NCIC CTG Overview
Structure and Opportunities

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NCIC CTG

NCIC Clinical Trials Group
NCIC Groupe des essais cliniques

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

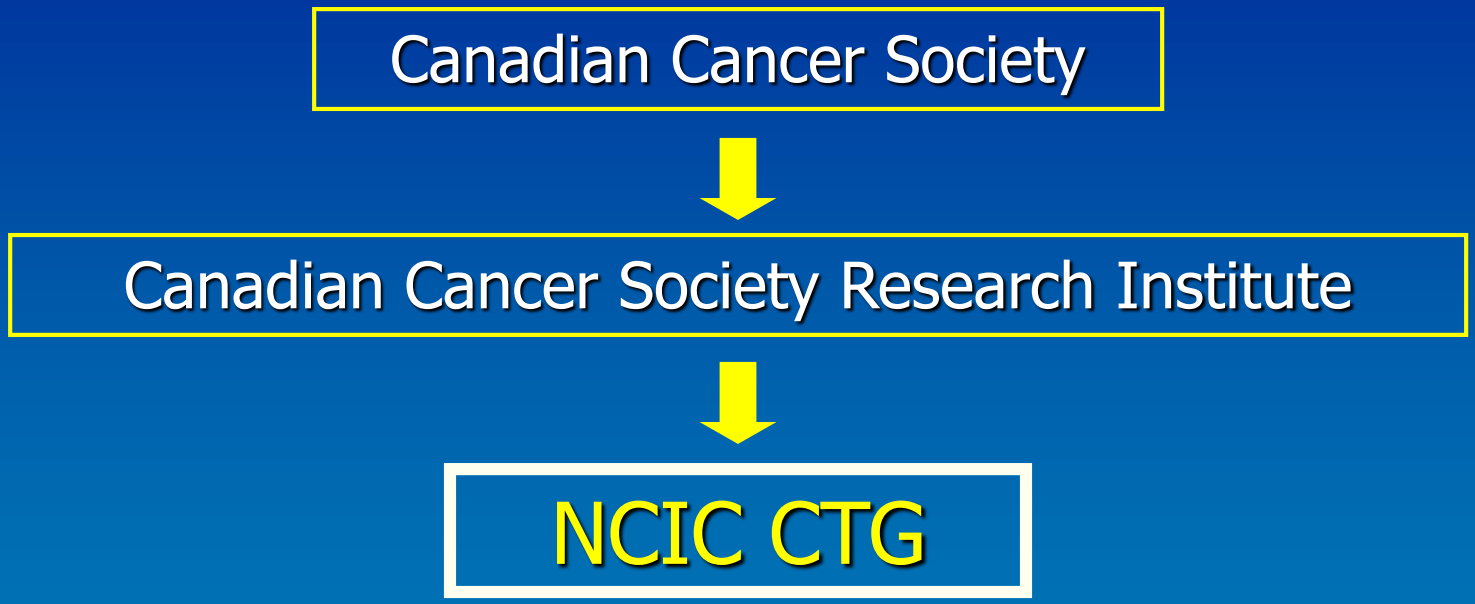
Funding

CCSRI

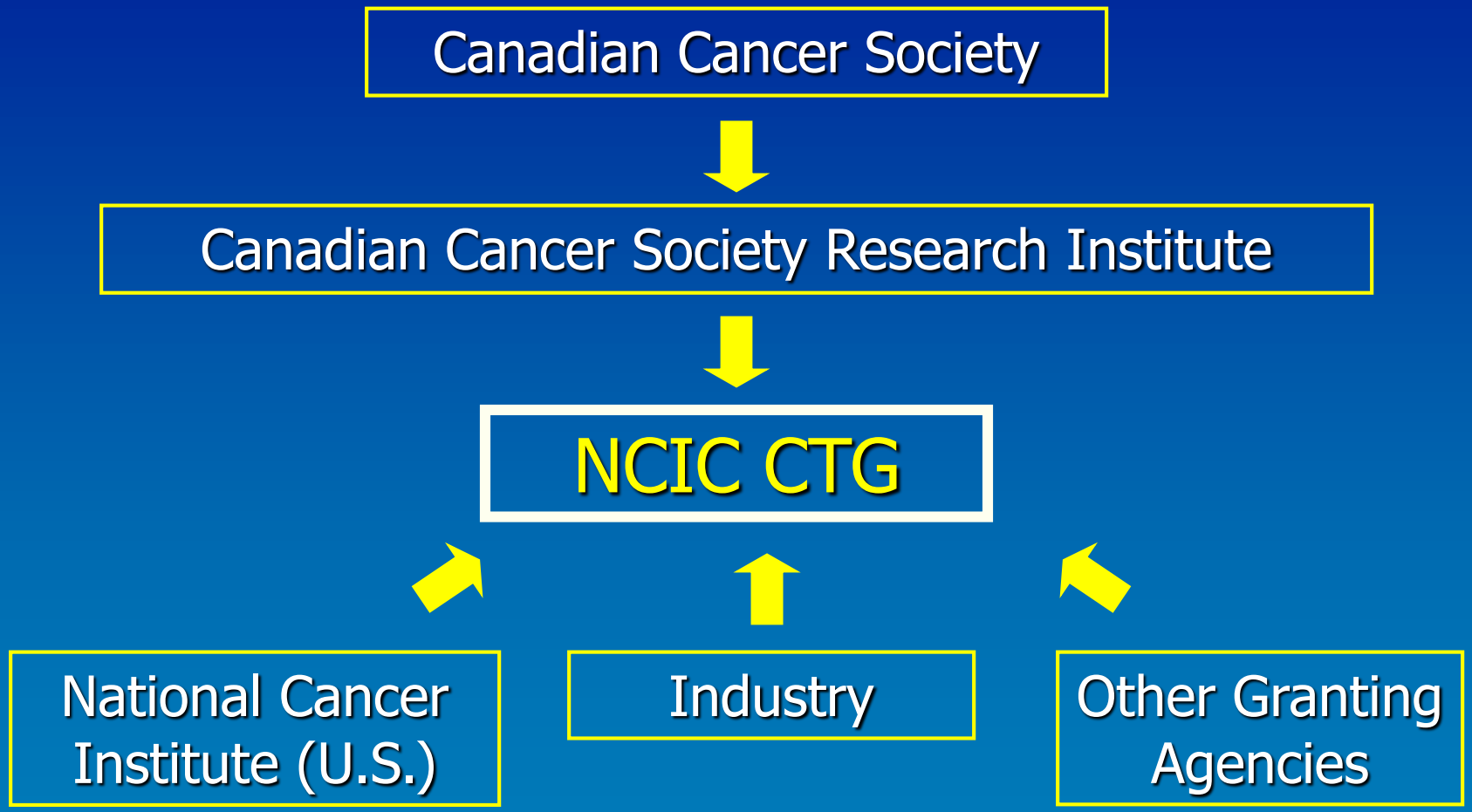
- **Funds:** Impact grants
  Innovation grants
  Prevention grants
  other
- **Funds two national networks / programs**
  ARCC
  NCIC CTG

Funding

Funding


Canadian Cancer Society
Canadian Cancer Society Research Institute
NCIC CTG

Funding


Canadian Cancer Society
Canadian Cancer Society Research Institute
NCIC CTG
National Cancer Institute (U.S.)
Industry
Other Granting Agencies

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

Structure

NCIC CTG

Can be considered in two major categories:

External

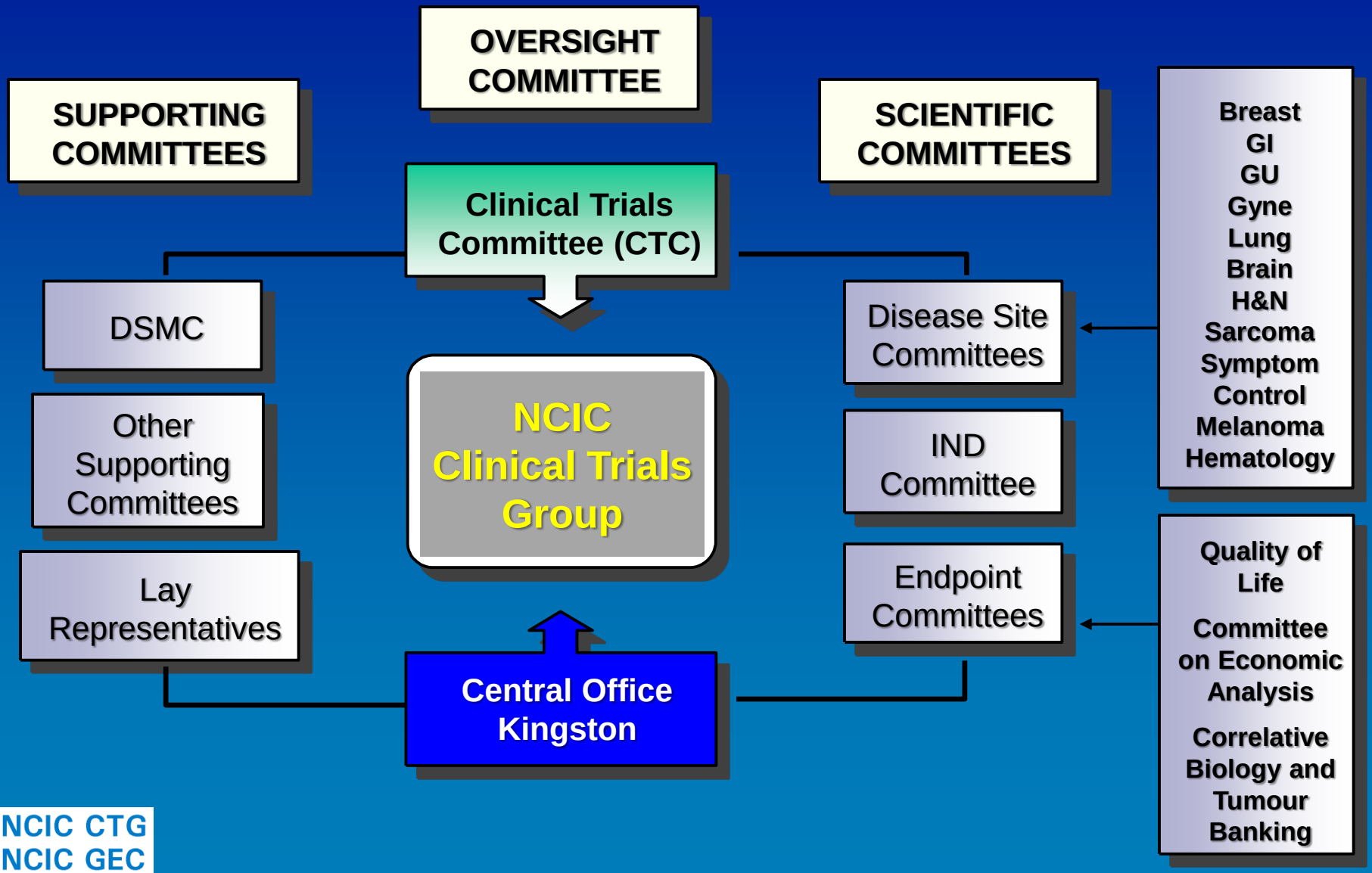
- Network of ~ 80 Canadian investigative sites
- Committee structures involving nearly 1000 investigators and other research personnel

Internal

- Head office in Kingston - 110 staff, 12 faculty

External Organization

External Structure



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

External Organization

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

Internal Structure

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

External Structure

Phase III Program

Scope:

- Randomized controlled trials
- Selected phase II studies (enablers)

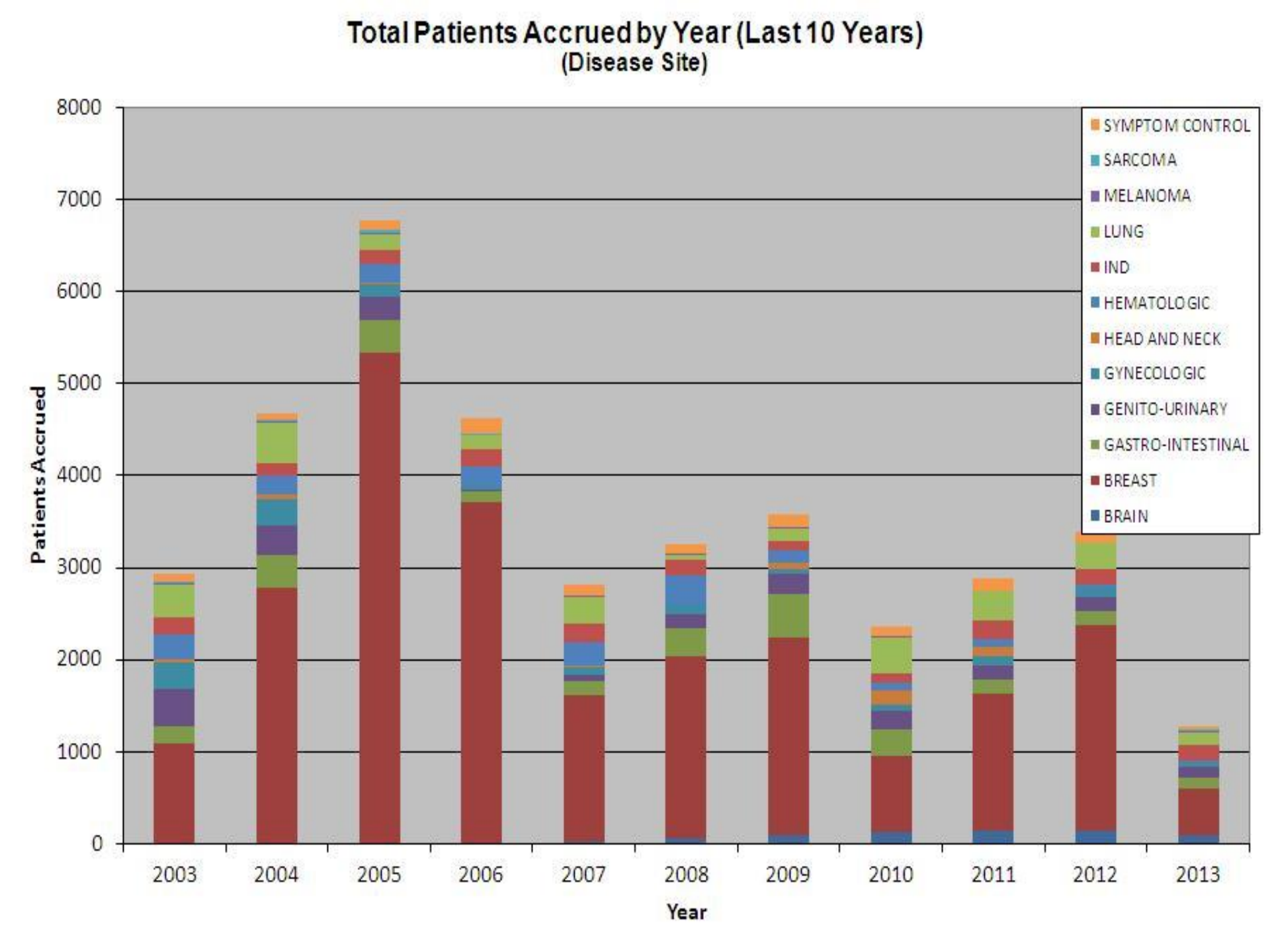
Broad Accomplishments

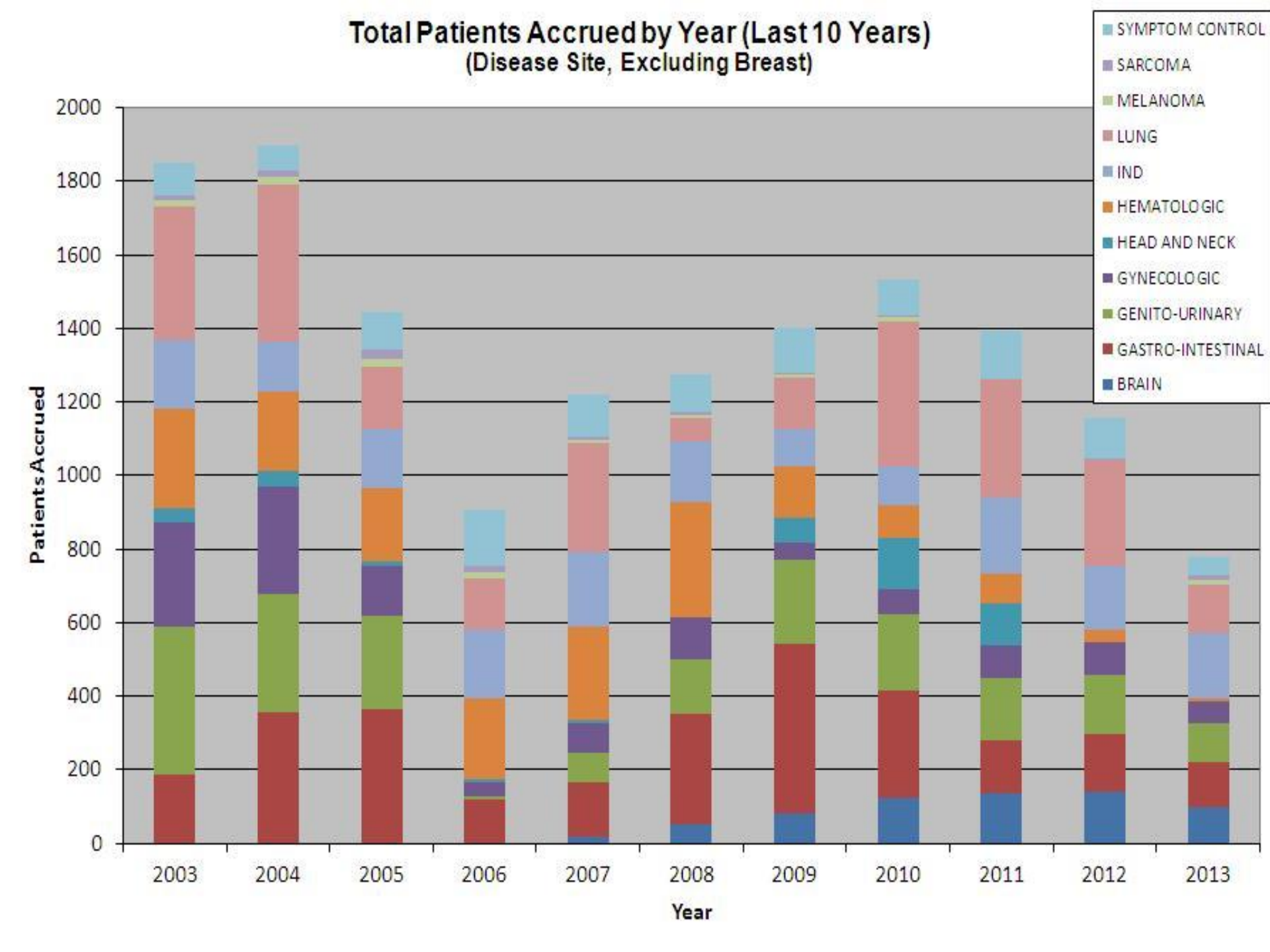
1980 – August 2013:

- 481 trials
- 75,600 patients

In 2004-2010 grant cycle:

- 200 trials were in some form of conduct
- 23,000 new patients were accrued


Total Patients Accrued by Year (Last 10 Years)
(Disease Site)
8000
7000
6000
5000
4000
3000
2000
1000
0
Patients Accrued
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Year
SYMPTOM CONTROL
SARCOMA
MELANOMA
LUNG
IND
HEMATOLOGIC
HEAD AND NECK
GYNECOLOGIC
GENITO-URINARY
GASTRO-INTESTINAL
BREAST
BRAIN


Total Patients Accrued by Year (Last 10 Years)
(Disease Site, Excluding Breast)
SYMPTOM CONTROL
SARCOMA
MELANOMA
LUNG
IND
HEMATOLOGIC
HEAD AND NECK
GYNECOLOGIC
GENITO-URINARY
GASTRO-INTESTINAL
BRAIN
Patients Accrued
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Year

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)

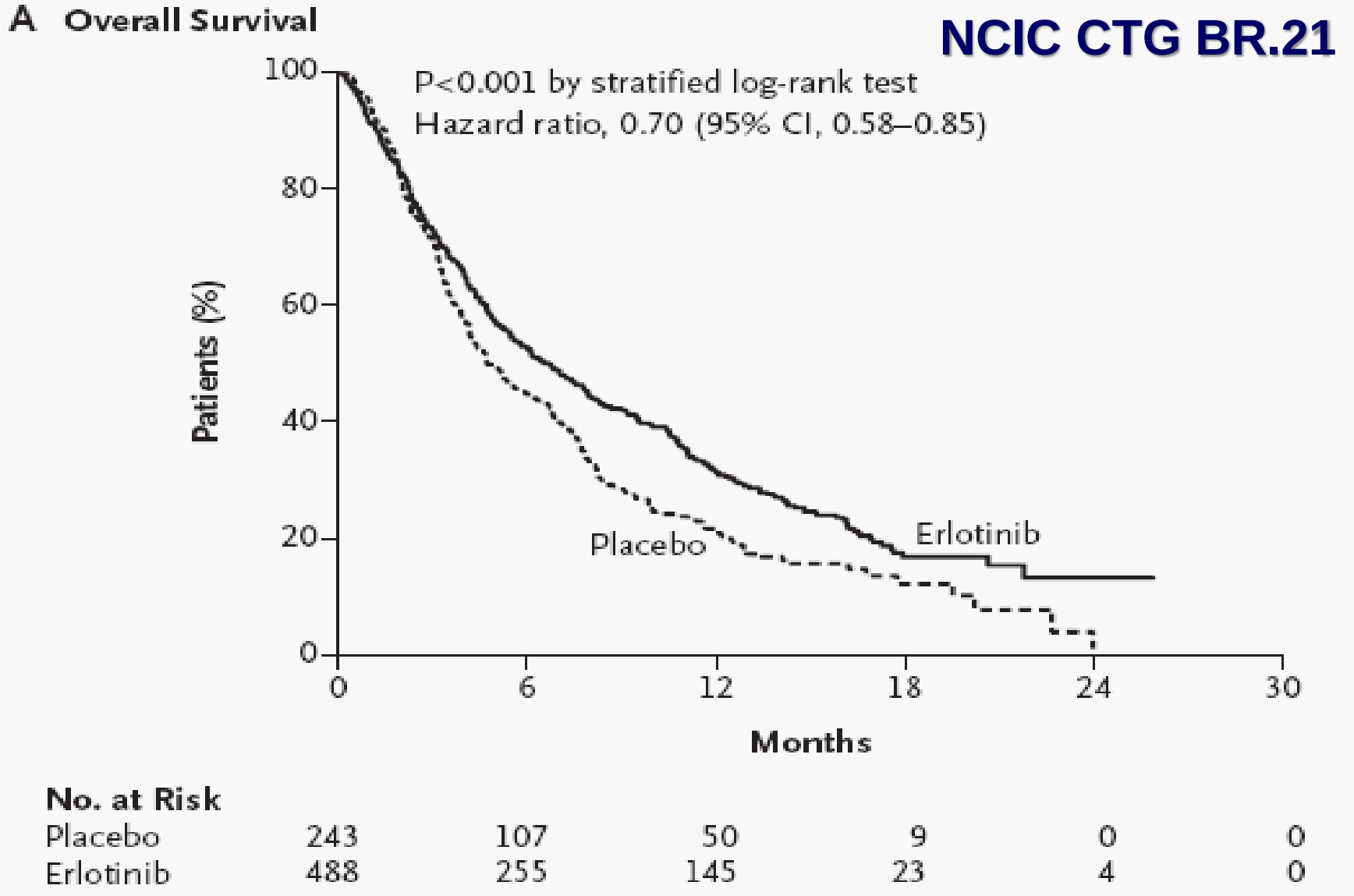
Changes to Canadian Health Care Practices

- 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)

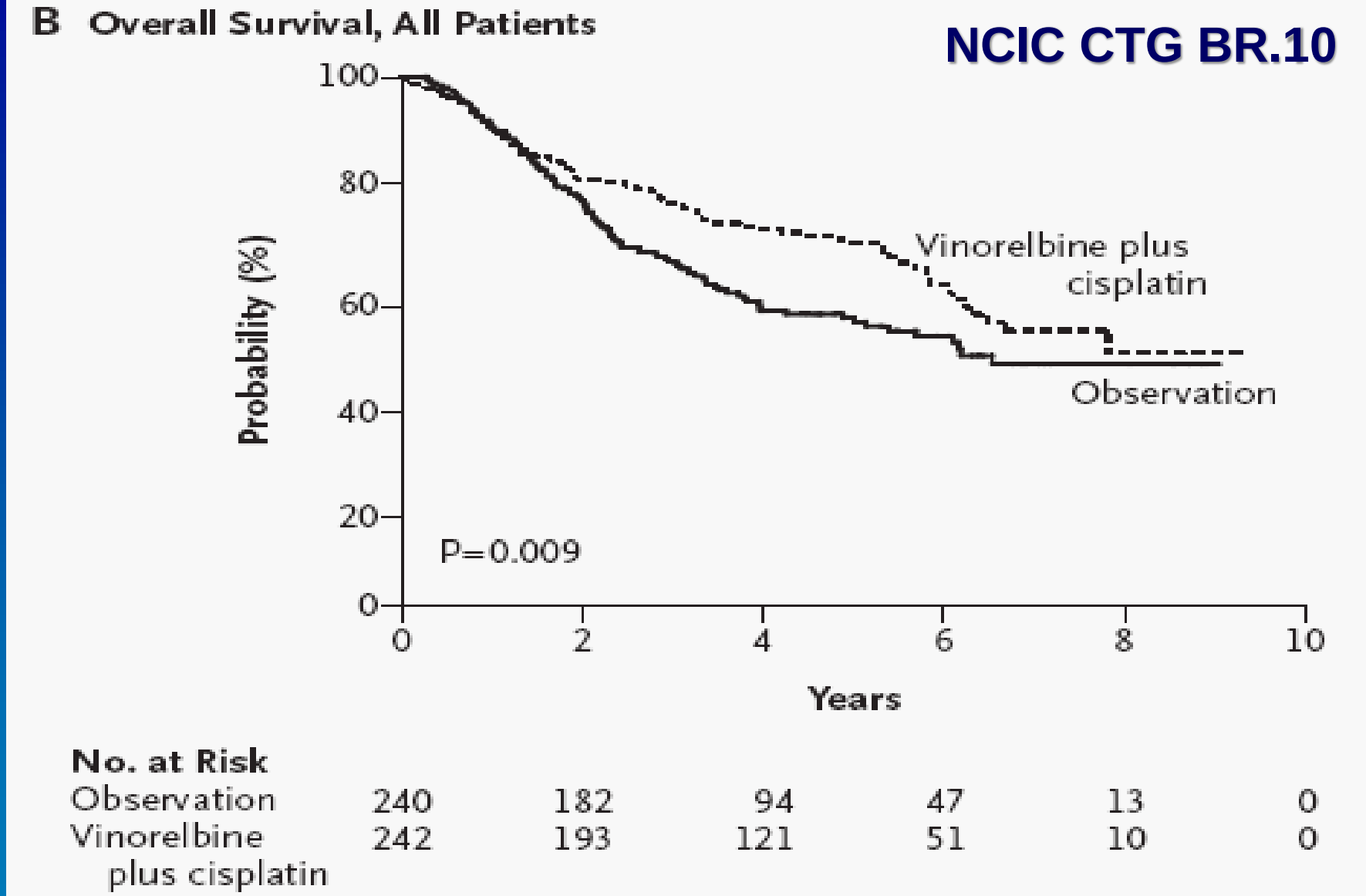
Changes to Canadian Health Care Practices

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

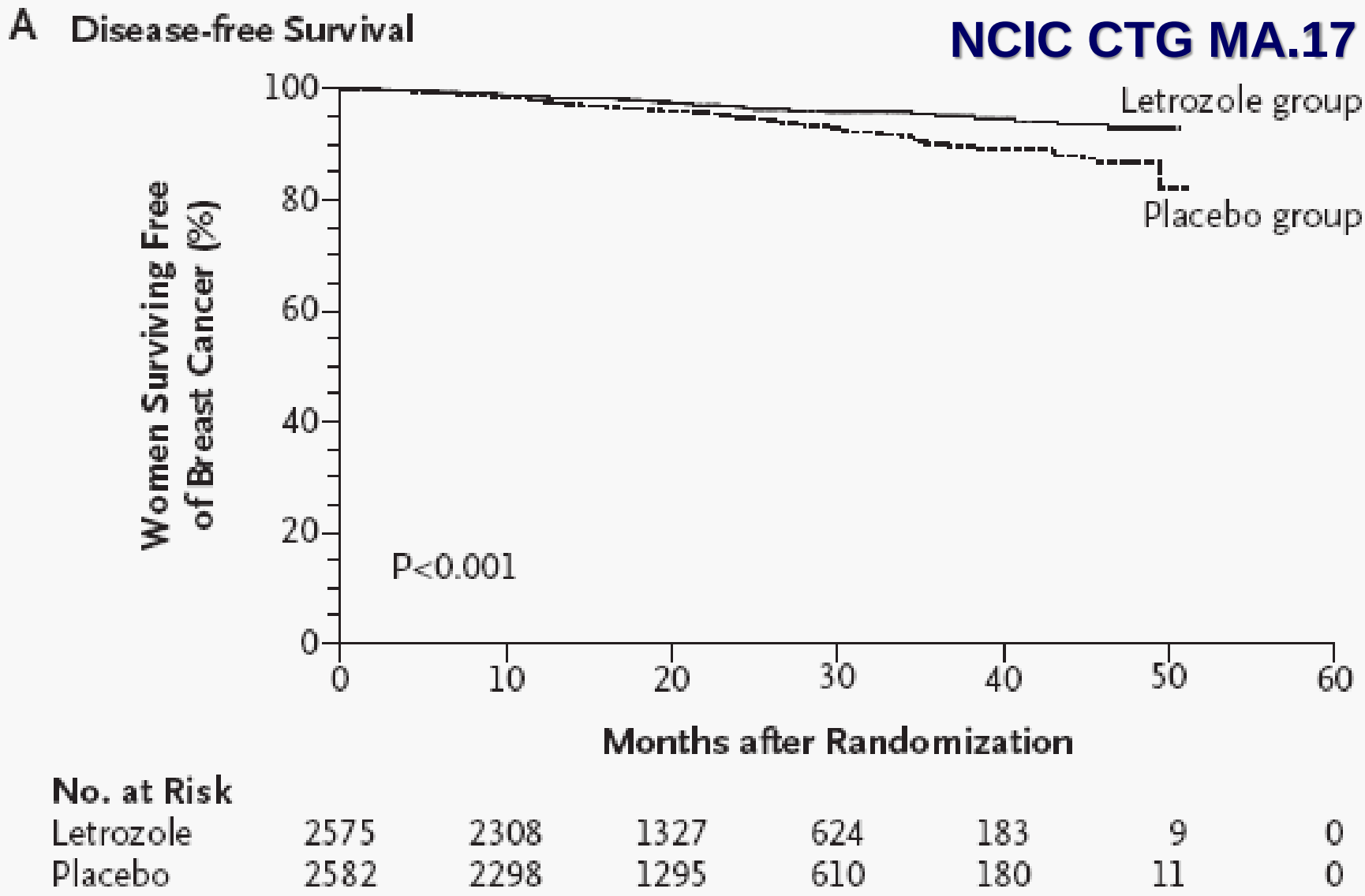
NCIC CTG BR.21



NCIC CTG BR.10

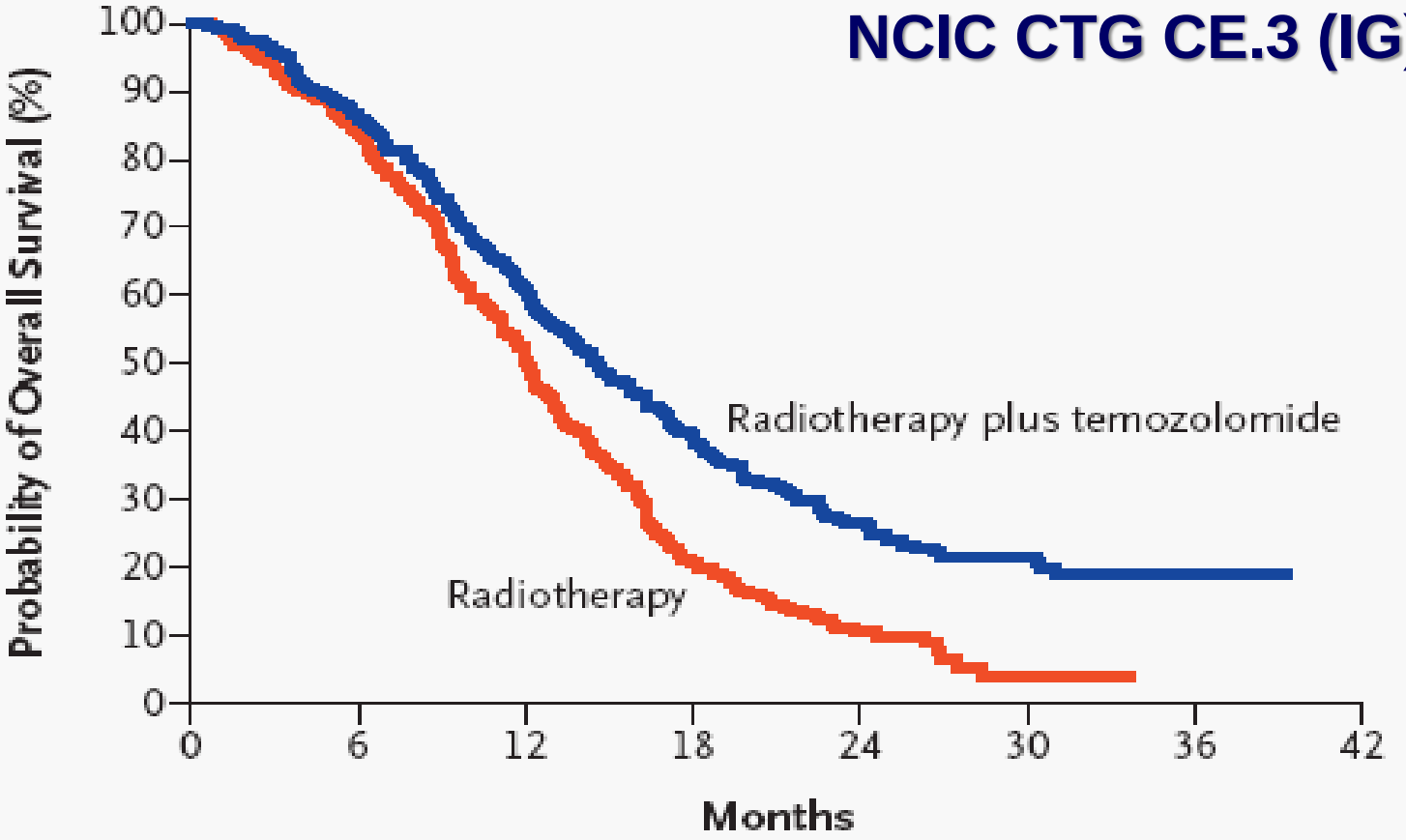


NCIC CTG MA.17



No. at Risk							
Letrozole	2575	2308	1327	624	183	9	0
Placebo	2582	2298	1295	610	180	11	0

NCIC CTG CE.3 (IG)



No. at Risk							
Radiotherapy	286	240	144	59	23	2	0
Radiotherapy plus temozolomide	287	246	174	109	57	27	4

NCIC CTG CO.17

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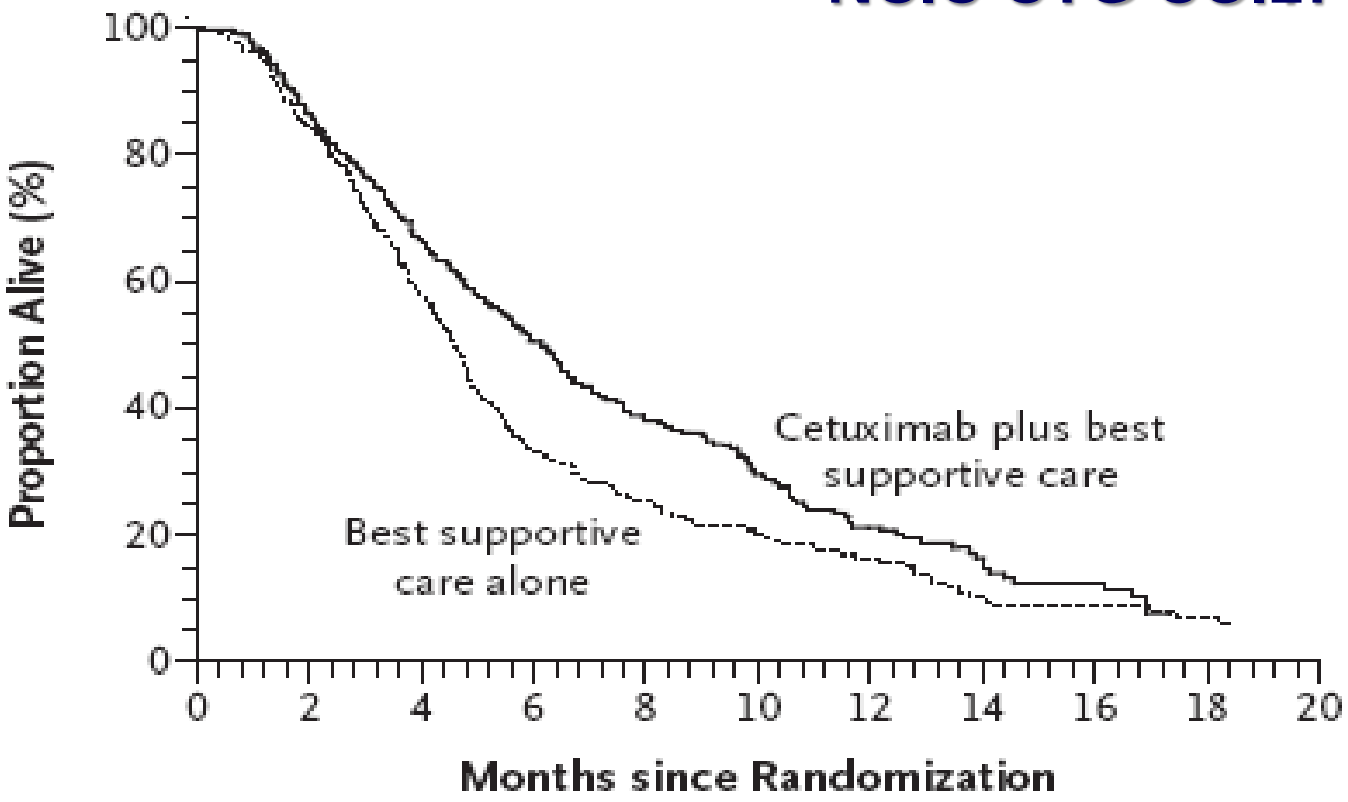
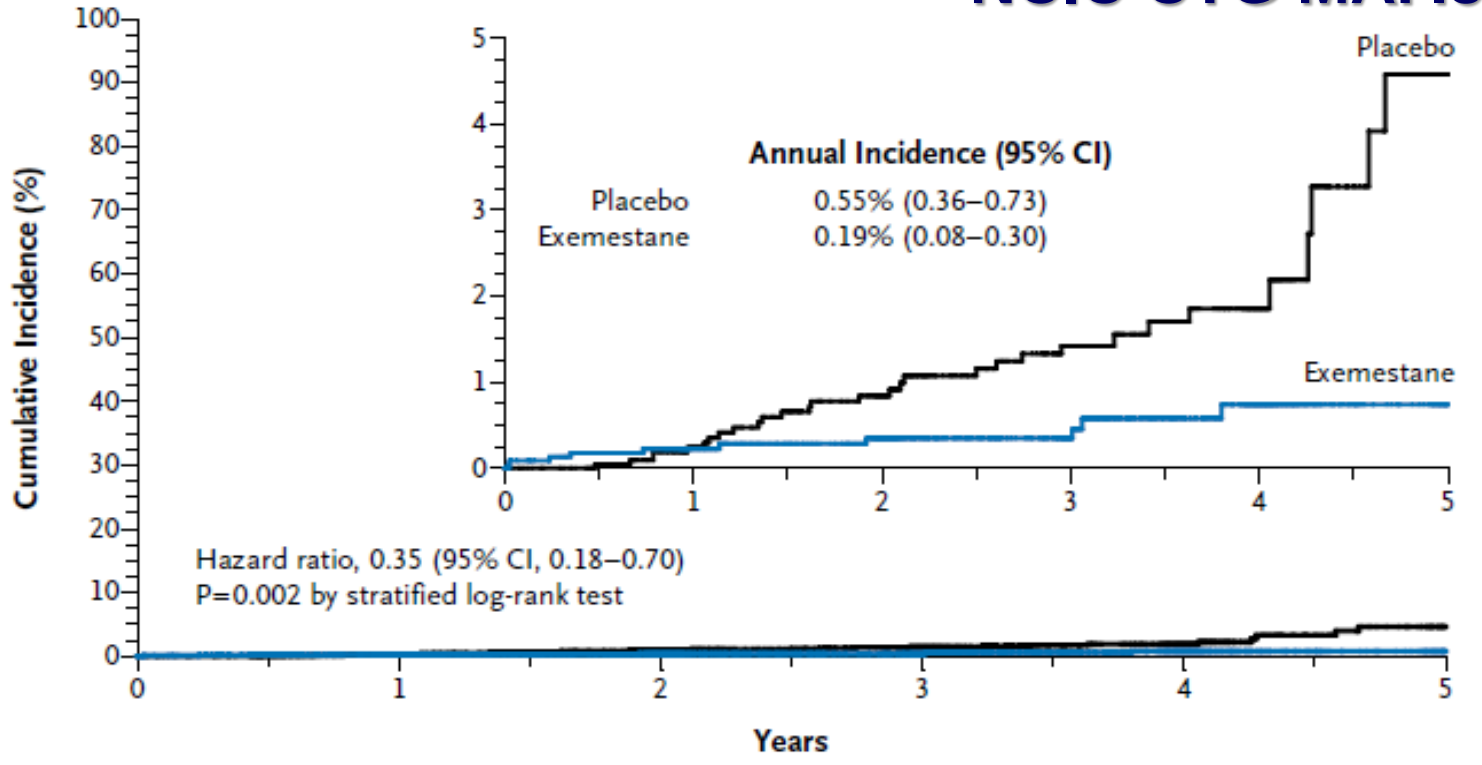


No. at Risk

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

NCIC CTG MAP.3



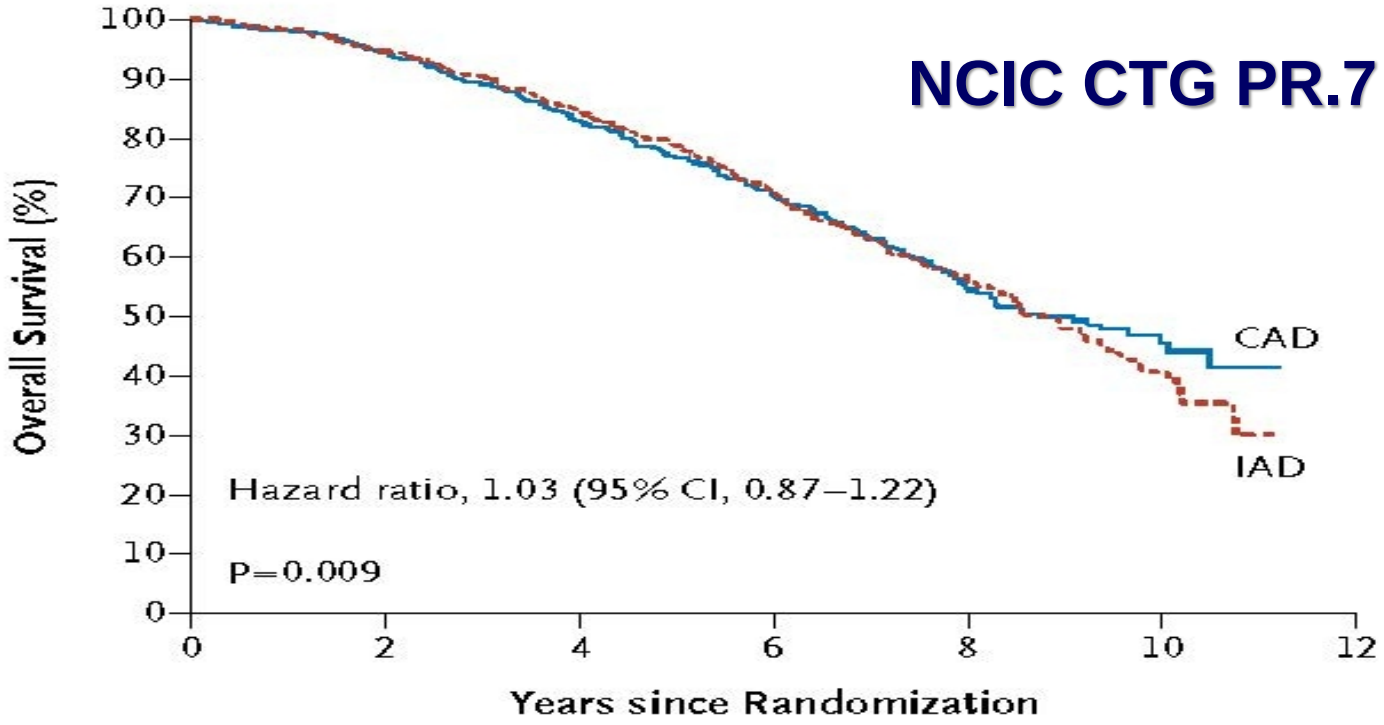
No. at Risk

Placebo	2275	1905	1468	986	477	82
Exemestane	2285	1902	1468	980	464	77

Figure 1. Cumulative Incidence of Invasive Breast Cancer.

CI denotes confidence interval.

NCIC CTG PR.7



No. at Risk							
CAD	696	652	561	319	125	35	0
IAD	690	651	571	327	140	34	0

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, 0.86 to 1.23). 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.