- metastatic breast cancer

The IND.241 platform study is supported by multiple peer reviewed grants including from CIHR, The Komen Foundation and Conquer Cancer (ASCO Foundation). The trial includes multiple correlative endpoints, including blood-based assays and radiomics which will help investigators understand mechanisms of disease progression and how best to select treatments for individual patients. To date, four sub-studies have been opened and multiple new sub-studies are expected to open in 2025.

Committee Executive

Dr. David Cescon
Chair

Dr. Yvette Drew
Incoming Chair

Dr. Quincy Chu
Past Chair

Dr. Lesley Seymour
IND Program Director

Laura Pearce
Senior Investigator

Dr. Dongsheng Tu
Senior Biostatistician

Dr. Wei Tu
Senior Biostatistician

Joan Petrie
Patient Representative

Carol Hill
Patient Representative

Michael Kolinsky
Alexander Wyatt
Anna Tinker
Daniel Renouf
Jonathan Spicer
John Hilton

Nathalie Levasseur
Christina Addison
April Rose
Michael Ong
Stephanie Lheureux
Amber Simpson

Annette Hay
Janet Dancey
Mariam Jafri
Pamela Brown-Walker
Pierre-Olivier Gaudreau
Maxwell Sherry

Terry Ng (Quality of Life Liason)
Lorrie Yunace (CRA Representative)
Stephanie DeLuca (Pharma Representative)
Erica Tsang

Brain Disease Site Committee

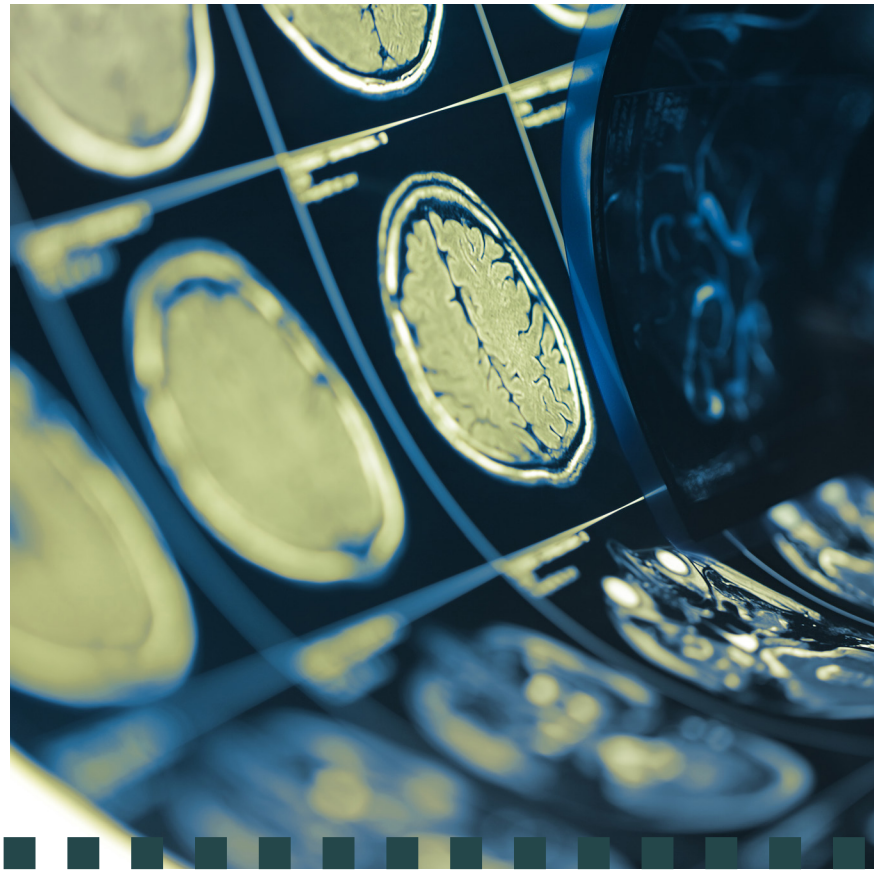
2024 Overview

This year the Brain Disease Site committee opened the much-anticipated international study CE.9 (LUMOS2) a collaboration with the Australian Cooperative Trials Group for Neuro-Oncology (COGNO). This umbrella study evaluates personalized therapy of multiple novel and molecularly targeted drugs, selected on the basis of tumour DNA analysis, for recurrent low and anaplastic gliomas. CCTG has activated the first site with first patient enrollment expected soon. New arms have been added to the trial with more to follow.

The committee is pleased to once again be collaborating with the European Organisation for Research and Treatment of Cancer (EORTC), on their upcoming CE.10 (VIGOR) trial. This trial investigates whether Vorasidenib should be used as a maintenance treatment after chemoradiotherapy treatment of patients with IDH-mutated grade 2 or 3 astrocyctomas.

In 2024 the CCTG-led CE.7 trial, comparing stereotactic radiosurgery with hippocampal-avoidant whole brain radiotherapy, reached 140 patients accrued, triggering a pre-planned interim analysis. Accrual was completed to CEC.6 (CODEL) questioning whether treatment with radiotherapy with concomitant and adjuvant temozolomide is superior to receiving radiotherapy with adjuvant PCV chemotherapy.

The Brain Disease Site Committee has a strong interest in developing phase I and II trials of novel targeted agents and welcomed to the committee Dr. Rebecca Harrison in the role of Investigational New Drug (IND) Liaison. The Committee's goal is to increase the opportunity for identification and prioritization of brain trials in IND. The Committee also formed the Brain Tumour Working Group to develop and evaluate trial concepts including one in meningioma and one in recurrent glioblastoma.



2025 Priorities

- Expand participation and enrolment to CE.9 (LUMOS2)
- Open CE.10 (VIGOR)
- Complete the CE7 interim analysis
- Identify opportunities for new trial concepts in IND and via the Brain Tumour Working Group
- Identify a new higher volume trial which CCTG can develop and lead

Committee Executive

Dr. Marshall Pitz
Co-Chair

Dr. David Roberge
Co-Chair

Chris O'Callaghan
Senior Investigator

Dr. Keyue Ding
Senior Biostatistician

Catherine Wreford
Patient Representative

Maureen Parkinson
Warren Mason
Galereh Zadeh
James Perry
Mary MacNeil
Rebecca Harrison (IND Liason)
Nicole Mittmann (Economic Analysis Liaison)
Anne Leis (Quality of Life Liaison)

Trial Spotlight

CEC.6 (CODEL) is a phase III intergroup study of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy with adjuvant PCV chemotherapy in patients with 1p/19q co-deleted anaplastic glioma or low grade glioma

This year saw the completion of accrual to CEC.6 (CODEL) trial comparing radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy with adjuvant PCV chemotherapy in patients with in 1p/19q co-deleted anaplastic or low-grade gliomas. This is a phase III intergroup study led by the US based ALLIANCE for Clinical Trials in Oncology.

The trial met its protocol-specified accrual target with a final enrolment of 264 patients, with CCTG centres contributing 33 patients to the study. Completion of the CODEL trial represents the culmination of 15 years of collaboration between Canadian, American and European academic CNS Oncology researchers. The evolving landscape of clinical brain tumour research and emerging data over this time was reflected in corresponding changes to the design of the CODEL trial. However, its successful completion will assist physicians in determining optimal therapy for a relatively rare population of patients with brain tumours.

Breast Disease Site Committee

2024 Overview

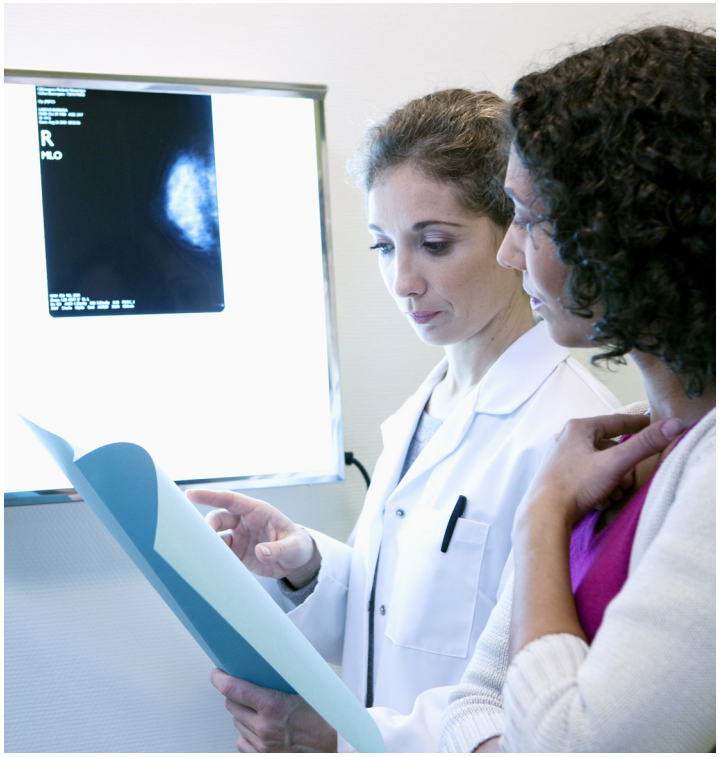
It has been a busy and productive year for the Breast Disease Site Committee, with the opening of several key clinical trials. The new MAC.30 (OFSET) trial compares the addition of adjuvant chemotherapy to ovarian function suppression plus endocrine therapy to ovarian function suppression plus endocrine therapy alone for early-stage breast cancer in premenopausal women.

The MAC.29 (OptimICE-pCR) trial was also activated, investigating a de-escalated treatment for patients with early-stage triple negative breast cancer. This US National Clinical Trials Network (NCTN) study will examine whether an additional treatment with immunotherapy is necessary for patients who have had a good response after initial neoadjuvant treatment.Another addition is the IND.241 platform study, which tests breast cancer tumors for DNA abnormalities using ctDNA to help predict which patients are most likely to benefit from specific targeted treatments. This precision medicine approach represents a major step forward in tailoring therapies based on individual tumor biology.

In 2024 the MA.40 trial successfully completed accrual, reaching the target of 250 study participants enrolled. This phase III trial investigates the use of either Ipatasertib plus Fulvestrant or placebo plus Fulvestrant in patients with non-curable disease following progression on a CDK4/6 inhibitor and an AI evaluated side effects during treatment and associated costs. The MAC.23 (RT CHARM) results were presented at the 2024 American Society for Radiation Oncology meeting and demonstrated that hypofractionation given postmastectomy with planned breast reconstruction does not increase complications and can be shortened by nearly half for this patient population.

2025 Priorities

- Focus on efforts to increase accrual to NCTN trials
- Continue to add trials to portfolio that are feasible and appealing to the breast cancer community
- Complete, analyze and present CCTG-led practice-changing trials (MA.39, MA.40)
- Continue CCTG trial concept development for conduct and support within the NCTN
- Explore new and recently successful collaborations–UniCancer France and BCT Australia & New Zealand
- Continued use of the breast tumour bank for genomic and translational studies
- Continued dialogue with industry partners to access novel therapeutic agents
- Work with IND to develop novel therapeutic agents to bring to phase 2 and 3 trials
- Enhance accessibility of breast trials to rural and marginalized communities



Committee Executive

Dr. Eileen Rakovitch
Co-Chair

Dr. Stephen Chia
Co-Chair

Dr. Wendy Parulekar
Senior Investigator

Dr. Lois Shepherd
Senior Investigator

Dr. Bingshu Chen
Biostatistician

Martina Wood
Patient Representative

Michelle Audoin
Patient Representative

Ruth Ackerman
Patient Representative

Dawn Barker
Patient Representative

Valerie Theberge
Jean-Francois Boileau
Philippe Bedard

Muriel Brackstone
Peter Watson
Arif Awan

Julie Lemieux (Quality of Life Liaison)
Danielle Rodin (Economic Analysis Liaison)
Abhenil Mittal (New Investigator Practicum)

Trial Spotlight

MAC.30 is a phase III adjuvant trial evaluating the addition of adjuvant chemotherapy to ovarian function suppression plus endocrine therapy in premenopausal patients with ER-Positive/HER2-Negative Breast Cancer

The MAC30 clinical trial is comparing two commonly used treatment approaches for pre-menopausal women with ER-positive, HER2-negative breast cancer who are at low to intermediate risk of recurrence. The study is evaluating whether adding chemotherapy to ovarian function suppression (OFS) plus hormonal therapy provides additional benefit, compared to OFS and hormonal therapy alone.

For this group of patients with early-stage breast cancer, the risk of recurrence is moderate, and chemotherapy is often included in standard care. However, chemotherapy comes with potential toxicity and can negatively impact quality of life during treatment. Researchers aim to determine how much additional benefit chemotherapy offers—and whether inducing early menopause through ovarian suppression may provide similar protection against cancer recurrence without the added burden of chemotherapy.

Gastrointestinal Disease Site Committee

2024 Overview

2024 was very busy for the Gastrointestinal Disease Site Committee with multiple newly approved trials and several previously approved trials being centrally activated.

The NE2 (STOPNET) international trial examining whether neuroendocrine tumour patients should continue somatostatin analogue therapy after treatment with peptide radionuclide therapy activated. This is a study from the CCTG and AGITG Commonwealth Neuroendocrine Tumour Research Collaboration (CommNETs) and opened almost simultaneously in Canada and Australia —the first of hopefully many CommNETs trials to be developed.

The ES3 (NEEDS) international esophageal cancer clinical trial was also opened, investigating whether omitting or delaying surgery for patients with squamous cell carcinoma of the esophagus who have a good response to initial chemoradiotherapy is as good in terms of patient survival as the standard treatment whereby all patients undergo surgical removal of their esophagus, and possibly better in preserving patient quality of life.
A focus on patient-driven research is behind the potential de-escalation of full rectal surgery with the CO32 (NEO-RT) trial. This study will test whether the addition of radiation therapy to chemotherapy can reduce the necessity for full rectal removal.

Important study results were also presented in 2024, including from the GA1 (TOPGEAR) trial presented at the 2024 European Society for Medical Oncology Congress (ESMO) and simultaneously published in the New England Journal of Medicine. This long-awaited trial, led by the AGITG in collaboration with the CCTG, TROG and EORTC groups, definitively demonstrated that the addition of radiation therapy to standard chemotherapy in patients with resectable gastric and gastro-esophageal junction adenocarcinoma does not improve patient quality of life nor extend their life expectancy.

2025 Priorities

- Complete accrual to PAC.3
- Optimize accrual to CRC.10, NE.1, NE.2, CO.32, GA.4 and ES.3 trials
- Activate HE.2, and CO.33 trials

Committee Executive

Dr. Sharlene Gill
Chair

Dr. Chris O'Callaghan
Senior Investigator

Dr. Dongsheng Tu
Senior Biostatistician

Hayden Bechthold
Patient Representative

Suzanne Wood
Patient Representative
(passed Feb 2025)

Howard Lim
Hagen Kennecke
Petr Kavan
Derek Jonker
Rebecca Auer

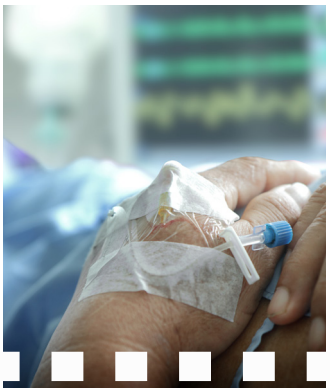
Eric Chen
Angela Hyde
Shivani Dadwal
Rachel Goodwin (IND liaison)
Kelvin Chan (Economic Analysis Liaison)
Winston Cheung (Quality of Life Liaison)

Trial Spotlight

CO.32 (NEO-RT) a phase 3 randomized trial of neoadjuvant chemotherapy, excision and observation versus chemoradiotherapy for early rectal cancer.

The CO.32 clinical trial, which opened in late 2024, is evaluating the effectiveness of chemotherapy alone versus chemotherapy combined with radiotherapy before limited rectal cancer surgery. The goal is to determine whether more patients can avoid a full rectal removal without compromising treatment outcomes—preserving bowel function and quality of life.

Researchers believe that omitting radiation may still allow for effective tumor control while reducing treatment-related side effects. If successful, this approach could offer patients a less invasive yet equally.



Genitourinary Disease Site Committee

2024 Overview

Activation was a key focus for the committee the year starting with the PR.24 (ASCENDE-SBRT), a CCTG-led NCTN trial evaluating the efficacy of stereotactic body radiotherapy (SBRT) compared to conventional external beam radiotherapy (EBRT) with brachytherapy boost in men with unfavourable, localized prostate cancer. The outcomes of this study are expected to inform future standards in managing localized prostate cancer.

Next was PR.25 (oPTion-DDR), another prostate cancer study focused on improving survival in patients with castration-resistant prostate cancer. This trial examines whether patients with DNA damage response gene alterations experience additional benefit when treated with a combination of carboplatin and docetaxel versus docetaxel alone. Importantly, PR.25 is the first GU trial to incorporate the measurement of social determinants of health using app-based technology.

The BLC6 (MODERN) trial also launched this year and explores whether tumour-informed circulating tumor DNA (ctDNA) can guide post-surgical immunotherapy decisions in bladder cancer. Researchers aim to determine if ctDNA levels from a blood test can identify which patients should receive immunotherapy and what type of immunotherapy may be most effective.

Congratulations are in order for Dr. Michael Ong, who secured CIHR funding for PR26 (Triple-Switch), a study expected to activate in early 2025. The committee is integrating the CCTG EDIIA framework into the protocol development for this trial. The GCC1 study completed accrual in 2024. This trial assessed the positive predictive value of miRNA 371 in patients with early-stage non-seminoma or seminoma germ cell tumours.

Correlative science, led by Dr. Alex Wyatt, continues to be central to the GU research program and will support the development of future biomarker-driven trials. Additionally, patient-reported outcomes have been incorporated into trial designs to ensure that the patient voice is reflected throughout the clinical research process.

2025 Priorities

- IND.234 publication of experience of operating a country-wide precision oncology trial: feasibility, lessons learned, efficacy
- Complete accrual for PR19
- Continue to work on accrual for BLC.6, PR.24, PR.25,
- PR.26 (Triple-Switch) to be activated and start accrual
- Develop EV-pembrolizumab de-escalation trial
- Develop trial evaluating treatments post adjuvant immunotherapy in renal cancer
- Continue to develop EDIIA engagement strategies for improving accrual

Committee Executive

Dr. Sebastien Hotte
Chair

Dr. Wendy Parulekar
Senior Investigator

Dr. Mariam Jafri
Senior Investigator

Dr. Keyue Ding
Senior Biostatistician

Erwin Wanderer
Patient Representative

Bill Richarson
Patient Representative

Lindsay Clarke
Patient Representative

Nawaid Usmani
Scott North
Kim Chi
Tamim Niazi
Wassim Kassouf
Michael Kolinsky (IND Liaison)

Trial Spotlight

PR.25 (oPTion-DDR) is a randomized phase III trial investigating platinum and taxane chemotherapy in metastatic castration resistant prostate cancer patients with alterations in DNA damage response genes

The CCTG PR.25 (oPTion-DDR) clinical trial uses a personalized medicine approach to investigate and evaluate markers to determine which metastatic prostate cancer patients would benefit from treatment with carboplatin, a drug used in other cancers but not routinely used in prostate cancer. A quarter of prostate cancer patients have alterations in their genes that normally repair damage. These genes are called DNA damage response genes which make cancer cells sensitive to a form of chemotherapy called platinum-based chemotherapy.

The study will compare the effects of a new drug compared to the current standard treatment for this disease. It will specifically test whether platinum-based chemotherapy used in combination with a non-platinum-based drug improves overall survival for advanced prostate cancer patients with DNA damage response gene alterations.

Gynecologic Disease Site Committee

2024 Overview

In 2024, the Gynecologic Disease Site Committee achieved several important milestones as part of its strategic agenda to improve cancer outcomes, optimize treatment selection through advanced molecular testing, and evaluate patient-reported outcomes related to anticancer therapies.1

A highlight was the launch of VU.2, a CCTG-led, CIHR-funded clinical trial focused on rare tumours. This study addresses the question of optimal surgical management for early-stage vulvar cancer, using molecular profiling of tumour tissue to guide treatment decisions.

There were also a number of high profile and practice defining publications from this committee in 2024 including:

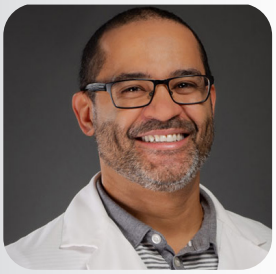
- CX.5 (NEJM 2024): efficacy and safety of a simple hysterectomy for low-risk early-stage cervical cancer.
- OVC.2 (JCO 2024): lack of efficacy of cediranib monotherapy in combination with olaparib compared to standard of care chemotherapy in platinum-resistant or primary platinum-refractory ovarian cancer.
- OV.26 (ESMO 2024): lack of efficacy of maintenance treatment with olaparib and cediranib compared to olaparib monotherapy in the relapsed ovarian cancer setting.

In addition, the accrual target for CX.6 was successfully reached. This trial will provide critical insights into the role of sentinel node biopsy in early cervical cancer, helping to shape future standards of care.

2025 Priorities

- Meaningfully participate in ongoing trials (EN.10, EN.11, VU.2)
- Analyze and publish secondary analyses generated by the CX.5 database
- Analyze the OV.25 trial (Acetylsalicylic Acid (ASA) in Prevention of Ovarian Cancer in Women with BRCA 1/2 Mutations)
- Complete and publish ongoing correlative analyses from closed CCTG led trials
- Seek additional opportunities to support trials testing molecularly driven treatment strategies within the International RAINBO consortium in endometrial cancer
- Mentor and train early/mid-career investigators within the CCTG network
- Generate innovative trial concepts designed to improve cancer outcomes in gynaecological malignancies.

Committee Executive



Dr. Stephen Welch
Co-Chair

Dr Mark Carey
Co-Chair

Dr. Wendy Parulekar
Senior Investigator

Dr. Dongsheng Tu
Senior Biostatistician

Carol Gordon
Patient Representative

Deb Clark
Patient Representative

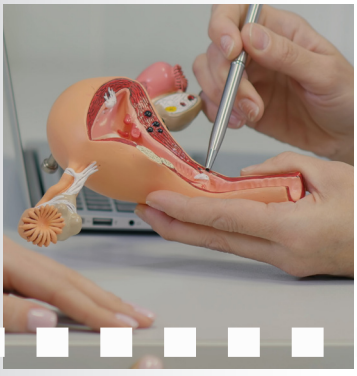
Marie Plante
Stephanie Lheureux
Laura Hopkins
Corinne Doll
Josee-Lyne Ethier (IND liaison)
Iwa Kong (Quality of Life liaison)
Janice Smith Kwon (CEA liaison)

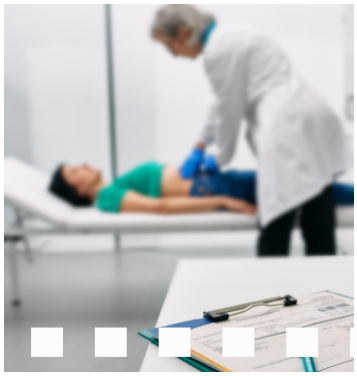
Trial Spotlight

EN.10 (RAINBO BLUE & TAPER) investigates adjuvant therapy in POLE-Mutated and p53-wildtype/NSMP early-stage endometrial cancer

EN10 (RAINBO BLUE & TAPER) trial applies state-of-the-art molecular testing to guide post-surgical treatment decisions for patients with early-stage endometrial cancer. The goal is to identify individuals at low risk of cancer recurrence based on the molecular characteristics of their tumours. These patients may safely receive reduced radiotherapy—or potentially avoid both radiotherapy and chemotherapy altogether—without compromising outcomes.

Using a lab-based method known as molecular stratification, researchers aim to personalize treatment plans, ensuring that low-risk patients are not overtreated. The trial will demonstrate the feasibility of routine molecular classification and support its implementation as a standard approach for all newly diagnosed endometrial cancer patients across Canada.





Head & Neck Disease Site Committee

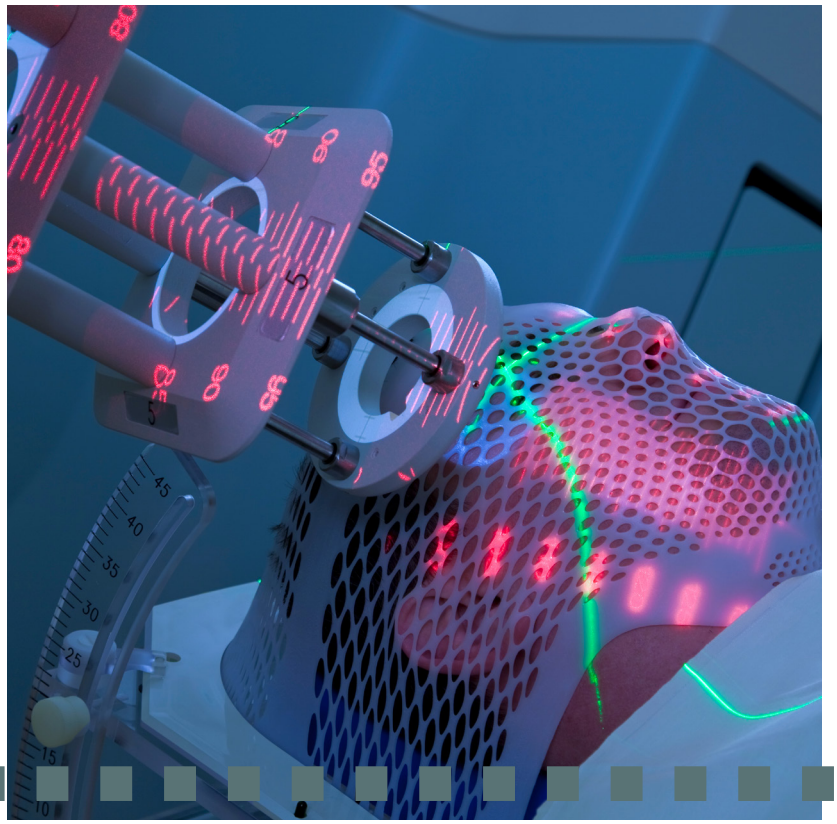
2024 Overview

2024 began on a strong note for the Head & Neck Disease Site Committee, with the completion of the final analysis for the HN.10 (EVADER) clinical trial. The results were presented at ASTRO 2024 and support the trial's central hypothesis: that lymph node regions in the neck, which are at risk but not directly invaded by tumour, can be safely spared from radiotherapy without compromising cancer control. This finding has important implications for reducing treatment-related side effects while maintaining effective cancer management.

The CIHR grant funded HN13 clinical trial was activated and will evaluate stereotactic body radiotherapy (SBRT) to treat advanced head and neck cancer patients who are unable to tolerate curative intent radiotherapy. This innovative trial will also piolet key strategies developed at the EDIIA workshop at Spring Meeting.

The Committee endorsed the CCTG SKC.1 trial which examines the efficacy of response adapted therapy post neoadjuvant immunotherapy for resectable stage III/IV cutaneous squamous cell carcinoma.

Plans for correlative studies are underway examining the microbiome in patients treated with curative intent therapy including immunotherapy (HN9) and the role of HPV related ctDNA, somatic mutations, and radiomics in patients treated with de-escalated radiotherapy (HN10). Patient reported outcomes are a committee priority—analyses are ongoing involving health related quality of life, swallowing function and patient reported toxicity measures.



2025 Priorities

- Conduct the final analysis of the HN9 trial
- Enroll to the HN.11, HN.13 and SCK.1 trials
- Analyze PRO data from the Disease Site Committee trial portfolio
- Conduct correlative analyses involving biospecimens from the HN.9, HN.10 studies
- Develop novel de-escalation treatment concepts in good prognosis head and neck cancer
- Collaborate with IND to develop a platform trial testing novel targeted therapies in metastatic head and neck cancer
- Engage in CCTG led education and training opportunities for investigators and research personnel

Committee Executive

Dr. Scott Bratman
Co-Chair

Dr. John Hilton
Co-Chair

Dr. Wendy Parulekar
Senior Investigator

Dr. Wei Tu
Senior Biostatistician

Mr. Bill Richardson
Patient Representative

Houda Bahig
Anna Spreafico (IND Liaison)
Christopher Lee (Quality of Life Liaison)
Ambika Parmar (Economic Analysis Liaison)
Enrique Sanz Garcia (New Investigator Practicum)

Trial Spotlight

HN.10 (EVADER) **was a phase II single arm trial of elective volume adjusted de-escalation radiotherapy in patients with low-risk HPV-related oropharyngeal squamous cell carcinoma.**

The CCTG HN.10 results were presented by study lead Dr Scott Bratman at the American Society for Radiation Oncology (ASTRO) 2024 meeting. Curative intent radiotherapy is usually delivered to lymph nodes at risk for cancer involvement. the side effects of this treatment can have a long-lasting impact on the quality of life for individuals diagnosed with early, good prognosis tumours.

The results of HN.10 have shown that a reduction in radiotherapy volume can be safely performed and further research in de-escalation treatment strategies is warranted. Importantly, this de-escalation strategy could be combined with others that are currently under investigation.

Hematology Disease Site Committee

2024 Overview

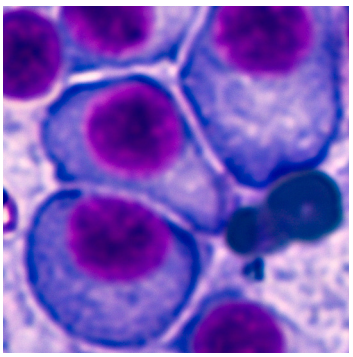
In 2024, international collaborations were a large part of the work for the Hematology Disease Site Committee. This year saw the opening of the myeloMATCH suite of clinical trials, described further under Trial Spotlight. Canadian investigators have been instrumental in developing the platform and protocols in collaborations with colleagues from across the National Cancer Institute US.

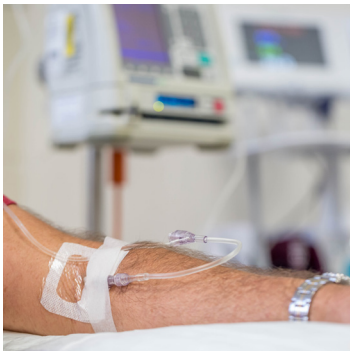
Other international collaborations include the CLC3 trial, testing early treatment for patients with chronic lymphocytic leukemia or small lymphocytic lymphoma. In Hodgkin lymphoma, the HD11 trial for people with relapsed and refractory disease is being conducted with the Australian Leukemia and Lymphoma Group, and the HD12 trial in newly diagnosed disease is being conducted in collaboration with multiple international partners including the United Kingdom.

The team is poised for significant increase in accrual including with the MY13 randomized phase III trial investigating time-limited versus continuous CD38 monoclonal antibody treatment for older people with multiple myeloma. New concepts are in development in a variety of lymphoproliferative neoplasms. Hematology continues to benefit from excellent investigator engagement. Additional initiatives to encourage young investigators are planned.

2025 Priorities

- Focus on opening and accruing to newer trials
- First CCTG hematology cell therapy trial
- Opening myeloMATCH ALC9 and MD1
- Exploring additional Canadian roles in myeloMATCH
- Advance new trials concepts in lymphoma
- Advance cell therapy research






Committee Executive

Dr. Anthony Reiman
Co-Chair

Dr. Sarit Assouline
Co-Chair

Dr. Annette Hay
Senior Investigator

Dr. Lois Shepherd
Senior Investigator

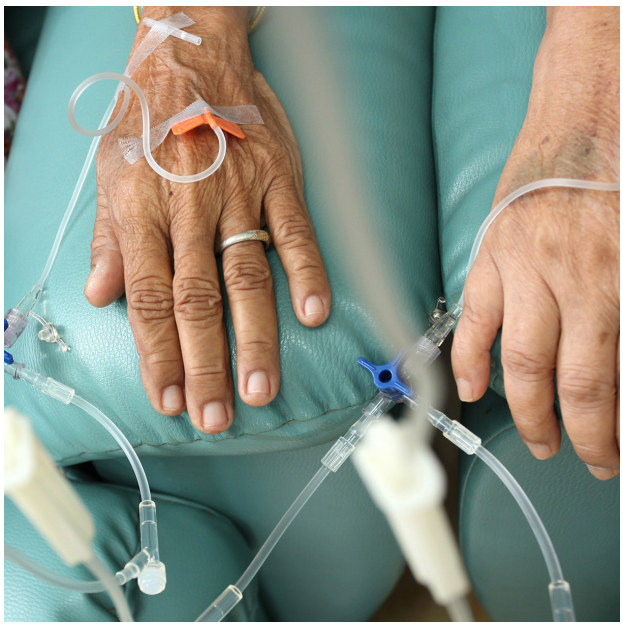
Dr. Bingshu Chen
Senior Biostatistician

Christopher Venner (Myeloma Working Group Co-Chair)
Diego Villa Restrepo (Lymphoma Working Group Co-Chair)
Laurie Sehn (Correlative Science Lead)
John Kuruvilla (Lymphoma Working Group Co-Chair)
Michael Crump (Past Chair)
Mary Lynn Savoie (Leukemia Working Group Co-Chair)
Tanya Skamene (IND Liaison)
Anca Prica (Quality of Life Liaison)
Pierre Villeneuve (Economic Analysis Liaison)
Ivan Landego (New Invesitgator Practicum)
Alejandro Garcia-Horton (New Invesitgator Practicum)

Trial Spotlight

ALC.7 myeloMATCH is a master screening and reassessment protocol for tier advancement in the NCI myeloMATCH clinical trials

The myeloMATCH platform study is a series of precision medicine clinical trials for patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). At the core of this initiative is the ALC7 screening study, which uses biomarker testing to match patients with the most appropriate myeloMATCH trial based on the molecular features of their disease. Patients who are not matched to a specific trial will receive standard-of-care treatment and continue to be followed through the Tier Advancement Pathway.



In 2024, the first two myeloMATCH treatment trials opened: AL6 compares standard AML treatment with two new combination regimens and ALC8 evaluates novel experimental therapies that may more effectively eliminate AML than current treatments.

CCTG's participation in these studies represents a major advancement in the delivery of personalized, biomarker-driven care for patients with myeloid cancers in Canada, helping to bring cutting-edge therapies to those who need them most.

Thoracic Disease Site Committee

2024 Overview

The Thoracic Disease Site Committee had number of key trials concluded and for 2024 the focus has turned to the planned secondary analysis. The positive results from the IND.227 international trial showed statistically significant overall survival benefits (published in The Lancet). These results led to FDA approval of pembrolizumab in combination with pemetrexed and platinum chemotherapy as first-line treatment for malignant pleural mesothelioma and now the related secondary analyses have begun.

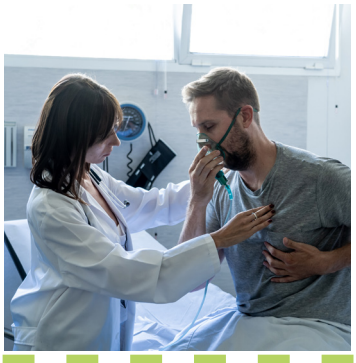
The international BR.31 phase III trial compared durvalumab against placebo following adjuvant chemotherapy for surgically resected non-small cell lung cancer (NSCLC). The results were presented at the European Society for Medical Oncology (ESMO) 2024 Congress. The study did not meet its primary endpoint, which was improvement in disease-free survival and related secondary analyses are moving forward.

The interventional second stage of the BR.36 trial was activated evaluating the efficacy of circulating tumor DNA (ctDNA) response-adaptive immuno-chemotherapy in participants with metastatic NSCLC. Results from the first stage were published in Nature Medicine and the study was a poster presentation at ASCO 2024.

The CCTG IND.242A sub study of the phase II pre-operative platform trial in patients with surgically resectable NSCLC enrolled patients in 2024. The CCTG-led NCTN BR.38 (CURB2) international trial is near activation and will evaluate if the addition of radiation therapy to extra-cranial oligoprogressive metastatic disease can prolong progression-free survival and/or overall survival compared to standard of care systemic therapy alone in participants with NSCLC.

2025 Priorities

- BR.31 primary publication
- BR.31 secondary analyses and publications
- CC227 secondary analyses and publications
- Open and accrue to BR38
- Accrual for BR36 and BRC.8 (MAVERICK) trials
- New trials involving early-stage NSCLC, treatment toxicity, and elderly patients
- Define priorities for the next grant cycle

Committee Executive

Dr. Penelope Bradbury
Co-Chair

Dr. Alexander Sun
Co-Chair

Dr. Pierre-Olivier Gaudreau
Senior Investigator

Dr. Keyue Ding
Senior Biostatistician

Emi Bossio
Patient Representative

Janet Dancey
Scott Laurie
Biniam Kidane
Scott Laurie
Frances Shepherd
Glenwood Goss

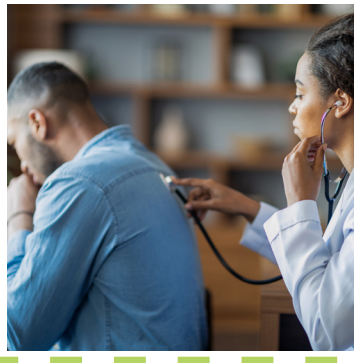
Normand Blais
Barbara Lynn Melosky
Ming-Sound Tsao (CS/TB Liaison)
Quincy Chu (IND Liaison)
Alexander Louie (Economic Analysis Liaison)
Elizabeth Faour (New Investigator Practicum)

Trial Spotlight

BR.36 is a biomarker-directed, multi-center phase II/III study of ctDNA molecular response adaptive immuno-chemotherapy in patients with non-small cell lung cancer

CCTG BR.36 is using blood tests to determine treatment options for patients with non-small cell lung cancer. Liquid biopsies hold immense promise in revolutionizing cancer care by enabling precision medicine—delivering the right treatments to the right patients at the right time. By identifying ctDNA, liquid biopsies provide critical insights into a patient's cancer without the need for invasive tissue biopsies.

This trial represents a significant advancement in personalized cancer treatment, using advanced liquid biopsy techniques to tailor therapies based on molecular responses. The interventional, second stage of the trial builds on the promising results from stage 1, which highlighted the optimal timepoint for molecular response readout. Investigators believe that this study has the potential to enhance outcomes for patients with metastatic NSCLC.



Melanoma & Skin Cancer Disease Site Committee

2024 Overview

The Melanoma & Skin Cancer Disease Site Committee continues to advance trials evaluating immunotherapy and understanding the biological determinants of its efficacy. The innovative ME.17 trial, launched in late 2024. This study evaluates fecal microbiota transplantation (FMT) combined with immune checkpoint blockade (ICB) to improve outcomes for advanced melanoma.

MEC.6, a phase II trial of adjuvant nivolumab with or without cabozantinib for resected mucosal melanoma, is accruing well. Researchers are exploring immunotherapies that boost the immune response and inhibit tumor growth and spread.

CCTG has finalized agreements to provide samples to the Terry Fox Research Institute MOHCCN, ME.13L, and the Can-PIVOT and Can-PREDICT projects. A new NCTN Melanoma Steering Committee is being formed to support trial proposal development. Additional academic-led trials in adjuvant and neoadjuvant settings are under consideration.

2025 Priorities

- Complete accrual for ME.13, ME.13L, and ME.15
- Open ME.18 following Clinical Trials Committee approval
- Explore early-phase IND trial of novel therapies in metastatic melanoma
- Continue engaging surgeons, building on strong ME.15 recruitment
- Represent CCTG on the new NCTN Melanoma Steering Committee

Committee Executive

Dr. Ian Watson
Co-Chair

Dr. Marcus Butler
Co-Chair

Dr. Janet Dancey
Senior Investigator

Dr. Bingshu Chen
Senior Biostatistician

Sally Nystrom
Patient Representative

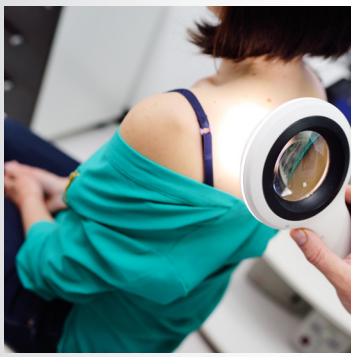
Vanessa Bernstein
Rahima Jamal
Wilson Miller
Carman Giacomantonio
Nicole LookHong (Economic Analysis Liason)
Michael Ong (IND Liason)
Christopher Lee (Quality of Liason)

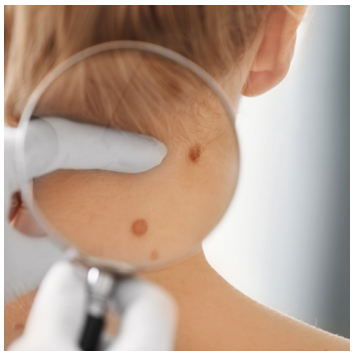
Trial Spotlight

ME.17 a phase II randomized trial of LND101 for fecal microbiota transplantation in combination with immune checkpoint blockade in patients with advanced melanoma

ME.17 is one of the world's largest randomized trials of fecal microbiota transplantation (FMT) in cancer. It evaluates whether adding FMT to standard immune checkpoint blockade (ICB) improves outcomes for advanced melanoma. ICB is the current standard of care however many patients will still experience disease progression. This study will use an encapsulated stool sample from healthy donors to change the patients' gut microbiota with the intent of making the current treatment for advanced melanoma more effective.

If this trial is successful, this approach could significantly improve survival and transform care for advanced melanoma.





Sarcoma Disease Site Committee

2024 Overview

SRC8 was centrally activated in late 2024 and will investigate whether a combination of immunotherapy and chemotherapy is more effective than chemotherapy alone for adults with advanced sarcoma, specifically undifferentiated pleomorphic or poorly differentiated sarcoma subtypes. The committee hopes to support this when the trial expands to include de-differentiated liposarcomas.

The committee continued to support the SR7 trial to compare the effects of receiving chemotherapy before surgery. The international study is currently accruing well at the six sites with 11 Canadian patients accrued out of 122 patients enrolled worldwide (4.4% of the total sample size of 250).

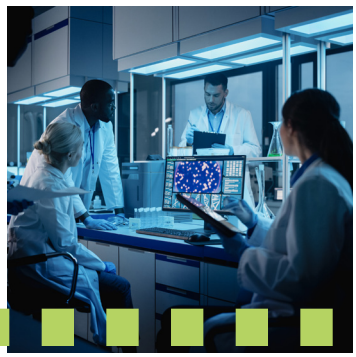
The team also moved forward with the work to open the GCAR1 Phase I feasibility and safety study of Chimeric Antigen Receptor (CAR) T-cell therapy for patients with relapsed GPNMB-Expressing solid tumors. The sarcoma IND working group forged ahead with new IND concepts and are actively involved in promoting the sarcoma trials with the IND committee.

The team keeps working to support targeted therapy development, focused on linking drug mechanism to sarcoma biology—including presentations by Canadian basic science community at CCTG meetings. The committee prides itself on keeping sarcoma patients at the front of the research agenda by ensuring sarcoma patients are included in basket trials and master protocols which will help to make targeted studies of rare tumors feasible.

The DSC is building on the extremely successful CCTG SR.2 trial and the SARC.32 trial by evaluating radiotherapy treatments and immunotherapy in extremity soft tissue sarcoma. The innovative trial SR.8 trial was approved by CTC and offers the opportunity to reduce patient burdens (number of radiotherapy treatments and length of immunotherapy) in this extremity sarcoma.

2025 Priorities

- Continue accrual onto SR.7 and SRC.8
- Confirm funding mechanism for SR.8
- Develop trial concepts for patients with LMS
- Open GCAR1 and accrue patients onto the trial




Committee Executive

Dr. Rebecca Gladdy
Co-Chair

Dr. Shantanu Banerji
Co-Chair

Dr. Mariam Jafri
Senior Investigator

Dr. Dongsheng Tu
Senior Biostatician

Jasmine Heuring
Patient Representative

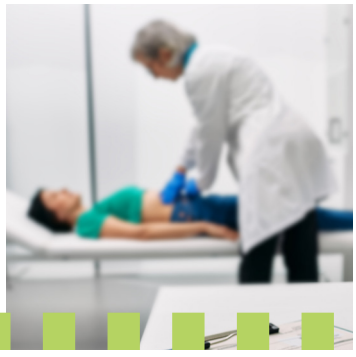
Dr. Abha Gupta
Dr. Philip Wong
Dr. Jan-Willem Henning
Dr. Torsten Nielsen
Dr. Christine Simmons
Dr. Albiruni Razak (IND liaison)

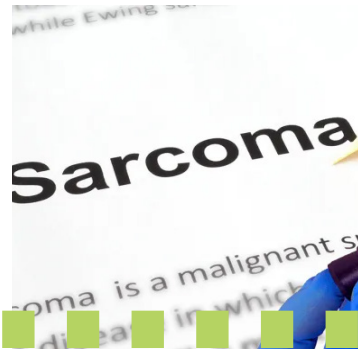
Trial Spotlight

SRC.8 is a randomized phase III trial of doxorubicin + pembrolizumab versus doxorubicin alone for the treatment of undifferentiated pleomorphic sarcoma (UPS) and related poorly differentiated sarcomas

The SRC8 clinical trial is exploring whether a combination of immunotherapy and chemotherapy is more effective than chemotherapy alone for adults with advanced sarcoma—specifically undifferentiated pleomorphic or poorly differentiated subtypes. The trial will assess the potential benefits of adding a well-established immunotherapy drug, known for its manageable side effect profile, to help the immune system better recognize and destroy cancer cells.

Immunotherapy is emerging as a promising alternative to traditional chemotherapy, addressing some of its limitations. This trial represents an important step toward expanding immunology-based treatment options for sarcoma.





Committee of Economic Analysis

2024 Overview

The Committee for Economic Analysis (CEA) continued their work to include economic analyses and advance innovative methods for collecting and analyzing economic data. Through collaboration among Investigators, Patient Representatives and the Disease Site Committees, these efforts ensure that economic considerations are integrated into CCTG clinical trials to support evidence-informed decision-making in cancer care.

The CEA will be leading an economic analysis of the CO.21 (CHALLENGE) trial, investigting the benefits of a structured exercise program after adjuvant therapy for colon cancer. There are over 30 trials that include economic analyses secondary studies and more in development including the HE.2 and CO.33.

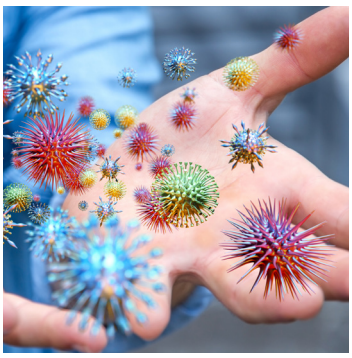
The committee focused on initiatives aimed at reducing data collection with the goal of executing economic analyses with less impact on patients, trial sites, and CCTG Operations & Statistics Centre staff. The New Trial Economics Collection Form identifies the type and objectives of economic analysis proposed for a trial—focused on data collection and essential elements that will impact a cost-effectiveness analysis.

The committee has also evaluated additional outcomes of importance to patients. The new Financial Toxicity Working Group was focused on incorporating the collection of a patient-reported tool (FACIT-COST) into trials including HD.11. The Comprehensive Score for Financial Toxicity (COST) is a tool developed by the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system to assess financial distress in patients with cancer. In collaboration with partners, the CEA has also investigated the concept of time toxicity (health system contact days) and its impact on costs and work productivity in the LY.12 trial.

Finally, the CEA has revised its guidance on when economic analyses should be considered in a CCTG trial. Considerations for CEA-designed sub studies include analysis that could include: individual-based statistical, model-based, linking with external data (e.g. administrative datasets), and to advance CEA methodology.

2025 Priorities

- Model-based working group – conduct model-based analyses
- Time toxicity collaboration - contact days and correlation with costs/indirect costs in LY.12
- Administrative data linkage plans - SC.24 and LY.12 linked economic analysis
- CO.17 as platform for multi-province demonstration project
- Analyze data where FACIT-COST incorporated - HD11




Committee Executive

Dr. Kelvin Chan
Co-Chair

Dr. Matthew Cheung
Co-Chair

Dr. Annette Hay
Senior Investigator

Carol Gordon
Patient Representative

Dr. Bingshu Chen
Senior Biostatistician

Wei Tu
Senior Biostatician

Dr. Tim Hanna
Dr. Nicole Mittmann
Dr. Natasha Leighl
Dr. Jeffrey Hoch
Dr. Neil Reaume (GI)
Dr. Pierre Villeneuve (Hem/SC)
Mr. Carlo De Angelis (PHARMA)
Dr. Nicole LookHong (Melanoma)
Dr. Anca Prica (Hem/QoL)
Dr. Alexander Louie (Lung)
Dr. Ambika Parmar (Head/Neck)
Dr. Danielle Rodin (Breast)
Dr. Marc Kerba (Supportive Care)
Dr. Winson Cheung (Quality of Life)
Dr. Janice Smith Kwon (Gynecology)
Dr. Stuart Peacock (Pharma)
Patti O'Brien (Study Coordinator)

Trial Spotlight

CCTG CX.5 (SHAPE) economic analysis - Cost-effectiveness analysis of simple hysterectomy compared to radical hysterectomy for early cervical cancer

The CX.5 SHAPE trial was an international phase III trial comparing simple to radical hysterectomy. Simple hysterectomy was superior for quality of life and sexual health. The subsequent cost-effectiveness economic analysis was published in 2024. Simple hysterectomy for early cervical cancer was shown to be less costly and more effective in terms of quality-adjusted life expectancy compared to radical hysterectomy.

Opportunity costs in this patient population are high. This patient population includes young women who often face significant disruptions to their lives, including time away from work or care giving responsibilities, due to surgery and the management of postoperative complications. The inclusion of opportunity costs did not change the outcome of this analysis.

Providing a simple hysterectomy with nodal assessment instead of standard radical hysterectomy was shown in the CX.5 study to improve quality of life, and decrease overall health care costs. The CX.5 SHAPE trial should revolutionize cervical cancer treatment worldwide as this study concludes that simple hysterectomy should replace radical hysterectomy as the standard of care.

Quality of Life Committee

2024 Overview

The Quality of Life Committee (QOLC) has continued their focus on sustaining scientific rigor and clinical relevance in measuring, interpreting, and reporting Quality of Life (QOL) and Patient Reported Outcomes (PRO) in CCTG clinical trials. Through a workshop at the Spring Meeting 2024, the committee deepened their understanding of PRO-CTCAE, a patient-reported outcome measurement system from the National Cancer Institute (NCI) to capture symptomatic adverse events experienced by patients in cancer clinical trials.

Members participated in the NCI's CTSU (Cancer Trials Support Unit) ePRO (electronic Patient-Reported Outcome) initiative where their integration requirements were clarified. This is a mobile application, to gather patient responses to questionnaires and diaries. They also explored the capabilities of the new CCTG SPROUT mobile application to capture patient reported outcomes and shared this knowledge to other QOLC members.

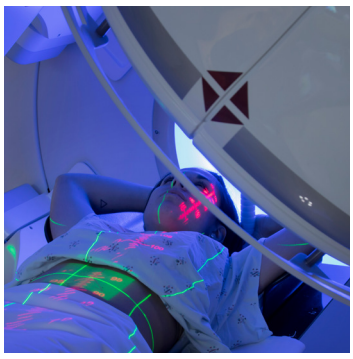
The committee contributed to the international standardization of how PRO data is collected, analyzed, presented, and shared. QOLC members actively participated in key international initiatives focused on PRO guidance and methodology, including PROBE and CATAPULT—databases of clinical trials that used the EORTC QLQ-C30—as well as SISAQOL, CONSORT-QOL, PROTEUS, and SISAQOL-IMI, which support the development of standardized guidance and methods.

The CCTG led HE.1 clinical trial was published in Lancet Oncology in late 2024. The study confirmed the quality-of-life benefits of palliative radiation therapy for symptomatic hepatocellular carcinoma and liver metastases. Low dose radiation should be considered a standard palliative intervention for hepatic cancer pain.

Work continues to increase patient engagement in research priority setting, trial design, and presentation of trial results. The committee improved the CRA guidance and support for the collection of the QOL questionnaires. Also, there was a collaboration with the IND disease site team to improve the utilization of PROs in phase I clinical trials. The committee continued the partnership with the CCTG Committee on Economic Analysis to explore themes of financial and time toxicity.

2025 Priorities

- Improve access to key presentations and relevant documents
- More integration with patient-centric trials
- Support the CCTG SPROUT mobile application roll out

Committee Executive

Dr. Joelle Helou
Co-Chair

Dr. Winson Cheung
Co-Chair

Ms. Louise Bird
Patient Representative

Dr. Joseph Pater
Senior Investigator

Dr. Dongsheng Tu
Senior Biostatician

Dr. Julie Lemieux (Breast)
Dr. Michael Brundage
Dr. Hira Mian (Hem)
Dr. Kelvin K-W Chan
Dr. Matthew Cheung
Dr. Doris Howell (Supportive Care)
Dr. Anca Prica (Hematology)

Dr. Jolie Ringash (Rad Onc)
Mr. David Boren
Dr. Biniam Kidane (Lung)
Dr. Iwa Kong (Gynaecologic)
Dr. Michael McKenzie (Supportive Care)
Dr. Christine Simmons
Dr. Christopher Lee (LUNG/MEL)
Dr. Anne Leis (Brain)

SPROUT ePRO Mobile App

The CCTG System Patient Reported OUTcomes (SPROUT) is an electronic Patient-Reported Outcomes (ePRO) system developed to streamline the collection of questionnaire-based data directly from clinical trial participants. The type of data collected varies by study and may include patient-reported outcome measures such as quality of life assessments or health utility evaluations.

Currently the web version of SPROUT is used by centre representatives and site data managers to distribute and collect survey data. The CCTG IT team is developing a more accessible SPROUT mobile application for iOS and Android. The SPROUT app will extend data collection beyond clinic visits by enabling patients to complete surveys anytime, anywhere.

Features include:

- **Offline Capability:** Allows participants to complete surveys without internet access; participants can sync data when back online.
- **Flexible Survey Formats:** Supports a range of input types including single/multiple choice, sliders, text, and conditional branching logic.
- **Push Notifications:** Alerts about pending or uncompleted surveys.
- **Privacy & Security:** Fully encrypted and compliant with relevant privacy standards.
- **Accessibility:** Built-in features to ensure usability for a diverse participant population.

The SPROUT app will be available to trial participants in late 2025.

Correlative Sciences & Tumour Biology Committee

2024 Overview

This year, the Correlative Sciences & Tumour Biology Committee (CSTB) has focused on refreshing its membership under the new leadership of Co-Chairs Alex Wyatt and Alan Spatz to align with current priorities and a renewed strategic direction. A data sciences SOP is in development to improve transparency and access to correlative data generated through CCTG trials and create opportunities for meta-analyses.

Engagement has begun around Artificial Intelligence (AI), and Machine Learning (ML) approaches to digital pathology. This evolving field has the potential for faster, more accurate analysis and eventually improved diagnostic accuracy, and personalized medicine.

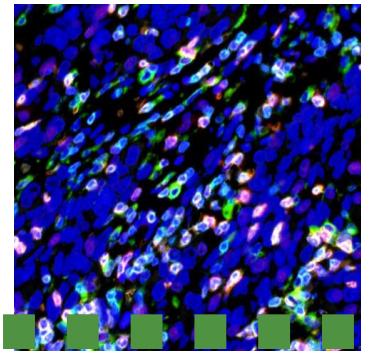
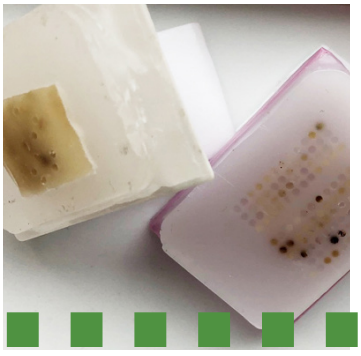
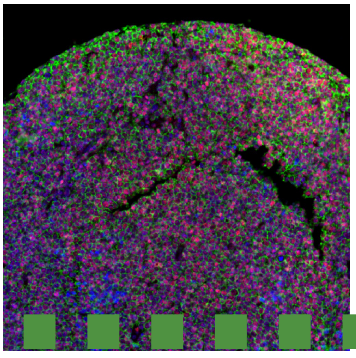
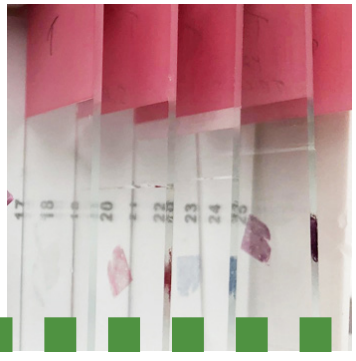
Standardization of circulating tumor DNA (ctDNA) assessments is underway in CCTG trials. Areas of focus include establishing consistent collection protocols, timepoints, and analytical platforms across studies. The executive is also working with industry partners to develop alliances that span the trial portfolio and enhance the utility of ctDNA correlatives. CCTG played a leadership role in outlining the necessary steps for ctDNA kinetics to be integrated into the RECIST response assessment framework as a highlight (Wyatt CCR2024: FoCR2025).

The PM2 CAN-IMPACT-IO study is under development to support biospecimen collection, model system development and correlatives for patients on CCTG trials involving immunotherapy. This will allow CCTG investigators to enhance their mechanistic understanding of response to therapies, treatment resistance, and to share models more widely across Canada.

This year, operational efforts were dedicated to the development of a new home for the CCTG Tumour Tissue Data Repository (TTDR) and the large-scale expansion of its histopathology and biobanking resources. The expected opening in the fall of 2025 will enhance the capabilities of the TTDR and support the growth in biobanking capacity.

2025 Priorities

- Membership renewal and update - identify new members/areas of expertise
- Establish focus groups: ctDNA and AI
- Identify cross-trial study opportunities and standardization of ctDNA time points to facilitate future meta-analyses and consideration of broader efforts to understand how to integrate this technology into response metrics.
- Proposals for broad industry alliances to support the engagement of investigators (e.g. master agreements with vetted partners)
- Increase use of TTDR samples and facilities

Committee Executive

Dr. Alex Wyatt
Co-Chair

Dr. Alan Spatz
Co-Chair

Dr. Lois Shepherd
Senior Investigator

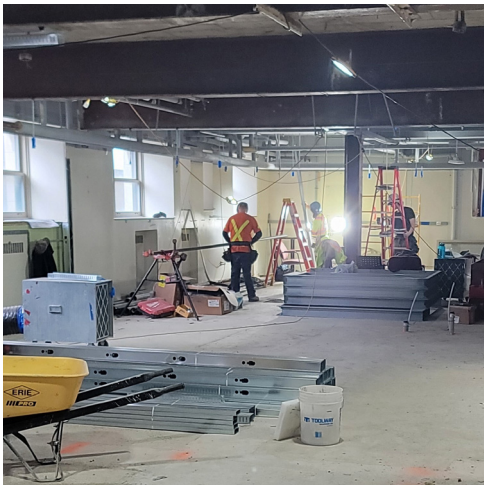
Dr. Jonathan Loree
Senior Investigator

Dr. Keyue Ding
Senior Biostatistician

Marie-Térèse Little
Patient Representative

Sharlene Gill
Harriet Feilotter
Tricia Cottrell
Geoffrey Liu
Marcus Butler
Scott Bratman
Ming-Sound Tsao (PATH)
Shakeel Virk (PATH)
Peter H. Watson (PATH)

TTDR Expansion Update



The expansion of CCTG's Tumour Tissue Data Repository (TTDR) will enhance the current capacity for ongoing and new CCTG initiatives that include: Precision Medicine Platforms, Cellular Therapy, and Immunotherapy. The new space includes a larger centralized capacity for genomic, transcriptomic and proteomic studies that will leverage expertise among member sites.

As well as the expansion of the facilities, the TTDR will be introducing advanced technologies to support new CCTG initiatives including the Vectra Polaris Quantitative Imaging system for multiplexed immunofluorescence and advanced image analysis. Equipment upgrades include: Leica Bond RX and Akoya Digital slide scanner; nucleic acid isolation equipment; automated slide stainer

The addition of Real Time PCR platforms, QIA symphony, BioTek Synergy Microplate Readers, Vectra Polaris Quantitative Imaging System, and Indica Labs Halo Image Analysis Modules will enable the repository and laboratory to perform additional assays, more easily share data and allow researchers from across Canada access to research materials from CCTG trials.

Along with the physical space there is work underway to implement sample barcoding and a database upgrade that will improve functionality, and digital pathology. This is an ExCELLirate Canada, Canada Foundation for Innovation (CFI) funded project.

Supportive Care Committee

2024 Overview

This year saw the long-awaited completion of the CO.21 physical activity intervention study to improve outcomes for colon cancer patients. The trial closed and final analysis continues in preparation for submission to ASCO 2025.

A tremendous team effort went into the preparation of two CCS Breakthrough Team Grants: i) the Canadian Psilocybin-Assisted Cancer Therapy (CAN PACT) proposal, led by Dr. Carlson at University of Calgary and ii) Advancing the Science of Remote Symptom Monitoring for Immune-Checkpoint Inhibitor Treatment Toxicities: Effectiveness, Biosignatures of toxicities, Wearables, Artificial Intelligence, and Implementation (SOPRANOS), led by Dr. Lambert at McGill University. Both programs of research were multidisciplinary in nature and marked by exceptional patient partnerships and meaningful partner engagement throughout the process.

The SC.28 Mindfulness App trial continues to accrue with five sites locally activated and the SC.29 investigating stereotactic body radiation therapy for bone cancer was centrally activated with interested sites working to open the study. The CCTG Clinical Trials Committee (CTC) has approved the SC.31 TEMPO prostate cancer-caregiver virtual support trial, and the SC.30 RATIONAL study looking at supportive care interventions to prevent serious infection. The committee is anticipating a successful CIHR announcement for this trial in early 2025.

The partnership with Australasian Leukaemia & Lymphoma Group (ALLG) is progressing and they have submitted a grant to join the SC.26 EASE trial investigating emotion and symptom-focused engagement for acute leukemia next year.

The committee continues to collaborate with Dr. Chris Ma who received CIHR funding to conduct a phase 1/2 trial for placebo vs Vendolizumab to reduce checkpoint-inhibitor-related colitis and is in discussion with Takeda about support for a future definitive phase III trial with CCTG.

2025 Priorities

- Analyses of SC.27
- Operationalize ALLG's joining SC.26
- Support accrual to SC.28
- Support SC.29 opening in centers and accrual
- Centrally activate SC.30 and SC.31, open and accrue
- Establish a network of investigators and patient partners to test the potential of psychedelic-assisted therapy as an approach to support patients with advanced cancer and demoralization.
- Submit SOPRANOS implementation trial to CIHR

Committee Executive

Dr. Michael McKenzie
Co-Chair

Dr. Margot Burnell
Co-Chair

Dr. Harriet Richardson
Senior Investigator

Dr. Wei Tu
Senior Biostatician

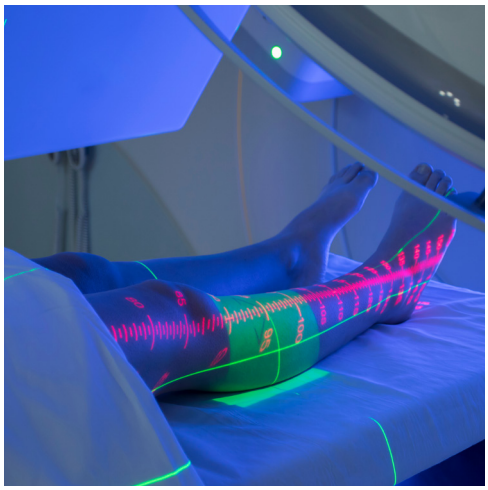
Hilary Horlock
Patient Representative

Dr. Tina Hsu
Dr. Martin Chasen
Dr. Arjun Sahgal
Dr. Lynda G. Balneaves
Dr. Linda Carlson
Dr. Camilla Zimmermann
Dr. Doris Howell (Quality of Life)
Carlo De Angelis (Pharma)

Trial Spotlight

CCTG SC.29 is a randomized phase III study comparing stereotactic body radiotherapy (SBRT) versus conventional palliative radiotherapy (CRT) for participants with painful non-spine bone metastases

The CCTG SC.29 symptom control trial is evaluating the use of high precision stereotactic body radiotherapy (SBRT) to conventional palliative radiotherapy (CRT) for patients with advanced cancer and a painful non-spine bone metastasis. Researchers believe that SBRT may be better for pain relief than the standard conventional radiation therapy. SBRT represents a high dose treatment typically offered in the curative cancer setting; however, its role as a palliative treatment to improve pain for these patients is unknown.



SBRT targets painful areas of cancer, while keeping the radiation away from the healthy tissue around the cancer minimizing normal tissue damage which could impact quality of life. CRT is directed at painful areas but using a lower dose and does not spare the normal tissues.

CCTG at the heart of pan-Canadian initiatives to advance the national understanding of immunotherapy

The Canadian Cancer Trials Group (CCTG) is at the forefront of national efforts to advance the evaluation of novel immunotherapies through its clinical trials. To better determine which patients benefit from these treatments, CCTG has a strategic partnership with the Marathon of Hope Cancer Centres Network (MOHCCN). The Network is leading several pan-Canadian initiatives aimed at improving the effectiveness, safety, and personalization of immunotherapy. This collaboration is critical to understanding how best to use immunotherapies to increase survival, minimize toxicities, and improve quality of life for Canadian cancer patients.

According to Dr. Janet Dancey, "CCTG investigators have designed multiple trials to determine the optimal immunotherapy, doses, schedules, or treatment duration. To determine better which patients may benefit, CCTG and MOHCCN are partnering to improve precision medicine by identifying markers that predict treatment response." These markers can be used to tailor treatment strategies to individual patients, potentially allowing for shorter treatment durations, fewer side effects, and improved overall well-being without compromising survival outcomes.

CAN-IMPACT-IO is the CCTG PM2 study to facilitate the collection and analysis of samples and clinical data from patients enrolled in CCTG-led immunotherapy trials. This national immunotherapy bio-specimen collection platform provides a foundation for linked research programs across Canada. Patients who consent to participate will allow their clinical trial data and bio-specimens to be analyzed as part of the MOHCCN cohort studies: CAN-PREDICT-IT and CAN-PIVOT.

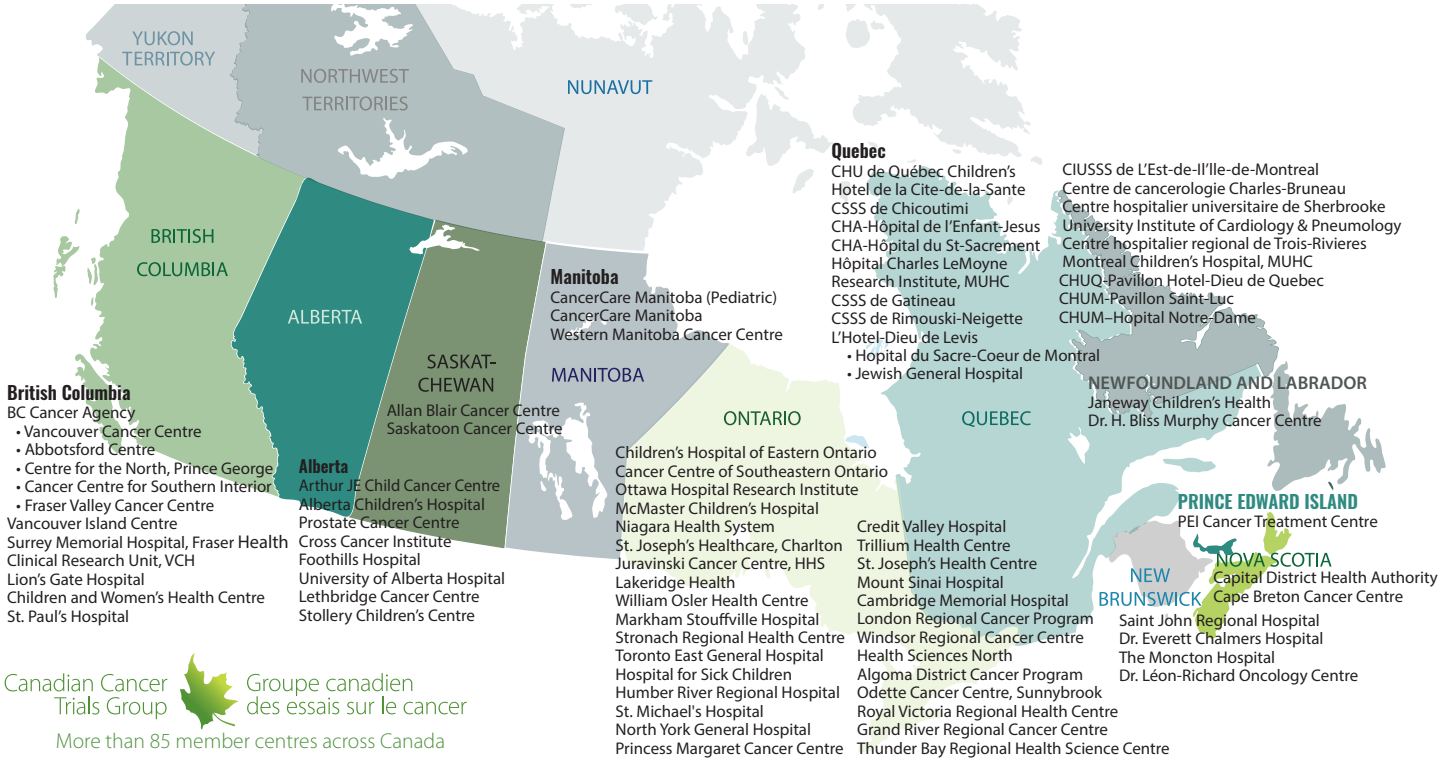
CAN-PREDICT-IT aims to enhance the personalization of cancer treatment by identifying biomarkers that predict which patients are most likely to benefit from specific immunotherapy interventions. By collecting and analyzing diverse data types—including clinical, genomic, and imaging information—this initiative seeks to develop multi-modal predictive biomarkers to support more targeted and effective treatment strategies. Through collaboration with CCTG's clinical trials portfolio, researchers will be able to recruit participants directly from ongoing trials. The insights generated will not only guide patient selection in current studies but will also inform future clinical trial designs, helping to match patients to therapies tailored to their tumor biology. This represents an important step forward in advancing precision medicine and optimizing outcomes for Canadian cancer patients receiving immunotherapy.

CAN-PIVOT is a national platform focused on investigating both primary and acquired resistance to cancer immunotherapy. This project will generate whole-genome and transcriptome sequencing (WGTS) data, combined with comprehensive clinical information such as diagnosis, treatment regimens, and outcomes. The goal is to identify molecular and clinical factors associated with resistance to immunotherapy. Understanding these mechanisms will enable researchers to design new therapies that overcome resistance and sensitize tumors to treatment, ultimately improving survival and cure rates. At the same time, this approach will help avoid potentially life-threatening toxicities in patients who are unlikely to benefit from immunotherapy.

ME.13 STOP-GAP and its associated bio-marker sub study, is another major initiative supported through this partnership. ME13 (STOP-GAP) is a phase III randomized trial investigating the optimal duration of immune checkpoint inhibitor (ICI) therapy in patients with metastatic melanoma. A key challenge in this disease area is the inability to predict which patients will respond to ICIs. Through the sub study, researchers will collect and analyze blood and tissue specimens from consenting trial participants to perform Whole-Genome and Transcriptome Sequencing (WGTS), and integrate this data with detailed clinical histories, including treatment response. This work aims to identify predictive bio-markers that can determine which patients are likely to benefit from ICI therapy, and whether shorter treatment durations can preserve efficacy while reducing toxicity and improving quality of life.

Taken together, these initiatives position the Canadian Cancer Trials Group and the Marathon of Hope Cancer Centres Network as leaders in building the scientific evidence, infrastructure, and collaborative frameworks necessary to transform immunotherapy in cancer care. The partnership exemplifies how coordinated, patient-centered research can advance precision medicine, personalize treatment, and improve outcomes for cancer patients across Canada. These efforts will accelerate scientific discovery and ensure that future generations of patients benefit from more effective, tailored, and compassionate cancer therapies.

CCTG network of Cancer Centres



Solving Cancer Together

CCTG Strategic Plan 2022-2027

Solving Cancer Together means driving scientific progress and advancing new treatments to improve patient outcomes. The group remains committed to supporting new and ongoing trials and strengthening our scientific efforts. Through the actions of our patient representatives, network leaders and members, international collaborators, industry partners, central office team, and funders, we are creating meaningful change.

Network Engagement, Collaboration, and Partnership with Patients

- Virtual Network Roadshow
- Launch of Network Support Fund Pilot
- Policy development to support Network Leadership completed with monitoring of uptake in progress

Opportunities for Career Development

- Hired Education Lead and established role of Director of Education
- Launched new CRA Practicum for Network and lunch and learn sessions
- Developed new CCTG leadership training program to be initiated in 2025

Research Collaborations

- NCTN Program Leader recruited
- NCTN Program Grant Renewal to be submitted (Feb 2025) with risk mitigation strategies
- CCS Program Grant Midterm completed
- MOU's with International partners renewals in progress with aim to establish ways of working

Correlative Science Expansion

- TTDR renovation in progress with move planned 2025
- Database migration to new data model key focus for 2024 (data cleaning, testing, mapping)
- Expansion in parallel to supporting trials and key projects throughout the year

Patient engagement

- Established stipends for PRC and travel funding for trial patients
- Implemented patient facing communication materials across trials
- Recruitment and onboarding of new members

EDIIA

- Action Plan V1 complete and plans for the future underway
- EDIIA integrated into trial documents, templates, data
- Workshop for pilot trials with roll out underway

Operations and Efficiency Initiatives

- Increased communication: Annual Report and quarterly trials update
- CDISC compliance continued and expanded to additional trials
- Decentralized trial approach and patient sharing implemented with ongoing efforts to expand
- Collaborating with 3CTN and NCTN initiatives
- Streamlining data collection - internal and NCTN SCTIC initiative
- Increased collaborators contracting > ~240 contracts executed to support trials and projects

Compliance Initiatives

- Navigated new EU CTR with the transition of 3 trials (HN9, BL13, BR31)
- Reviewed ICH GCP R3 review for opportunities impacts for GCP
- Resolved ethics discussions regarding data sharing/broad consent with stakeholders & ICF discussions to support uptake across provinces

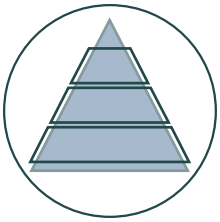
2024 Highlights Scientific Priorities & Platforms

This year saw strong growth in the trial portfolio, with progress in precision medicine, rare cancers, and patient-centered studies. A total of 18 new trials were activated—exceeding the annual target of 15—and 18 trials were analyzed across both the IND and phase III programs. The Group was also proud to launch the Network Support Fund to strengthen site activation and accrual, and to establish new policies and processes to support network leadership. Work began on the 2027–2031 Strategic Plan, marking an important step in shaping future priorities.

In addition, CCTG successfully completed the Japanese Health Authority inspection by the Pharmaceuticals and Medical Devices Agency (PMDA) to support trial registration. Extensive industry engagement is underway to foster new trial concept submissions, and major grant milestones were met with the submission of both the CCS Grant Midterm Review and the NCTN Grant Renewal (February 2025).

Cell Therapy

- CFI and Match Funding ($10M) implementation in progress and additional BioCanRx funding received in 2024
- Pilot initial studies (2023-2025) in progress:
- Novel Therapy Trials: 2 Phase 1 trials with FIH academic cell therapy constructs (rare solid tumors; hematology)
- SOC Trials: I.245 SOC supportive trial, with other concepts like supportive care, tox prevention and bridging therapy with SOC cell therapy



Pre-operative Clinical Trials

- IND.242 Neoadjuvant platform trial 1st cohort completed and future development underway
- Expanding biobanking and digital pathology capacity is in progress with TTDR expansion planned for completion 2025
- Ongoing engagement of pathology and surgical trainees at NICTC, CCTG ECI practicum

Data Science

- Genomic SOP in developed for review with Network
- Data linkage included obtaining final linked dataset (CCTG, CCO, StatCan) from the LIFE study
- Initiated exploratory collaborations with large Canadian longitudinal cohorts such as CanPath and CLSA
- Fellow and Post Doc recruited has strengthened capabilities in genomic analyses

Funding Successes & Grant Applications

19 grants submitted, 11 funded, totaling $13,726,698M

SPOTLIGHT: ME17 is a phase II randomized trial of LND101 for fecal microbiota transplantation in combination with immune checkpoint blockade in patients with advanced melanoma. This study was made possible by an investment of $1 million from Canadian Cancer Society (CCS) and $1 million from the Weston Family Foundation combined with $1,786,273 funding from CIHR. It is one of the world's largest randomized controlled clinical trials using fecal microbiota transplantation to improve the effectiveness of the standard of care for advanced melanoma.

CIHR funding 2024

Fantastic funding news this year for CCTG, with four grant applications to the Canadian Institutes of Health Research (CIHR) successfully funded. CIHR is Canada's federal funding agency for health research, and this strong outcome reflects the quality and impact of the CCTG-led proposals.

MY.13 is a phase III trial of fixed-duration Daratumumab versus continuous Daratumumab among transplant ineligible older adults with newly-diagnosed multiple myeloma

The MY.13 study received $3,056,172 over 8 years to investigate time-limited versus continuous Daratumumab treatment for older people with multiple myeloma. Researchers would like to know if they need to stay on it continuously or if they can discontinue daratumumab safely and be monitored. (Dr Hira Mian, study chair)

PAC.5 is a randomized phase III multicentre trial of lanreotide for the prevention of postoperative pancreatic fistula

The PAC.5 clinical trial was awarded $742,052 to test lanreotide for the prevention of one of the most severe complications of pancreatic surgery, postoperative pancreatic fistula (POPF). Many pancreatic surgery patients experience major postoperative complications, the most critical is POPF, leading to worsened quality of life and life-threatening conditions. (Dr. Paul Karanicolas, principal investigator)

PR.26 (TRIPLE-SWITCH) is a randomized phase III clinical trial for the addition of docetaxel to androgen receptor pathway inhibitors in patients with metastatic castration sensitive prostate cancer and suboptimal PSA response

The PR.26 prostate cancer trial received $2,487,015 to investigate docetaxel, a chemotherapy drug that has been used for the treatment of prostate cancer. It disrupts cell microtubules, targeting both testosterone dependent and independent mechanisms. While hormone therapy is recommend for metastatic prostate cancer, it is not know who benefits from the early addition of chemotherapy. (Dr. Michael Ong, study chair)

VU.2 (STRIVE) a study on the stratIfication of vulvar squamous cell carcinoma by HPV & p53 status to guide excision

The VU.2 trial was awarded almost 1 million to investigate treatment options for early-stage vulvar cancer patients based on tissue analysis. The analysis will help to identify people who require additional surgery to prevent the cancer from returning and those who do not need a second surgery.
(Dr. Jessica McAlpine and Dr. Amy Jamieson, study co-chairs)

2024 CCTG Publications

Publications this year reflected the impact of our practice-changing clinical research, showcasing CCTG's role as both a research leader and valued collaborator working alongside our international and intergroup partners. For the group there were a total of 71 peer reviewed publications, 71 abstracts with 10 phase III and 8 IND analysis.

CX.5 a randomized phase III trial comparing radical hysterectomy and pelvic node dissection vs simple hysterectomy and pelvic node dissection in patients with low-risk early stage cervical cancer

The results of the CX5 (SHAPE) clinical trial, published in the New England Journal of Medicine (NEJM), conclude that a simple hysterectomy is a safe treatment option for women with low-risk early-stage cervical cancer. The Canadian led phase III international trial chaired by Dr Marie Plante, compared radical hysterectomy and pelvic node dissection with simple hysterectomy and pelvic node dissection. The global impact of these results is important as surgical de-escalation may allow women in low and middle-income countries, easier access to less radical surgical intervention with fewer surgical urological complications.

HE.1 a phase III study of palliative radiotherapy for symptomatic hepatocellular carcinoma and liver metastases

The Canadian led HE1 trial results, published in Lancet Oncology, confirm the quality-of-life benefits of palliative radiation therapy for symptomatic hepatocellular carcinoma and liver metastases.
One dose of palliative radiation therapy directed to the liver, reduces pain and discomfort for patients who are often not a good fit for standard therapies. The study chaired by Dr Laura Dawson concludes that low dose radiation should be considered a standard palliative intervention for hepatic cancer pain.

HDC.1 a phase III randomized study of nivolumab (Opdivo) or brentuximab vedotin (Adcetris) plus AVD in patients with newly diagnosed advanced stage classical hodgkin lymphoma

The HDC.1 trial results, published in the New England Journal of Medicine (NEJM), showed that the immune checkpoint inhibitor nivolumab plus chemotherapy significantly reduced the risk of disease progression and death compared with standard treatment in previously untreated stage III or IV Hodgkin lymphoma, making it the new standard of care. This (SWOG S1826) intergroup study was a successful collaboration in trial development between the Children's Oncology Group (COG) and the US National Clinical Trials Network cooperative groups and pediatric centres in Canada through CCTG.

PR13 (RADICALS-RT) Radiotherapy and Androgen Deprivation In Combination After Local Surgery

The PR13 (RADICALS-RT) follow-up study, published in the Annals of Oncology, confirms that routine preventative radiotherapy is not required after prostate cancer surgery. RADICALS-RT (MRC-PR10) researchers concluded that while radiation is effective when used at an early sign of relapse, they found that radiotherapy soon after surgery resulted in a higher risk of unwanted side-effects, such as urinary and bowel problems. This global practice changing work represents a meaningful collaboration between CCTG and international academic groups in the UK, Denmark and Ireland.

CCTG Annual Report: Clinical Trials Glossary

- **ALC.6** (ALLIANCE A041501) A phase III trial to evaluate the efficacy of the addition of Inotuzumab Ozogamicin (a conjugated anti-cd22 monoclonal antibody) to frontline therapy in young adults (ages 18-39 years) with newly diagnosed precursor B-cell all
- **ALC.7 (myeloMATCH)** A master screening and reassessment protocol for tier advancement in the NCI myeloMATCH clinical trials
- **ALC.9 (ERASE)** (ALLIANCE A221505) Eradicating Minimal Residual Disease in Patients with Acute Myeloid Leukemia (AML) prior to Stem Cell Transplant a myeloMATCH treatment trial
- **BL.13** A randomized phase II trial assessing Trimodality therapy with or without adjuvant durvalumab (MEDI4736) to treat patients with muscle-invasive bladder cancer
- **BLC.6 (MODERN)** An integrated phase 2/3 and phase 3 trial of MRD-based optimization of adjuvant therapy in urothelial cancer
- **BR.31** A phase III prospective double-blind placebo controlled randomized study of adjuvant MEDI4736 in completely resected non-small cell lung cancer
- **BR.34** A randomized trial of durvalumab and Tremelimumab +/- platinum based chemotherapy in patients with metastatic (Stage IV) Squamous or Non-Squamous Non-Small Cell Lung Cancer (NSCLC)
- **BR.36** (CRI-CCTG-0002)A biomarker-directed, multi-center phase II/III study of ctDNA molecular response adaptive immuno-chemotherapy in patients with non-small cell lung cancer
- **BR.38** (CURB2) Consolidative Use of Radiotherapy to Block Oligoprogression in patients with metastatic non-small-cell lung cancer-a randomized phase III trial
- CC227 - in development
- **CE.10 (VIGOR)** Vorasidenib as maintenance treatment after first-line chemoradiotherapy in IDH-mutant grade 2 or 3 astrocytoma: A placebo-controlled randomized phase III study
- **CEC.6 (CODEL)** A phase III intergroup study of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy with adjuvant PCV chemotherapy in patients with 1p/19q co-deleted anaplastic glioma or low-grade glioma
- **CLC.3** (SWOG S1925)Randomized phase III study of early intervention with venetoclax and obinutuzumab versus delayed therapy with venetoclax and obinutuzumab in newly diagnosed asymptomatic high-risk patients with chronic lymphocytic leukemia/small lymphocytic lymphoma
- **CO.17** A phase III randomized study of cetuximab (erbituxtm, c225) and best supportive care versus best supportive care in patients with pretreated metastatic epidermal growth factor receptor (egfr)-positive colorectal carcinoma
- **CO.21 (CHALLENGE**) A phase III study of 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
- **CO.32 (NEO-RT)** A phase 3 randomized trial of neoadjuvant chemotherapy, excision and observation versus chemoradiotherapy for early rectal cancer.
- **CO.33 (BATTMAN)** Botensilimab + balstilimab vs best supportive care as therapy in chemo-refractory, advanced, colorectal adenocarcinoma:
- **CRC.10** (NRG-GI008) Colon adjuvant chemotherapy based on evaluation of residual disease (CIRCULATE-NORTH AMERICA)
- **CX.5 (SHAPE)** A randomized phase III trial comparing radical hysterectomy and pelvic node dissection vs simple hysterectomy and pelvic node dissection in patients with low-risk early-stage cervical cancer.
- **EN.10 (RAINBO BLUE & TAPER)** Adjuvant therapy in POLE-Mutated and p53-wildtype/NSMP early-stage endometrial cancer
- **EN.11 (RAINBO GREEN)** Refining adjuvant treatment in endometrial cancer based on molecular features, transportec platform trials
- **ES.3 (NEEDS)** Neoadjuvant chemoradiotherapy for esophageal squamous cell carcinoma versus definitive chemoradiotherapy with salvage surgery as needed
- **GA.1 (TOPGEAR)** (TROG 0808) A randomized phase II/III trial of preoperative chemoradiotherapy versus preoperative chemotherapy for resectable gastric cancer
- **GA.4** A randomized phase II study of paclitaxel and ramucirumab +/- zanidatamab in HER2 positive advanced gastroesophageal adenocarcinoma
- **GCAR.1**- in devleopment
- **HD.11** A randomized phase II trial of pembrolizumab and brentuximab vedotin versus GDP followed by high dose chemotherapy and autologous stem cell transplantation for relapsed/refractory classical hodgkin lymphoma
- **HD.12 (RADAR)** A randomized phase III trial with a PET response adapted design comparing ABVD +/- ISRT with A2VD +/- ISRT in patients with previously untreated stage IA/IIA Hodgkin lymphoma
- **HDC.1** (SWOG S1826) A phase III randomized study of nivolumab (opdivo) or brentuximab vedotin (adcetris) plus AVD in patients (age >/= 12 years) with newly diagnosed advanced stage classical hodgkin lymphoma
- **HE.1** A phase III study of palliative radiotherapy for symptomatic hepatocellular carcinoma and liver metastases
- **HE.2 (SLIDE-HCC)** A phase II study of STRIDE (durvalumab + tremelimumab) with lenvatinib versus STRIDE alone in patients with unresectable hepatocellular carcinoma
- **HN.10 (EVADER)** A phase II single arm trial of elective volume adjusted de-escalation radiotherapy in patients with low-risk HPV-related oropharyngeal squamous cell carcinoma.
- **HN.13** A Phase III Randomized Controlled Trial Comparing Palliative Stereotactic Body Radiotherapy vs. Palliative Standard Radiotherapy in Patients with Advanced Head and Neck Cancer
- **HN.9** Randomized phase II study of cisplatin plus radiotherapy versus durvalumab plus radiotherapy followed by adjuvant durvalumab versus durvalumab plus radiotherapy followed by adjuvant tremelimumab and durvalumab in intermediate risk HPV-positive locoregionally
- **IND.227** A phase II randomized study of pembrolizumab in patients with advanced malignant pleural mesothelioma
- **IND.241** A liquid-biopsy informed platform trial to evaluate treatment in CDK4/6-inhibitor resistant ER+/HER2- metastatic breast cancer
- **IND.242** Neoadjuvant platform trial in patients with surgically resectable Non-Small Cell Lung Cancer (NSCLC)
- **LY.12** A phase III study of gemcitabine, dexamethasone, and cisplatin compared to dexamethasone, cytarabine, and cisplatin plus/minus rituximab [(R)-GDP VS (R) -DHAP] as salvage chemotherapy for patients with relapsed or refractory aggressive histology non-Hodgkin's lymphoma prior to autologous stem cell transplant and followed by maintenance rituximab versus observation.

- **MA.30** A phase III adjuvant trial evaluating the addition of adjuvant chemotherapy to ovarian function suppression plus endocrine therapy in premenopausal patients with ER-Positive/HER2-Negative Breast Cancer
- **MA.39 (Tailor RT)** A randomized trial of regional radiotherapy in biomarker low risk node positive and T3N0 breast cancer
- **MA.40 (FINER)** Double-blind placebo controlled randomized phase III trial of fulvestrant and ipatasertib as treatment for advanced HER-2 negative and estrogen receptor positive (ER+) breast cancer following progression on first line CDK 4/6 Inhibitor and aromatase inhibitor
- **MAC.22 (TMIST)** (ECOG-ACRIN EA1151) Tomosynthesis Mammographic Imaging Screening Trial
- **MAC.23 (RT CHARM)** (ALLIANCE A221505) Phase III randomized trial of hypofractionated post-mastectomy radiation with breast reconstruction
- **MAC.29 (OptimICE-pCR)** (ALLIANCE A012103) De-escalation of therapy in early-stage TNBC patients who achieve pCR after neoadjuvant chemotherapy with checkpoint inhibitor therapy
- **MAC.30** A phase III adjuvant trial evaluating the addition of adjuvant chemotherapy to ovarian function suppression plus endocrine therapy in premenopausal patients with ER-Positive/HER2-Negative Breast Cancer
- **ME.13 (STOP-GAP)** A randomized phase III trial of the duration of anti-PD-1 therapy in metastatic melanoma
- **ME.13.L (STOP-GAP)** A biomarker sub-study of the CCTG ME.13 duration of anti PD-1 therapy in metastatic melanoma trial
- **ME.15 (MelMarT-II)** Melanoma Margins Trial: A phase III, multi-centre, multi-national randomized control trial investigating 1cm vs 2cm wide excision margins for primary cutaneous melanoma
- **ME.17** A phase II randomized trial of LND101 for fecal microbiota transplantation in combination with immune checkpoint blockade in patients with advanced melanoma
- **MEC.6** (ALLIANCE A091903) A randomized phase II trial of adjuvant nivolumab with or without Cabozantinib in patients with resected Muscosal melanoma
- **MY.13** A phase III non-inferiority randomized controlled trial of fixed duration versus continuous daratumumab among transplant ineligible older adults with newly diagnosed multiple myeloma
- **NE.1 (NET RETREAT)** A phase II study of 177Lutetium- DOTATATE retreatment vs. everolimus or sunitinib or cabozantinib in metastatic/unresectable gastroenteropancreatic tumours
- **NE.2 (STOPNET)** (AG0219NET) A randomized study of cessation of somatostatin analogues after peptide receptor radionuclide therapy in mid, hind-gut and pancreatic neuroendocrine tumours
- **OV.25 (STICs and STONEs)** A randomized phase II double-blind placebo-controlled trial of acetylsalicylic acid (ASA) in prevention of ovarian cancer in women with BRCA 1/2 mutations
- **OV.26** (CRUK/UCL ICON9) An international phase III randomised study to evaluate the efficacy of maintenance therapy with olaparib and cediranib or olaparib alone in patients with relapsed platinum-sensitive ovarian cancer following a response to platinum-based chemotherapy
- **OVC.2 (COCOS)** (NRG GY005) A randomized phase II/III study of the combination of Cediranib and Olaparib compared to Cediranib or Olaparib alone, or standard of care chemotherapy in women with recurrent platinum-resistant or -refractory ovarian, fallopian tube, or primary peritoneal cancer
- **PAC.3 (ALLIANCE A021806)** Perioperative versus adjuvant chemotherapy for resectable pancreatic cancer
- **PM.2 (CAN-IMPACT-IO)** Canadian initiative to measure, predict and assess cancer treatment outcomes in patients treated with immuno-oncotherapeutics
- **PR.13 (RADICALS)** Radiotherapy and androgen deprivation in combination after local surgery
- **PR.19** A randomized phase II trial evaluating high dose rate brachytherapy and low dose rate brachytherapy as monotherapy in localized prostate cancer
- **PR.21** A randomized phase II Study of 177Lu-PSMA-617 vs docetaxel in patients with metastatic castration-resistant prostate cancer and PSMA-positive disease
- **PR.24 (ASCENDE-SBRT)** Androgen suppression combined with elective nodal irradiation and dose escalated prostate treatment: a non-inferiority, phase III randomized controlled trial of stereotactic body radiation therapy versus brachytherapy boost in patients with unfavourable risk localized prostate cancer
- **PR.25 (oPTion-DDR)** A randomized phase III trial investigating platinum and taxane chemotherapy in metastatic castration resistant prostate cancer patients with alterations in DNA damage response genes
- **PR.26 (TRIPLE-SWITCH)** A randomized phase III clinical trial for the addition of docetaxel to androgen receptor pathway inhibitors in patients with metastatic castration sensitive prostate cancer and suboptimal PSA response
- **SC.24** A randomized phase II/iii study comparing stereotactic body radiotherapy (SBRT) versus conventional palliative radiotherapy (CRT) for patients with spinal metastases
- **SC.26 (EASE)** Emotion and Symptom-focused Engagement: A multi-site randomized controlled trial of an intervention for individuals with acute leukemia
- **SC.27** living with cancer in the time of COVID-19: A cohort study of the impact of the COVID-19 pandemic on cancer patients during treatment and survivors
- **SC.28 (SEAMLESS study)** A pragmatic multi-site randomized waitlist-controlled trial of a smartphone app-based mindfulness intervention for french and english speaker cancer survivors
- **SC.29** A randomized phase III study comparing stereotactic body radiotherapy (SBRT) versus conventional palliative radiotherapy (CRT) for participants with painful non-spine bone metastases
- **SC.30 (RATIONAL-PT)** Role of antibiotic therapy or immunoglobulin on infections in haematology platform trial
- **SC.31 (TEMPO)** Using SMART to optimize the stepped care delivery of TEMPO – a tailored, dyadic, web-based physical activity and self-management program for men with prostate cancer and their caregivers
- **SKC.1** (NRG-HN014) Randomized phase III trial of neoadjuvant immunotherapy with response-adapted treatment versus standard-of-care treatment for resectable stage III/IV cutaneous squamous cell carcinoma
- **SR.7 (STRASS 2)** (EORTC 1809-STBSG) A randomized phase III study of neoadjuvant chemotherapy followed by surgery versus surgery alone for patients with high-risk retroperitoneal sarcoma
- **SR.8 (HARMONY)** Hypofractionated alternative radiation with modulation of neoadjuvant/peri-operative immunotherapy in sarcoma
- **SRC.8** (ECOG-ACRIN EA7222) A randomized phase III trial of doxorubicin + pembrolizumab versus doxorubicin alone for the treatment of undifferentiated pleomorphic sarcoma (ups) and related poorly differentiated sarcomas
- **VU.2 (STRIVE)** Stratification of vulvar squamous cell carcinoma by HPV and p53 status to guide excision

www.cctg.ca

The Canadian Cancer Trials Group is proud to be a national program of the Canadian Cancer Society (CCS). CCTG is the only non-American partner of the US National Clinical Trials Network and collaborates with research cooperative groups around the world. The CCTG Operations and Statistical Centre, based at Queen's University, is recognized as a Canada Foundation for Innovation Major Sciences Initiative facility.

Canadian Cancer Society Société canadienne du cancer

Queen's University

NCI National Clinical Trials Network
a National Cancer Institute program