Canadian Cancer Trials Group Symptom Control

Experience and emerging themes

Rebecca Wong
Chair, Symptom Control Committee

Institute of Medicine 1997

APPROACHING DEATH
IMPROVING CARE AT THE END OF LIFE

A symptom based strategy for biomedical research

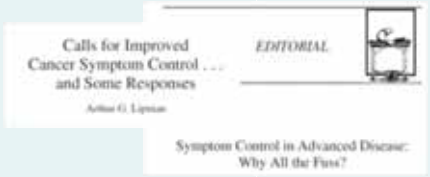
https://www.nap.edu/read/5801/chapter/1

2001 Senn et al Europ J Cancer 2001

Prevalent symptoms of advanced cancer

Pain	84%	Constipation	52%
Easy fatigue	69%	Early satiety	51%
Weakness	66%	Dyspnoea	50%
Anorexia	66%	Weight loss	50%
Lack of energy	61%	Cough	49%
Dry mouth	57%	Anxiety	48%

Orphan topics
Mucositis/dysphagia
Anorexia/weight loss
SOB.cough
Diarrhea/obstipation
Rehabilitation and psychological disorders


Calls for Improved Cancer Symptom Control . . . and Some Responses
EDITORIAL
Symptom Control in Advanced Disease: Why All the Fuss?

Lipman et al J Pain & Palliative Care Pharmacotherapy v17(2)2003

Outline

- A few comments on cooperative groups
- CCTG – structure
- Our trials in the last 5 years
- Our plan for the next 5 years
- A few thoughts on collaboration

Challenges with symptom control randomized trials

- Measuring symptoms/patient reported outcomes is hard
  - Pt collaboration
  - Appropriate tool
  - Validated outcome definitions
- "Burden" of trial participation & factors influencing
  - Willingness of health care team to approach and pts to accept trial participation
  - Ability to participate
- Attrition
  - Physical ability
  - Death

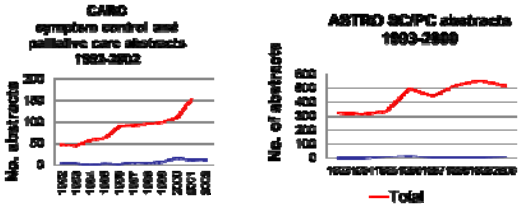
Modern

Enablers of symptom control trials

- It matters, affects all cancer patients
- Methodological advances
  - QoL, PROs, proCTCAE
  - Electronic tools
  - Validated/consensus outcome measures - Clinical relevance
- Clinical alignment
  - Palliative care units, palliative radiation oncology programs
  - Survivorship programs

5

Need for evidence…



"lower acceptance rate due to lack of perceived importance of SCPC research"

Sweeney et al

"lower no. is a function of lower no. submitted, not acceptance"

Roenn et al

Barnes Support care Cancer 12:91-94, 2004, Barnes 54,1, 211-214, 2002
Sweeney et al changing patterns of SC and palliative care paper presentations at the annual meeting of the ASCO JCO 19:3438-3439.2001
Roenn Role of symptom control and palliative care abstract presentations JCO 20(3), 880-882, 2002

6

Some Palliative Care Research Cooperatives from around the World

- Canadian Cancer Trials Group
- Base: Queen's University Kingston
- Since 1982
- trials that matter
- >80 Centers >2100 Canadian investigators
- Phase III, Phase I

https://www.ctg.queensu.ca/public/symptom-control/symptom-control-disease-site?orderByCode=Lorder_no%20DESC

- European Palliative Care Research Center
- Base: Norwegian University of Science and Technology (NTNU's FoM) at Trondheim University
- Since 2009
- 15 international 7 national
- Observation to phase III

https://www.ntnu.edu/prc

- Palliative Care Research Cooperative
- Coordinating center: U of Colarado, California, Duke
- Since 2010
- Evidence for improving QoL of patients with advanced and or potentially life-limiting illnesses, and their caregivers
- Pilot studies → RCTs

http://palliativecareresearch.org

- Palliative Care Clinical Studies Collaborative
- Base: Flinders University Adelaide
- Supporting access to appropriate medicine, maintain comfort and function during the terminal phase of illness
- Pilot, Phase III, IV

https://www.caresearch.com.au/Caresearch/tabid/2476/Default.aspx

MASCC

- Since 1990
- MASCC & International Society of Oral Oncology since 1998
- International membership 60 countries 5 continents
- Dedicated to research, practice and education
- Journal Supportive Care in Cancer
- Annual meeting
  - 2016, 1075 delegates from 50 countries
- MASCC Study Groups
  - Research, educational projects, guidelines

8

NCCTG – Alliance

Symptom Control Trials:
A 20-Year Experience

Charles L. Loprinzi, MD, Debra L. Barton, RN, PhD, Amanah Jatoi, MD, Jeff Sloan, PhD, Jim Mantenuto, MD, Daniel Stanimirovic, MD, Ravi Rao, MD, Paul Novotny, MS, Amit Sood, MD, Axel Grothey, MD, Lori Wirtzfeld, MD, and Harold Wiesenfeld, MD

SupportiveOncology 5,3, 119-128, 2007

1st trial:
Allopurinol mouth wash for 5FU induced mucositis
65 protocols

9 positive trials
Megestrol & cachexia
Erythropoietin in anemia
Fentanyl for cancer pain
Capsaicin for postsurgical neuropathic pain
EMLA Cream for procedural pain

Symptom	initiation Yr
Mucosal toxicity	1986
Anorexia/cachexia	1987
Pain	1988
Hot flashes	1989
Skin toxicity	1990
Sexual symptoms	1992
Neuropathy	1993
Lymphedema	1994
Anemia	1997
Cognitive dysfunctio	2000
Osteoporosis	2001
Insomnia	2004
Fatigue	2005

9

Cooperative groups with symptom control related focus

10

Cancer Control

On symptom control, supportive care, palliative care, survivorship…

- **Many definitions**
- **From diagnosis to end of life**
  - **pre diagnosis (preventive strategies) to post end of life (impact on families and society)**

11

Aligning affiliation with peer expertise?

	Psychosocial underpinning of illness	Active dying and death	Quantifying symptoms and QoL	Long term effects after cure has been achieved
Palliative care	++++	++++	+++	++
Supportive care	+++	+++	++++	++
Symptom control	++	++	++++	+
Survivorship	++	+	+++	++++

12

Canadian Cancer Trials Group: Canada's largest cancer clinical trial cooperative group

- **Mission:**
  - To develop and conduct clinical trials aimed at improving the treatment and prevention of cancer with the goal of **reducing morbidity and mortality** from this disease.
- **Scope of activities:**
  - phase I-III trials, all treatment modalities, endpoints; methods development; education and training; includes pediatrics and AYA, survivorship
- **Network, operations and statistical center:**
  - >80 centres; >2100 Canadian investigators
  - at Queens 11 faculty and 100 staff

CCSRI National Program since 1980

Courtesy Dr. Janet Dancey

CCTG Accomplishments

- 1500 to 3000 annually, >78,000 patients
- Trials run in 40 countries, 5 continents
- >500 trials ongoing or completed
  - 280(140 CTG led) phase III ongoing or completed studies,
  - 230 (all CTG led) Investigational Drug trials,
- Biorepository: Samples from > 20,000 clinical trial patients.
- Annual Spring Meeting > 700 participants
- Mentoring, education and training opportunities
  - Studentships, fellowships, sabbaticals
  - Biennial young investigators course

Trial results have changed practice and improved outcomes

Navigating CCTG

Brain
Breast
GI
GU
Gyne
Hematology
H&N
Lung
Melanoma
Sarcoma
Symptom Control

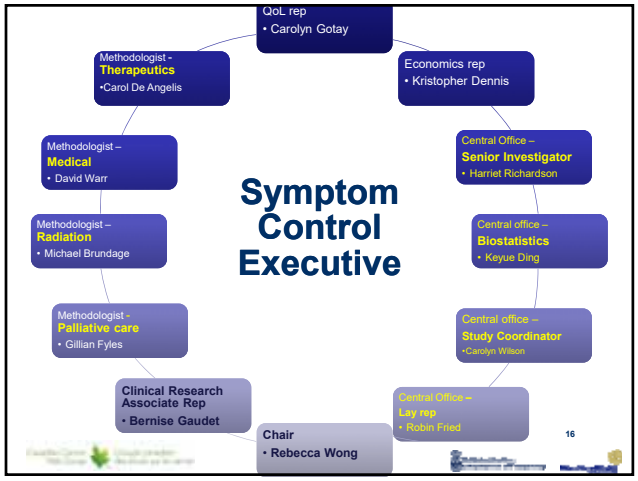
Quality of Life Committee on Economic Analysis Correlative Biology/Banking

Scientific Committees	Oversight Committees	Support Committees
Disease Sites	Clinical Trials	CRA
IND Program	Data Safety Monitoring	Pharmacy
Endpoints	Strategic Advisory	Auditing Monitory
		Lay/Patient
		Centre Representative
		RTQA

Central Ops and Stats Office at Queen's
100 Staff + 11 Faculty

> 80 Member sites and 2100 Investigators

15



16

Trial approval process

Idea	Emphasis on trial that matters design consideration, investigator support, feasible, strategic alignment
Proposal at annual spring meeting (or Exec mtg)	Demonstrate support surveys results, build coinvestigator network, industry interest, get on agendas,
Disease site executive	This can happen a few times! Be patient
Clinical Trials Committee	Formal submission written and in person presentation Details on design, up to date survey on feasibility, grant scoring methods, compete against other proposals,
Grant application (if needed)	Central office support
Trial activation	Congratulations *or the work now begins*!

Why take a trial through CCTG Symptom Control

- **Patient population**
- **Nature of question**
- **Trial design methodological expertise**
- **Data management expertise**
- **Generalizability of results**
- **Career development**

Symptom Control Committee – historical perspective

	Time	Topic	Pain	RT	Oth
IC1-7	1979-1989	Febrile neutropenia			x
SC1-9,11	1982-1995	Chemo induced emesis – Various			x
SC10	1992-1994	Pain – bone mets, clodronate	x		
SC15	1997-	RT - Lung symptoms		x	x
SC12,19	1995-2004	Radiation induced emesis – Dex		x	
SC17	1998-2001	Pain - Dextromethorphan	x		
SC18	2000-2002	Cachexia - Megace			x
SC20, 20u	2004-2012	RT – re-irradiation for bone pain	x	x	
SC23	2010-2014	RT – flare pain - Dex	x	x	
SC24	2015- now	RT – SBRT bone pain	x	x	
ES2	2003-2015	RT - Dysphagia			x
HE1	2015- now	RT - Liver pain			x
CO21	2008- now	Fatigue - Exercise			x

19

Lesson learned from challenging designs

	Time		Pain	RT	Oth
SC14	1998	Dyspnea - Theophylline			x
SC16	1998	Dry mouth - pilocarpine			x
SC22	2009-2011	Pain - methadone	x		

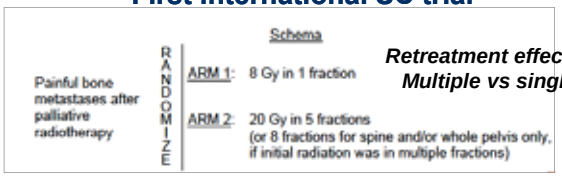
Some other topics	Pain	RT	Oth
Thoracotomy pain	x		x
Denusumab & painful bone metastases	x		x
Symptom clusters and psychosocial intervention			x

- Brilliant idea is a good start but…
  - Feasibility is critical
  - Network – investigator buy in, engagement, patient access
  - Champion

20

Our trials in the last 5 years

Trial Specifics – SC20
First international SC trial



Retreatment effective? Multiple vs single?

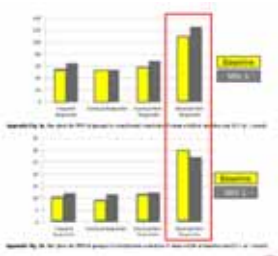
- *Design features*
  - *international consensus endpoint*
  - *non inferiority*
  - *response at 2m*
- Single fraction
  - non inferior to multiple fractions in providing pain relief
  - Associated with less toxicities
  - Not dependent on initial response
- QoL
  - Responding pts has superior qoL scores and less functional interference

N = 850
3 continents, 92 centers

The Lancet Oncology 15:164-71, 2014
J Clin Oncol 32: 3867-73, 2014

SC20U
Are urinary markers of osteoclastic activity associated with response to RT?

- Subgroup of 109 patients contributed urinary samples Baseline and at 1 month
- Tested for urinary markers of osteoclast activity
  - PYD (bone turnover-pyridinoline
  - DPD (Deoxypyridinoline)
  - NTX (N-telpeptide)
  - CTX (Alpha and Beta cross-laps of C-telopeptide
- Pts divided into four categories
  - Frequent responders
  - eventual responders
  - Eventual non responder
  - Absolute non responder

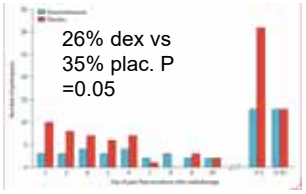


- **Absolute non responders have significantly higher urinary markers (PYD, DPD) both at baseline and at 1 month**

Rad Oncol 115:141-8, 2015

SC23
Does Dex prevent flare pain following RT?

N = 298

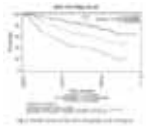


- **Dex 8mg od x 5 was effective in preventing pain flare**
- **No significant toxicities associated with Dex arm**

The Lancet Oncol 16: 1463-72:2015

Secondary analysis

Survival prediction KPS & primary site model (n = 204)



Rad Onc 118,547-551,2016

Pain classification mild, moderate, severe Using function & QoL (n = 822)

Optimal cut points 4,8

Supp care cancer 24:1617-1623, 2016

Bone metatases & RT
Pain
Functional interference
QoL
Survival

Minimal clinically important difference in EORTC QLQ BM22 & QLQ C15 PAL (n = 204)

MCID greater for improvement than deterioration

Qual Life res 25:2535-2541, 2016

25

Other trials

- **ES2 (TROG 03.01)**
  - **Clarified the role of RT in palliation of malignant dysphagia**
- **CO21**
  - **Phase III Exercise trial – important patients reported outcomes including fatigue - ongoing**
- **HE1**
  - **Phase III trial – single 8Gy to painful hepatomegaly – ongoing**

26

SBRT & Advanced Cancer Program

Cardinal metastases | Oligometastases | Trigger metastases

Lesion amenable to SBRT
(Well defined, smaller, e.g. lung, liver, bone, adrenal, nodes)

Local Control | Cure | SBRT inducing systemic effect

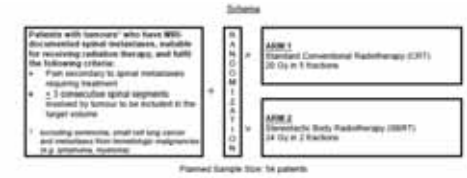
Correlative sciences
Prognostic, mechanisms for response

Trial methodology
Local effect, systemic effect
Pt reported outcomes, objective response reporting,

What is the role of Ablative RT in patients with metastatic disease?

SC24

Goal: proof of principle
Can local control improve symptom control?



Primary endpoint

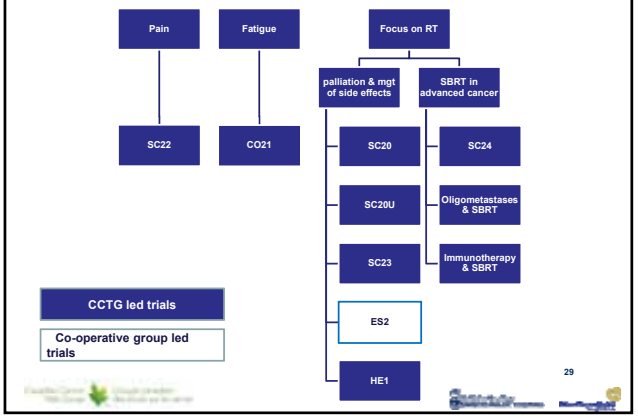
Feasibility of randomization and accrual within 18 months

Clinical endpoints

Complete pain (composite) response, Partial pain response at 3 and 6 mths
Any pain response (>2 point change)
Quality of life (EORTC QLQ C30, QLQ BM22) *(collected using eplatform)*
Local progression free survival at 3 & 6 mths
Adverse events
Correlative: sphingomyelinase levels (baseline and after fr 1)
Radiotherapy quality

28

Overall Committee Portfolio



29

Our next 5 years

- **Trials**
  - SBRT and advanced cancer platform trials (SC24, Oligometastases & immunotherapy trials)
  - Immune therapy related toxicity intervention trial
  - Cancer pain trial (e.g. dexmedetomidine for intractable pain)
  - Fatigue trial in early advanced cancer using prehabilitation framework
- **Cross Trial Infrastructure**
  - E - Patient reported outcomes collection (e.g. Raisin)
  - Imaging (radiomics, RTQA)
  - Correlative sciences including sphingomyelinase, ctDNA, immune markers
- **Methodology**
  - Novel endpoints design and validation
    - Time to QoL progression
    - Time to change of treatment strategy
  - Active accrual strategies
    - Trial implementation plan at study start up
    - Lay representatives

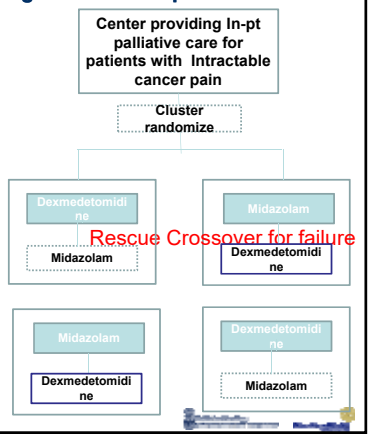
30

Future trial designs – In development

Intractable pain
dexmedetomidine vs standard

Outcomes of interest:
Feasibility for enrolment ,
Quantify primary outcome metric in study and control groups

Clinical outcomes:
No. of breakthrough doses of analgesia
No. of breakthrough doses for sedation
Proportion of patients with RASS 0
Proportion of patients with acceptable symptom control
Toxicity
QoL



PI: Dr. Neil Hillard

Future trial design – in development

Life style intervention
Fatigue & related symptoms
Prehabilitation

"early" incurable
disease
ECOG 0-1
Similar disease trajectory
(e.g. Colorectal cancer)

Prehabilitation Intervention

SOC

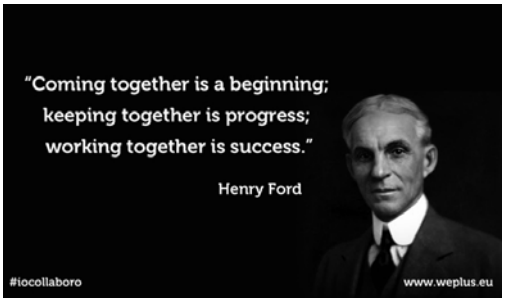
To be determined by pilot work:
Time to PS (e.g. ≥ 3)
Standardized performance tests (e.g. 6MWD), disability, (WHO DAS2.0), QoL, Social distress (SDI21), Depression, adverse events, OS, Economic analysis

32

PI: Dr. Amy Deckert, Gary Rodin

Symptom Control Committee - Today

- Scope
  - Symptom burden due to cancer & its treatment
- Strategic priorities
- Guided by key symptom experienced by cancer patients
- Investigator engagement
  - Pain
  - Fatigue
  - Focus on radiotherapy (palliation and side effects of)
  - Defining the role of SBRT in advanced cancer
- Modalities
- Other priorities
  - New methodologies to describe the impact of symptom control strategies
  - incorporate correlative endpoints into symptom control trials



*You have a clinical research idea, which likely will require multi-centre collaboration. How will you go about **identifying collaborators and collaborating centers**?*

- Cooperative Group(s) if likely
- If not
  - Search for others who have published on the topic
  - Cross reference with people I know/ centers I have worked with, ask for contacts "snowball" approach
  - Look for citations for others working in the area
  - Send emails to key people with thought out proposals
  - Cost effective research centers (e.g. India, Southeast Asia)

Acknowledgement: Dr. Vickie Baracos, Jolie Ringash, Kristopher Dennis,Tetteh Ago, Laura Dawson, Michael Lock, Candice Johnstone, Andrea Bezjak, Marc Kerba, Tracy Balboni

Are there any research collaborative Groups that you would consider proposing your idea to establish the collaborative network? If so which ones?

- Canadian: CCTG
- International: US NCI Site groups, NRG, EORTC, PRC, TROG, AGITG, IAEA,
- Committees at: CARO, ASTRO, MASCC,
- Research groups: CPROG (canadian Palliative Radiation Oncology Group), palliative care consensus group, SPRO (society of Palliative radiation Oncology)

*Can you provide some **favorable features** about the group that would encourage you to select them as your collaborative groups of choice?*

- Similar research/clinical care philosophies
- Track record for successful collaboration within an area of interest
- Large mature network
- Open membership
- Ability to accrue
- Communications:
  - regular contact, up to date websites,
- Mentors:
  - champions for idea under investigation, groups with funding to support ideas
- Infrastructure
  - Good infrastructure to help in best practices
  - Ability to provide technical assistance (e.g. QA)
- Sensitivity to whether they may be 'upset" that you were chosen to lead this particular effort

37

*Can you provide some **unfavorable features** about the group(s) that would discourage you from approaching them as your collaborative group of choice?*

- Complex organizations with multiple levels of "vetting"
- "Politics" that likely of success is extremely low, or at least try multiple venues
- Poor accrual, technical ability
- History of long time to study activation
- Inefficient collaborative groups
- Lack of funds, lack of regular connection to establish ongoing partnerships, limited uptkae on new ideas

38

*What are some key enablers and barriers to multi center clinical trial collaborations that you would pass on to **your mentee**? Favorite junior colleague wanting to follow your footsteps?*

- Know the subject matter
- Be part of the network
  - Join research groups
  - Go to meetings, meet people, keep in touch
  - Go to coop group meetings if you want them to advocate for you or your study idea
- Build relationships – this is important!
  - Departmental leadership research support
  - Call to ask questions – even those you already have answers for
  - Don't think too highly of yourself
  - Make a favorable first impression
  - Get to know the opinion leaders (and their friends)
  - Go to dinner when invited (and write a thank you after)
  - Find a reason to write a short nice note

39

- On mentors
  - Find a successful mentor
  - Work with generous collaborators
- On being a collaborator
  - Make sure your voice is heard
  - Contribute to others' proposals
  - Try not to "Take sides" in too strong a way
  - Be a collaborator (likely to get reciprocal support)
- Overall
  - Be willing to "bang your head against the wall" many many times
  - Work with what interests you and make you a better doctor (vs your CV)
  - Accept some ideas/ many hours/years of work will come to nothing
  - Do not take no for an answer (wisely)
  - Do not give up!

40

Take home message

- Symptom Control Committee of CCTG – a successful national and international collaborator
- Ready partner for symptom control trials within the palliative care/ advance cancer domain
- Pre-habilitation, intractable pain – anyone?

Canadian Cancer Trials Group / Groupe canadien des essais sur le cancer

NCIC Clinical Trials Group

Conducting trials that matter to patients

Example of recent publications (30-60/year)

The NEW ENGLAND JOURNAL of MEDICINE

say in Breast Cancer. Sparano

2. Regional Nodal Irradiation in Early-Stage Breast Cancer. Whelan T.J., et al. N Engl J Med 2015; 373:307-316
3. Intermittent versus Continuous Androgen Deprivation in Prostate Cancer. Hussain M., et al. N Engl J Med 2013; 368:1314-1325
4. ABVD Alone versus Radiation-Based Therapy in Limited-Stage Hodgkin's Lymphoma Meyer R.M., et al. N Engl J Med 2012; 366:399-408
5. Intermittent Androgen Suppression for Rising PSA Level after Radiotherapy. Crook J.M., et al.N Engl J Med 2012; 367:895-903
6. Exemestane for Breast-Cancer Prevention in Postmenopausal Women. Goss P.E., al. N Engl J Med 2011; 364:2381-2391
7. Neoadjuvant Chemotherapy or Primary Surgery in Stage IIIC or IV Ovarian Cancer Vergote I., et al. N Engl J Med 2010; 363:943-953

8. Bold = CCTG led trials

NCIC Clinical Trials Group

- Funders (last 2 years): Grants to support trials from 15 public funders/charities; 27 industry
- 2008-present >$64M public funding/$240M industry
- 13 drug marketing applications by 11 pharma companies for new or altered indications to government regulators
- 11 biotech company partnerships (5 Canadian), in development, trials with 6 additional biotechs, (2 Canadian).

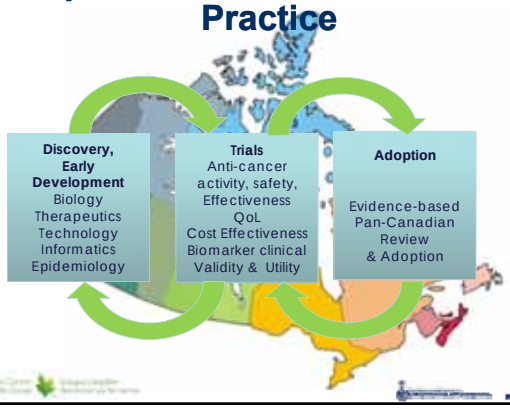
45

CCTG Today

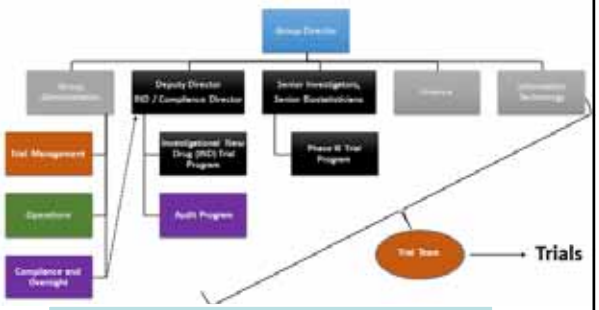
- Scientific trends: novel therapeutics including RT, immunotherapy, precision medicine, rare cancers, innovative trial approaches
- Capabilities: trial design, regulatory, legislative, legal and ethics expertise to conduct phase I-III trials including registration trials
- Relationships, partnerships, collaborators:
  - Researchers, consortia, nationally and internationally
  - Academic, industry, regulatory agencies, cancer agencies
- National initiatives and international initiatives:
  - Initiative to Streamline Clinical Trials
  - Canadian Cancer Clinical Trials Network
  - Molecular Laboratories Strategy with CCRA
  - CTRNeT
  - RECIST working group

46

Capabilities: Markers, Trials & Practice

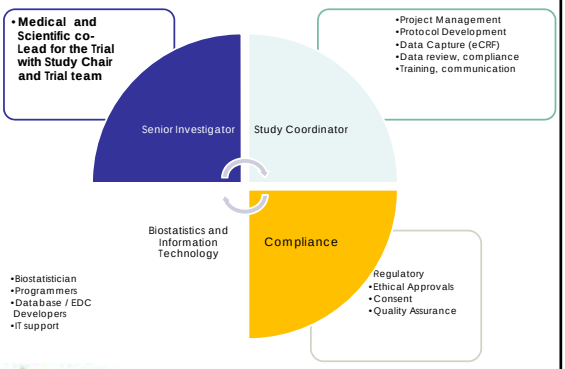


CCTG Operations and Statistical Centre



Central Ops and Stats Office at Queen's
100 Staff + 11 Faculty

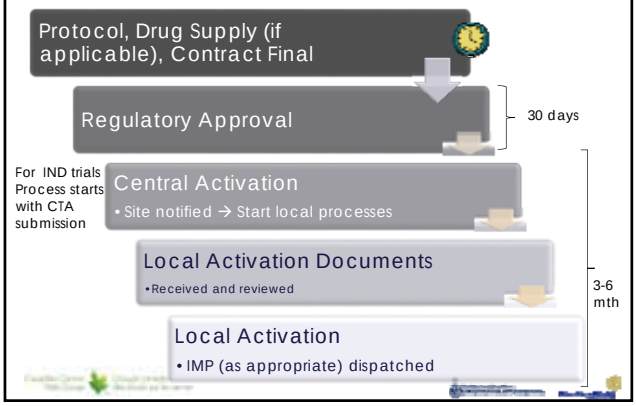
Trial Team Roles and Responsibilities



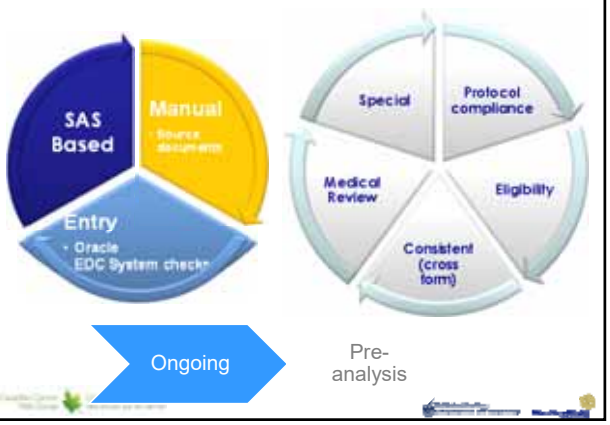
Standardized Systems

- Standard Operating Procedures
- Training
- Protocols, Informed Consent Forms, and electronic Case Report Forms (eCRFs)
- Trial and Site Activation
- Data Management and Analysis
- Quality Assurance for trial conduct, data including RTQA

Trial Activation Process



Data Review



MODELS OF COLLABORATION

Key Considerations

- Sponsorship: CCTG is sponsor and responsible for trial oversight, conduct, holds database and performs analysis
- Consensus decisions with partners; industry partners review publications, may have copy of trial database.
- Communication
- Network of sites and investigators
- Regulatory capacity
- Pharmacovigilance
- Quality assurance
- Standard operating procedures
- Contracts and Insurance

Impact

- Patient access to new treatment options and emerging therapies
- Practice changing research driven by academic cooperative groups, networks, consortia
- Increases applicability of results to multiple regions
- Reduces time to activate, accrue, and analyze

55

Opportunity

- Group collaboration
- Rapid site selection and accrual
- Efficient and cost effective
- Establishment links to international networks & consortia

Thank You

CCTG is a national program of the Canadian Cancer Society

Canadian Cancer Trials Group https://www.ctg.queensu.ca/default.html

NCI National Clinical Trials Network

INNOVATION.CA
CANADA FOUNDATION FOR INNOVATION | FONDATION CANADIENNE POUR L'INNOVATION

Summary of All Activities 1 July 2010 – September 30, 2016

- **Trials led in Phase III Program** **7**
- **(including 2 Symptom control trials within GI site portfolio)**
- **Intergroup trials** **1**
- **(1 symptom control trial within GI site portfolio - TROG)**
- **IND trials** **0**
- **Total CCTG-related accrual*** **1858**
  - **Canadian accrual to all SC trials** **1196**
  - **US / international accrual to CCTG trials** **575**
  - **Canadian accrual to SC trials led by GI group** **457**

* SC & SC trials led by GI
SC trials: 1196, SC trials led by GI

58

Awards

Young Investigator Awards
Successful applicants must be less than 40 years old and their abstracts must rank in the top 20% of those submitted.

59

Challenges, Threats and Opportunities

- **Engagement of investigators**
  - **Broad scope**
  - **Build and maintain network**
  - **Need to expand beyond RT to other clinical areas (e.g. palliative care, psychosocial oncology, toxicity mgt in novel therapeutics, correlative sciences)**
- **Efficient trial accrual strategies**
- **Funding source to support symptom control priorities**
- **Clinical areas of opportunities**
  - **Technological abilities & support for clinical trials in Canadian RT communities - SBRT in advanced cancer**
    - **Immunotherapeutics & associated toxicities**

60

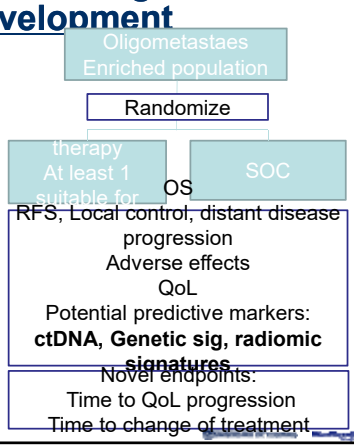
Major Accomplishments

- Established two new standards of care to control cancer pain
  - Repeat irradiation with a single 8Gy is effective for pain relief in painful bone metastases
  - Dexamethasone 8mg is effective in preventing flare pain following single fraction radiation for painful bone metastases
- Developed an overarching programmatic approach designed to establish the role of stereotactic body radiotherapy in patients living with advanced cancer
- Build sustained collaboration across CCTG scientific committees and international cooperative groups
- Incorporation of correlative science into each of our symptom control trials

61

Future trial designs – In development

Oligometastases
RCT
Intractable pain
dexmedetomidine vs standard
Life style intervention
Fatigue & related symptoms
Prehabilitation



62

Why take a trial through CCCTG Symptom Control

- Patient population
  - Trial proposal requires multicenter collaboration
  - National
  - International, collaborative group
    - E.g. TROG, AGITG
- Nature of question
  - "Public good" trials (low "Commercial value")
- Trial design methodological expertise
  - Trial design, patient reported outcomes/QoL/Economics
  - Correlative science/Biobank
- Data management expertise
  - Quality assurance, (e.g. QoL, RTQA)
- Generalizability of results
- Career development

63

Activities 2017-2022 - cont

- Capacity building
  - RT community
    - *Priority CCTG has given*
    - *Alignment between excellence in clinical research and pt care in palliative RT delivery*
  - Beyond the RT community
    - *Executive*
    - *Revisit co-chair model, working groups*
    - *Succession planning*
    - *Recruitment of new/young investigators & their senior mentors*
  - Training and engagement of new/young investigators
    - *Demonstrated successes with secondary analyses*
    - *Young investigators leading most of our newer proposals*
  - Cross DSG & International collaborations
  - Momentum

64

Our next 5 years

1. Reduce the burden of cancer
   - SBRT in advanced cancer investigation platform
2. Reduce the morbidity of cancer
   - SBRT in advanced cancer
   - Dexmedotomidine in intractable pain
   - Conduct a fatigue management trial
   - Conduct a trial to manage immuno-therapy related toxicities
   - Explicit trial accrual strategies with an emphasis on lay representative engagement
   - Continue to build correlative hypothesis
3. Demonstrate value of cancer treatments to QoL
   - Incorporate health economic measures to trials

65

Activities 2017-2022 - cont

- **Methodology and Endpoint Evaluation**
  - **Novel endpoints design and validation**
    - Time to QoL progression
    - Time to change of treatment strategy
  - **Active accrual strategies**
    - Trial implementation plan at study start up
    - Lay representatives

66

CCTG Accomplishments

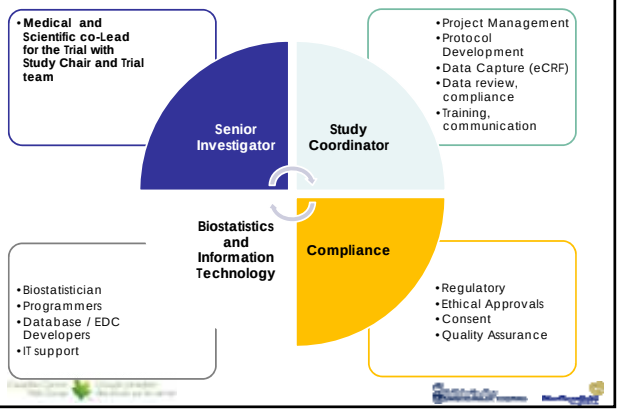
- **$25-35M/year research enterprise; consistently rated outstanding**
- **>500 trials ongoing or completed**
  - **280(140 CTG led) phase III ongoing or completed studies,**
  - **230 (all CTG led) Investigational Drug trials,**
- **>78,000 patients; 1500 to 3000 annually.**
- **Trials run in 40 countries, 5 continents**
- ***Trial results have changed practice and improved outcomes***
- **Biorepository: Samples from > 20,000 clinical trial patients.**
- **Annual Meeting > 700 participants**
- **Mentoring, education and training opportunities**
  - **Studentships, fellowships, sabbaticals**
  - **Biennial young investigators course**

CCTG Today

- **Scientific trends:** novel therapeutics including RT, immunotherapy, precision medicine, rare cancers, innovative trial approaches
- **Capabilities:** trial design, regulatory, legislative, legal and ethics expertise to conduct phase I-III trials including registration trials
- **Relationships, partnerships, collaborators**:
  - Researchers, consortia, nationally and internationally
  - Academic, industry, regulatory agencies, cancer agencies
- **National initiatives and international initiatives:**
  - Initiative to Streamline Clinical Trials
  - Canadian Cancer Clinical Trials Network
  - Molecular Laboratories Strategy with CCRA
  - CTRNeT
  - RECIST working group

68

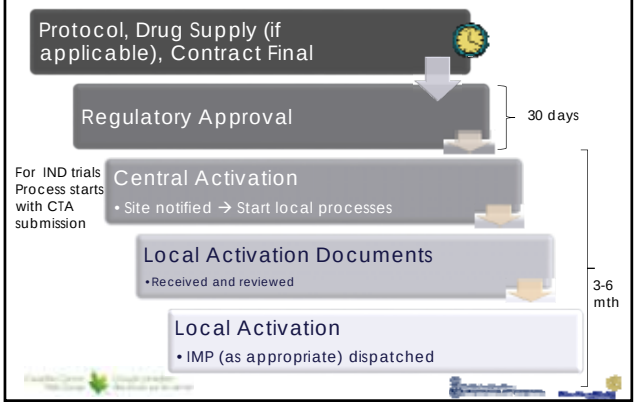
Trial Team Roles and Responsibilities



Standardized Systems

- Standard Operating Procedures
- Training
- Protocols, Informed Consent Forms, and electronic Case Report Forms (eCRFs)
- Trial and Site Activation
- Data Management and Analysis
- Quality Assurance for trial conduct, data including RTQA

Trial Activation Process



Why Radiation Oncology & Symptom Control worked for CCTG?

- Alignment of clinical need and research "specialized palliative clinics"
- Need for peers - CPROG
- Focus from Canadian Association Radiation Oncologist
- Focus from CCTG
- Strategic building workshops CARO-CCTG
- Collaboration
- Successful trials

72

Our next 5 years

- **Capacity building**
  - Lessons learned from the RT community
    - *Priority CCTG has given*
    - *Alignment between excellence in clinical research and pt care in palliative RT delivery*
  - Beyond the RT community
  - Training and engagement of new/young investigators
  - Cross DSG & International collaborations

73

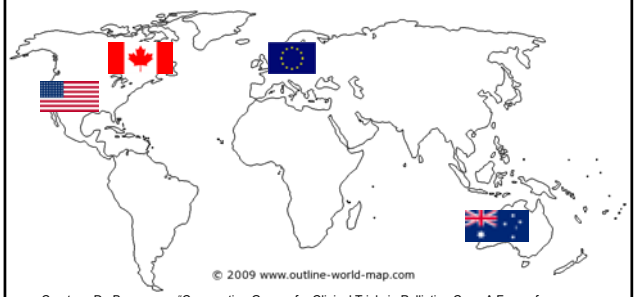
Challenges
CCTG - in the palliative care space

- Methodology
- Sustained success demonstration
- Sustained environment to engage investigators
- Building the investigator network within CCTG

a bridge to ✓

74

Some Palliative Care Research Cooperatives from around the World



Courtesy Dr. Baracos on "Cooperative Groups fro Clinical Trials in Palliative Care: A Forum for International Collaboration": Canadian Palliative Radiation Oncology Group Nov 2016

On symptom control, supportive care, palliative care, survivorship…

- Many definitions
- From diagnosis to end of life
  - pre diagnosis (preventive strategies) to post end of life (impact on families and society)
- WHO on palliative care
  - *Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.*
- MASCC on supportive care
  - *Supportive care in cancer is the prevention and management of the symptoms and side effects of cancer and its treatment across the cancer continuum from diagnosis to the end of life. It includes support for patients, their families, and their caregivers.*
- NCI dictionary on survivorship
  - *In cancer, survivorship focuses on the health and life of a person with cancer post treatment until the end of life. It covers the physical, psychosocial, and economic issues of cancer, beyond the diagnosis and treatment phases. Survivorship includes issues related to the ability to get health care and follow-up treatment, late effects of treatment, second cancers, and quality of life. (Patients) Family members, friends, and caregivers are also considered part of the survivorship experience.*

76