NCIC CTG Overview:
A New Investigator’s Perspective

Annette Hay, Clinical Trials Fellow
Disclaimer

For He's a Jolly Good Fellow
Objectives

- Demonstrate range of opportunities available
  - Personal experience
  - Sample projects
- Outline processes to answer research question
Phenotype of research trainees I’ve encountered

NCIC CTG Trainees

- Statisticians
- Scientists
- Doctors
Fellowships at NCIC CTG

- Thoracic Oncology Clinical Trials Fellowship
- Drug Development Fellowship
- Astra Zeneca Breast Cancer Fellowship
- OSI Translational Research Fellowship
- Astra Zeneca Clinical Trials Fellowship
Tailored Opportunities

Hematological

• Study development, protocol writing, phase I (LY.15)
• Data review, analysis, manuscript writing, phase III (LY.12)
• Economic analysis (LY.12)
• Collaboration with Germans in Hodgkin Lymphoma (HD.6)
• Editorial & review articles
• Clinical work
Tailored Opportunities

Methodological

• Community Health and Epidemiology MSc
  – Controlled clinical trials
  – Health economics
  – Health policy

• Predictive value of phase II trial designs

• Apprenticeship
Secondary analyses

• Clinical trial enrolment first priority
• Opportunities for secondary analyses
  – Comparative
  – Database interrogation
  – Correlative science
  – Methodological: economics, statistical . . .
An Individual Patient-Data Comparison of German Hodgkin Study Group HD10 and HD11 Combined Modality Therapy and NCIC Clinical Trials Group HD.6 ABVD Alone

Individual Patient Data Comparison
Limited-stage Hodgkin Lymphoma

- **2 ABVD + 20 Gy IFRT**
  - Early, favorable
  - HD10

- **4 ABVD + 30 Gy IFRT**
  - Early, unfavorable
  - HD11

- **4 – 6 ABVD alone**
  - Favorable
  - HD.6
  - Unfavorable

- **Advanced**

GHSG

NCIC CTG

Not necessarily to scale
Very good prognosis

B or Bulk

Limited-stage Hodgkin Lymphoma

Early, favorable HD10

Early, unfavorable HD11

Advanced

GHSG

NCIC CTG

HD.6

Favorable

Unfavorable

Advanced

Not necessarily to scale
Radiation improves disease control...
No difference in survival at 8 years

\[ \text{HR} = 1.09; \ 95\% \ CI \ 0.49, 2.40 \]

Hay et al, abstract 548, ASH 2012
Location of colon cancer (right-sided versus left-sided) as a predictor of benefit from cetuximab in NCIC CTG CO.17

Stephanie Y. Brulé, Derek J. Jonker, Christos Stelios Karapetis, Christopher J. O'Callaghan, Malcolm J. Moore, Ralph Wong, Niall C. Tebbutt, Craig Underhill, Desmond Yip, John Raymond Zalcberg, Dongsheng Tu, Rachel Anne Goodwin
Database interrogation

NCIC CTG CO.17

- Cetuximab versus best supportive care in pre-treated metastatic colon cancer, Jonker 2007

Study question

- In this population is primary tumour site (right vs. left) prognostic for outcome or predictive of benefit from cetuximab therapy?
Tumour site is not prognostic.

Figure 1. Location of the primary (RC vs LC) is not prognostic: OS and PFS by tumour location in patients on BSC alone.

Brule et al, abstract 3528, ASCO 2013
but is predictive of benefit from cetuximab

<table>
<thead>
<tr>
<th>KRAS WT subset</th>
<th>Median survival (months) CET vs BSC</th>
<th>Benefit CET vs. BSC HR (95% C.I.), p value</th>
<th>Predictive effect Interaction p value</th>
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<tr>
<td><strong>OS</strong></td>
<td></td>
<td></td>
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<tr>
<td>RC</td>
<td>6.2 vs 3.5</td>
<td>0.66 (0.36, 1.21), p=0.18</td>
<td>0.25</td>
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<tr>
<td>LC</td>
<td>10.1 vs 4.8</td>
<td>0.49 (0.31, 0.77), p=0.002</td>
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<tr>
<td><strong>PFS</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RC</td>
<td>1.9 vs 1.9</td>
<td>0.73 (0.42, 1.27), p=0.26</td>
<td>0.002</td>
</tr>
<tr>
<td>LC</td>
<td>5.4 vs 1.8</td>
<td>0.28 (0.18, 0.45), p&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Brule et al, abstract 3528, ASCO 2013
Exploratory analysis of angiotensin converting enzyme and aldosterone serum levels as prognostic and predictive biomarkers on the NCIC CTG BR24 trial

Jair Bar, Keyue Ding, Huijin Zhao, Scott Laurie, Lei Han, Frances Shepherd, Christina Addison, Glenwood Goss, Jim Dimitroulakos, Penelope Bradbury
Correlative science

BR.24
Advanced non-small cell lung cancer
296 patients

Carboplatin & paclitaxel

Carboplatin, paclitaxel & cediranib

Cediranib: VEGF inhibitor

Goss et al, JCO 2009
Correlative science

• Benefit from angiogenesis inhibitors has been linked to high blood pressure

• Exploratory analysis of angiotensin converting enzyme (ACE) and aldosterone (ALD) serum levels as prognostic and predictive biomarkers

• ACE and Ald levels retrospectively tested on 226 baseline serum samples

Bar et al, abstract 8048, ASCO 2013
High serum ACE level may be prognostic

High ACE level (≥ 115 ng/ml)

• Associated with better performance status (p=0.03)
• Longer overall survival (HR 0.52, p=0.025)

Bar et al, abstract 8048, ASCO 2013
High serum ACE level may be prognostic

High ACE level (≥ 115 ng/ml)

- Associated with better performance status (p=0.03)
- Longer overall survival (HR 0.52, p=0.025)

Low ACE may predict benefit from cediranib

Low serum ACE level (< 115 ng/ml)

- Improved overall survival with addition of cediranib to PC (HR 0.64, p=0.03)
NCIC CTG MAP.3: Symptoms and quality of life among racial/ethnic minority women taking the aromatase inhibitor exemastane for breast cancer risk reduction

Beverley Moy, Dongsheng Tu, Harriet Richardson, Elizabeth Maunsell, Paul Goss
MAP.3
4563 post-menopausal women at risk of breast cancer

Exemestane

Placebo

Canada, USA, Spain & France
Racial/ethnic minority women experience fewer adverse events on aromatase inhibitors

Ethnic minority compared with white women

- Fewer sweats (12% vs. 22%, p=0.005)
- Less vaginal dryness (8% vs. 16%, p=0.03)

Moy et al, abstract 6557, ASCO 2013
Racial/ethnic minority women experience fewer adverse events on aromatase inhibitors

Hispanic women compared with non-Hispanic experienced significantly less frequent

- Hot flashes
- Fatigue
- Sweats
- Insomnia
- Heartburn
- Arthritis

- Nausea
- Depression
- Back pain
- Cough
- Vaginal dryness

Moy et al, abstract 6557, ASCO 2013
How to do it too

ABOUT US

The NCIC Clinical Trials Group is a cooperative oncology group which carries out clinical trials in cancer therapy, supportive care and prevention across Canada and internationally. It is one of the national programmes and networks of the Canadian Cancer Society Research Institute (CCSRI), and is supported by the Canadian Cancer Society (CCS).

The information contained in this website is intended for use by NCIC Clinical Trials Group members at participating centres. If you are a cancer patient, your doctor can explain how this information applies to you, or you can call the Cancer Information Service of the Canadian Cancer Society at 1-888-939-3333.

We are located at Queen's University, Kingston Ontario at the Cancer Research Institute.

Password Management
Lost or Forgotten Passwords
Password Request Information
Contact Us
NCIC CTG Bulletin
Faculty Biographies
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Faculty Biographies
Public Listings

Information for New Centre Staff

A descriptive listing of all current trials is provided:

Phase III Site Committee Trials
  - Accrual: Phase III - Closed Studies

Investigational New Drug (IND) Program Trials
  - Accrual: IND Trials - Closed Studies

For Members Only (full study information)

Members

Single Study Members
Investigational New Drug Studies

**PHASE II STUDIES**

- Brain - I142 I204
- Breast - I163 I164 I197 I213
- Cervix - I184 I199
- Chronic Lymphocytic Leukemia - I193
- Colon - I146 I210
- Endometrial (non-sarcomatous uterine c.) - I148 I160 I192
- Fallopian Tube - I185
- Head and Neck - I157
- Liver (hepato-cellular) - I168
- Lung Cancer - Non-Small Cell - I211
- Melanoma - I156 I169 I189 I202
- Mesothelioma - I183 I207
- Multiple Myeloma - I145 I191
- Multiple Sites - I206
- Non-Hodgkins Lymphoma - I150 I152 I172 I182 I194
- Ovary - I149 I185
- Prostate - I165 I167 I195 I205 I209
- Renal (kidney) - I161
- Sarcoma - soft tissue - I155 I200

**PHASE I STUDIES**

- Acute Myeloid Leukemia - I141
- Brain - I162
- Colon - I171 I175 I187
- Lung Cancer - Non-Small Cell - I171 I175 I215
- Multiple Sites - I130 I134 I144 I147 I154 I178 I188 I203
- Myelodysplastic Syndrome - I141
- Neuroblastoma - I212
- Prostate - I153
- Rectal - I187
- Unknown or unspecified malignancy - I166 I166B I177 I179 I181

**PHASE I-II STUDIES**

- Acute Myeloid Leukemia - I186
- Brain - I170
- Breast - I198
- Colon - I208 I214
- Lung Cancer - Non-Small Cell - I196 I214
- Lung Cancer - Small Cell (= oat cell) - I190
- Myelodysplastic Syndrome - I186
- Pancreas - I173
A Randomized Phase II Study of Reolysin in Combination With Docetaxel and Prednisone or Docetaxel and Prednisone Alone in Patients With Metastatic Castration Resistant Prostate Cancer

Eligibility: Patients with a histological diagnosis of metastatic and/or locally recurrent castration resistant adenocarcinoma of the prostate. Tumour block available. Patients must be hormone refractory and have discontinued anti-androgens for at least 4 weeks prior to study entry. PSA >= 5 ng/mL at study entry. No prior chemotherapy for recurrent/metastatic disease. No prior docetaxel unless given adjuvantly and >= 12 months prior to enrollment. ECOG 0, 1 or 2. Adequate end-organ function.

Objectives: 1. To evaluate efficacy which will be based on the lack of disease progression measured at 12 weeks. 2a. To determine the tolerability and toxicity of Reolysin® and docetaxel when given in combination. 2b. To investigate additional potential measures of efficacy including CTC status, CTC conversion rate, change in PSA levels, Objective response rate and effect of both treatments on overall survival. 2c. Explore potential molecular factors predictive of response in archival tumour and baseline CTCs.

NCT Registration ID (from clinicaltrials.gov): NCT01619813
Participant: Limited to invited cancer centres only.

Status: Open
Activation Date: June 11, 2012

Chairs: (Canada) Dr. Bernhard Eigl, BCCA - Vancouver Cancer Centre, 1(604) 877-6000 Ext. 2707
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NCIC Groupe des essais cliniques
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NCIC CTG GROUP PUBLICATIONS & PRESENTATIONS

NCIC CTG Abstracts presented at the 2013 ASCO Annual Meeting
Chicago, Illinois
May 31 - June 4, 2013

NCIC CTG Abstracts presented at the
35th Annual San Antonio Breast Cancer Symposium
Henry B. Gonzalez Convention Center
San Antonio, Texas
December 4-8, 2012

NCIC CTG Abstracts presented at the
54th ASH Annual Meeting and Exposition
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NCIC CTG Primary Publications
Journals
Abstracts
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Correlative Science / Tumour Bank

The NCIC Clinical Trials Group (NCIC CTG) established the Tumour Tissue Data Repository (TTDR) in 1997 to support Correlative Science with the assistance of Rhone Poulenc Rorer (now Sanofi-Aventis). The NCIC CTGTTDR contains unique disease specific collections which are linked to an associated clinical dataset. This represents a "real" tumour bank in that tissue is collected from institutions across Canada and the world, catalogued and housed centrally in the Department of Pathology and Molecular Medicine at Queen's University.

Our Mission
NCIC Clinical Trials Group - Tumour Bank
 Logged in as: Public
 Location: Home - Disease Sites

Disease Sites
BRAIN
BREAST
GASTRO-INTESTINAL
GENITO-URINARY
GYNECOLOGIC
HEAD AND NECK
HEMATOLOGIC
IND
LUNG
MELANOMA
SARCOMA
SYMPTOM CONTROL

Inventory
Show Tissue Samples
Show TMA Samples
Show Fluid Samples

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NCIC Clinical Trials Group - Tumour Bank
Logged in as: Public
Location: Home - Disease Sites

Disease Sites
BRAIN
BREAST
GASTRO-INTESTINAL
GENITO-URINARY
GYNECOLOGIC
HEAD AND NECK
HEMATOLOGIC
IND
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SARCOMA
SYMPTOM CONTROL

Inventory
Show Tissue Samples
Show TMA Samples
Show Fluid Samples

NCIC Clinical Trials Group - Tumour Bank
Logged in as: Public
Location: Home - Disease Sites - GYNECOLOGIC

GYNECOLOGIC Trials
CX4
EN5
EN7
GT1
OV10
OV11
OV16
OV18
OV19
OV21

Inventory
Show Tissue Samples
Show TMA Samples
Show Fluid Samples

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**OV16 Details**

**Status:** Closed  
**Activation Date:** 2001AUG31  
**Closing Date:** 2005JUN29  
**Phase:** III

**Description:** A Phase III Study of Cisplatin Plus Topotecan Followed by Paclitaxel plus Carboplatin versus Paclitaxel plus Carboplatin as First Line Chemotherapy in Women with Newly Diagnosed Advanced Epithelial Ovarian Cancer

**Eligibility:** Patients with confirmed epithelial ovarian (or primary fallopian or peritoneal) cancer, Stage IIB to IV, with microscopic or macroscopic residual disease who have not received prior chemotherapy and have evidence of adequate organ function.

**Objective:** Primary: to compare progression free survival. Secondary: to compare overall survival, response rates, toxic effects, quality of life, and CA 125 normalization rates.

**Participation:** Not limited

**Lay Description:** The main purpose of this research study is to find out if first line treatment with four cycles of cisplatin combined with topotecan followed by another four cycles of paclitaxel combined with carboplatin will cause the tumour to shrink at least as well as, if not better than, standard treatment of paclitaxel combined with carboplatin given for eight cycles.

**Publications**  
[Show]

**Inventory**  

[Hide] Tissue Samples

<table>
<thead>
<tr>
<th>Disease Site</th>
<th>Trial Code</th>
<th>Patients Accrued</th>
<th>Patients - Blocks</th>
<th>Patients - Slides</th>
<th>Patients - Blocks and/or Slides</th>
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<tbody>
<tr>
<td>GYNECOLOGIC</td>
<td>OV16</td>
<td>819</td>
<td>315</td>
<td>325</td>
<td>364</td>
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[Hide] TMA Samples  
(Core size is 0.6 mm)

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<tr>
<th>Disease Site</th>
<th>Trial Code</th>
<th>Patients Accrued</th>
<th>TMA Blocks</th>
<th>Patients on TMA Blocks</th>
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<tbody>
<tr>
<td>GYNECOLOGIC</td>
<td>OV16</td>
<td>819</td>
<td>7</td>
<td>248</td>
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</table>

[Hide] Fluid Samples

<table>
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<tr>
<th>Disease Site</th>
<th>Trial Code</th>
<th>Patients Accrued</th>
<th>Patients - Whole Blood</th>
<th>Patients - Cellular Component of Blood</th>
<th>Patients - DNA extracted from Blood</th>
<th>Patients - RNA extracted from Blood</th>
<th>Patients - Plasma</th>
<th>Patients - Serum</th>
<th>Patients - Urine</th>
<th>Patients - Buccal</th>
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<td>GYNECOLOGIC</td>
<td>OV16</td>
<td>819</td>
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Process

- Draft brief protocol
  - Study question
  - Rationale
  - Data required to answer
  - Proposed methods
- Revise with central office input
- Obtain appropriate approval
- Follow processes
Potential Challenges

Question is not appropriate for CTG databases

– Data not collected
– Data not available in appropriate format
– Timing of analysis not appropriate
Potential Challenges

Question is not appropriate for CTG databases

- Data not collected
- Data not available in appropriate format
- Timing of analysis not appropriate

Resources

- Personnel
- Funding
Potential Challenges

Approval processes required
- Trial team, study chair, disease site committee
- REBs (Queen’s and host institution)
- Pharma