NCIC CTG Overview
Structure and Opportunities

Wendy Parulekar MD FRCP
Physician Coordinator
NCIC CTG
Overview of Talk

• Objectives
  – To describe the NCIC CTG:
    • who and what we are
    • funding
    • structure: internal / external
  – To describe scope of NCIC CTG activity
  – To understand opportunities for Investigators
NCIC Clinical Trials Group

• A research organization
• A clinical trials cooperative group
• Mandate is national
• Scope is international
• To include: all cancer disease sites
  all treatment modalities
Mission

The mission of the NCIC Clinical Trials Group (CTG) is to develop and conduct clinical trials aimed at improving the treatment and prevention of cancer with the ultimate goal of reducing morbidity and mortality from this disease.
NCIC CTG: An Overview

- 1979: NCIC decides to have formal group
- 1980: CTG established in Kingston under Joe Pater
- 1982: IND Program established
- 1988: NIH funding received; formalized in 1997
- 1997: Directions reviewed by NCIC Task Force on Clinical Studies
- 2010: Pediatric IND Program established
Funding

CCSRI

• **Funds:** Impact grants
  Innovation grants
  Prevention grants
  other

• **Funds two national networks / programs**
  ARCC
  NCIC CTG
Funding
Funding

Canadian Cancer Society

Canadian Cancer Society Research Institute

NCIC CTG
Funding

Other Granting Agencies:

- e.g. CIHR
- OICR
- Disease-specific agencies

- Format varies: special opportunities
  companion questions

- In general, is project-specific
Funding

Industry:

• Funding is project-specific
• Partner is pharmaceutical / biotech
• Often includes correlative biology
• Relationships include additional complexities
Structure
NCIC CTG

Can be considered in two major categories:

**External**
- Network of ~ 80 Canadian investigative sites
- Committee structures involving nearly 1000 investigators and other research personnel

**Internal**
- Head office in Kingston - 110 staff, 12 faculty
External Organization
External Structure

Refers to network of investigators

• Canada: approximately 80 sites
  provincial cancer centres
  university affiliations
  special clinics

• International: major cooperative groups
  single sites in many countries
External Organization

Centre Representatives

- Deal with local operations of trial conduct
- Receive correspondence concerning their site
  Agenda, Minutes, Surveys, Drafts
- Communicate information within centre
- Advisory role relationship with Central Office
External Organization

Disease Site Committees

- Responsible for scientific leadership
- Each committee has executive and chair
- External and internal representation
- Chair is external, may have international role
- Selection of executive is based on:
  - Scientific leadership
  - Participation
  - Geographic / modality balance
External Organization

Disease Site Committee Membership

- Each centre has Site Committee members
- Multiple members per centre based disease / therapeutic modalities
- Some Sites have Working Groups
- Members are to *communicate* within their centre, with their executive
External Organization

Outcome-Based Committees

Correlative Sciences and Tumour Biology

Quality of Life

Committee on Economic Analysis

- Scientific content to Sites / Trial Committees
- Methodologic research: measurement analysis
External Organization

Other Standing Committees include:

- Radiation Quality Assurance
- Audit and Monitoring Committee
- Clinical Research Associates
- Pharmacy Network
- Lay Representatives

- Role in trial conduct
- Methodologic research
NCIC Clinical Trials Group

Two programmatic components

Investigational New Drugs

Phase III
External Organization

Phase III Program

Agenda:

- Led by the Disease Site Committees
- Supported by the Working Groups
- Evaluated / prioritized by the Clinical Trials Committee (CTC)
- Conduct monitored by the DSMC
- Implementation assisted by: CRAs, Pharmacists
Investigational New Drug Program

Scope:
- Phase I-II testing of new agents
- Range from ‘1st in man’ to novel combinations
- Prioritized to evaluating targeted mechanisms

Agenda:
- Led by IND executive
- Implemented by IND Committee
Internal Organization
Refers to operations at Queen’s Centre for:

- Methodology and data management
- Trial coordination
- Quality management: assurance, monitoring, safety, regulatory / ethics
- Includes 12 faculty and about 110 staff
Roles of Central Office Staff

Director

- Administers program; formulates, implements policy

Physician Coordinators (Senior Investigators)

- Provide medical and group input into specific trials, serve as Central Office medical contacts for each site
Roles of Central Office Staff

Senior Biostatisticians

• Provide methodologic, statistical input into trials and analyses
• Each is responsible for a slate of sites
• Analyses conducted by biostatisticians, i.e. individuals with BSc or MSc training in statistics plus SAS / Oracle programming skills
Activity Level
Phase III Program

Scope:

• Randomized controlled trials

• Selected phase II studies (enablers)
Broad Accomplishments

1980 – August 2013:
• 481 trials
• 75,600 patients

In 2004-2010 grant cycle:
• 200 trials were in some form of conduct
• 23,000 new patients were accrued
Selected Deliverables

Publications:

- > 500 trial-related manuscripts and abstracts
- > 110 Central Office faculty research reports
- 18 meta-analyses

“Building Capacity”

- > 25 Fellows / PhD / Postdoctoral trainees
- > 20 Masters / PhD Theses
- 4 New Investigator Workshops (total N > 125)
Changes to Canadian Health Care Practices

- Aromatase inhibitors for breast cancer (MA.17)
- Adjuvant therapy for lung cancer (BR.10)
- Erlotinib for lung cancer (BR.21)
- Temozolomide for glioblastoma (CE.3)
- Cetuximab for colon cancer (CO.17)
- Chemotherapy for Hodgkin lymphoma (HD.6)
- Limited role of RT in endometrial cancer (EN.5)
- Important role of RT in prostate cancer (PR.3)
Changes to Canadian Health Care Practices

- Aromatase inhibitors prevent breast cancer *(MAP.3)*
- Regional RT for breast cancer *(MA.20)*
- Intermittent hormone Rx for prostate cancer *(PR.7)*
Overall Survival

P < 0.001 by stratified log-rank test
Hazard ratio, 0.70 (95% CI, 0.58–0.85)

No. at Risk

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B Overall Survival, All Patients

Probability (%)

P = 0.009

Years

No. at Risk
Observation 240 182 94 47 13 0
Vinorelbine plus cisplatin 242 193 121 51 10 0

NCIC CTG BR.10
Lung Cancer
Winton, NEJM 2005
A Disease-free Survival

Women Surviving Free of Breast Cancer (%)

No. at Risk

Months after Randomization

Letrozole group

Placebo group

P<0.001

Letrozole
Placebo

No. at Risk

2575 2308 1327 624 183 9 0

2582 2298 1295 610 180 11 0

Breast Cancer

Goss, NEJM 2003
NCIC CTG CE.3 (IG)

Glioblastoma
Stupp, NEJM 2005
A

Proportion Alive (%)

Months since Randomization

No. at Risk

Cetuximab plus best supportive care 287 245 189 136 87 60 37 20 13 4 1
Best supportive care alone 285 235 157 85 58 37 26 15 11 8 4

Colon Cancer

Jonker, NEJM 2007
**Figure 1.** Cumulative Incidence of Invasive Breast Cancer.
CI denotes confidence interval.

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Hazard ratio, 0.35 (95% CI, 0.18–0.70)  
P=0.002 by stratified log-rank test

Annual Incidence (95% CI)
- Placebo: 0.55% (0.36–0.73)
- Exemestane: 0.19% (0.08–0.30)
Figure 1. Overall Survival in the Intention-to-Treat Population.
The per-protocol analysis yielded very similar results to the analysis presented here, with an estimated hazard ratio for death with intermittent androgen-deprivation therapy (IAD), as compared with continuous androgen-deprivation therapy (CAD), of 1.03 (95% CI, 0.87 to 1.22). The P value for noninferiority (hazard ratio, <1.25) was 0.01.
NCIC CTG: Productivity

IND Program

• 197 trials
• *Enrolment of ~ 5,500 patients*
• Testing of more than 70 new agents
• Multiple examples of:
  ‘to phase III’ results
  successful correlative observations
IND Program: Goals

• Acquire new agents for study in Canada
• Generate results leading to phase III trials
• Advance phase I-II trial methodology
• Include laboratory / imaging correlative studies
• Train new specialists in drug development
Acquire Novel Agents for Study

High priority agents

- Novel / target - specific cytostatics / cytotoxics
- Antimetastatic agents or angiogenesis inhibitors
- Cytoprotectors or modulating agents
- Hormones / biologicals with immune basis
How to “Get In”
External Organization

- Come to meetings
- Be active in your centre
- Accrue to trials
- Bring your ideas forward
- Get on a committee

Disease Site Committee
Let any special backgrounds be known
Consider an operations committee
(e.g. Audit / Monitoring)
How to “Get In”

- Communicate your interest
  - within centre-to-centre and site reps
  - to us
  - to site chair
- Respond to surveys, questions about studies
- Accrue to active trials
- If medical / heme onc, consider IND trials
How to “Get In”

- Fellowship opportunities
- Secondary analyses
Summary

• We are a clinical trial research group with multiple sources of funding / collaborations

• Scope of activity – phase I-III

• Structure:
  – Internal head office in Kingston; virtual external office that includes national and international research personnel and sites / organizations
Summary

Multiple collaborative opportunities for investigators in the context of clinical research.