Improved Cancer Outcomes -- But Miles to Go Before We Sleep

Personal Reflections on 35 Years of Cancer Research

Elizabeth Eisenhauer OC MD FRCPC FRSC

Oncology Grand Rounds

September 2019

Disclosures/Conflicts of Interest

- During the past 5 years – none
- Prior to that - numerous clinical trials were supported at least in part by pharmaceutical firms but I received no personal payment for this research - and the data and results were analysed independently

Objectives

1. Understand the history of new cancer drug investigation in Canada via the NCIC CTG (now CCTG) Investigational New Drug Program
2. Learn some stories of success, and unexpected failures
3. Understand my personal evolution to believe that medical oncology must grow beyond a specialty focused on cancer treatment to influence Cancer Control more broadly

Outline – and along the way some personal lessons

- 1982 – when I started my first faculty position - the way we were
- A brief history of cancer and treatment to 1982
- 1980s – a time of change in Cancer Research
- Growing knowledge in Cancer Biology – new rationally designed treatments emerge
- Treatment is not enough
- All the lessons learned and moving forward

Then (1982)

THE NEW ENGLAND JOURNAL OF MEDICINE April 1, 1982

ALTERNATING DRUG COMBINATIONS IN THE TREATMENT OF ADVANCED HODGKIN'S DISEASE

ARMANDO SANTORO, M.D., GIANNI BONADONNA, M.D., VALERIA BONFANTE, M.D., AND PINUCCIA VALAGUSSA, B.S.

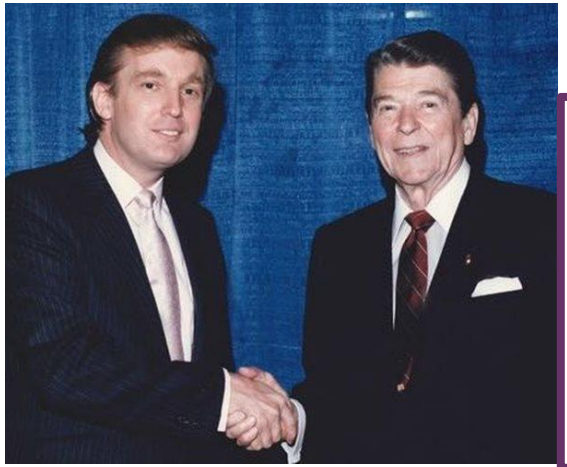
THE YALE JOURNAL OF BIOLOGY AND MEDICINE 55 (1982), 443-452

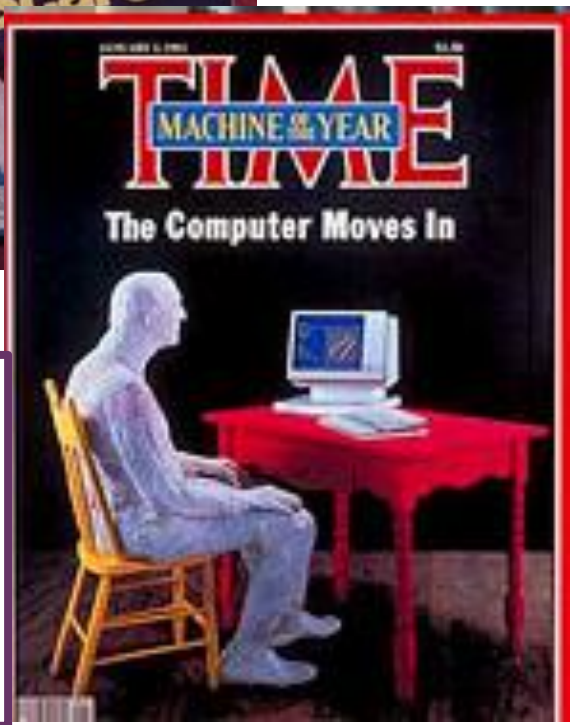
The Acquired Immunodeficiency Syndrome: Current Status

VINCENT QUAGLIARELLO, M.D.

Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut

Received November 18, 1982





Cancer Treat Rep. 1979 Nov-Dec;63(11-12):1727-33.

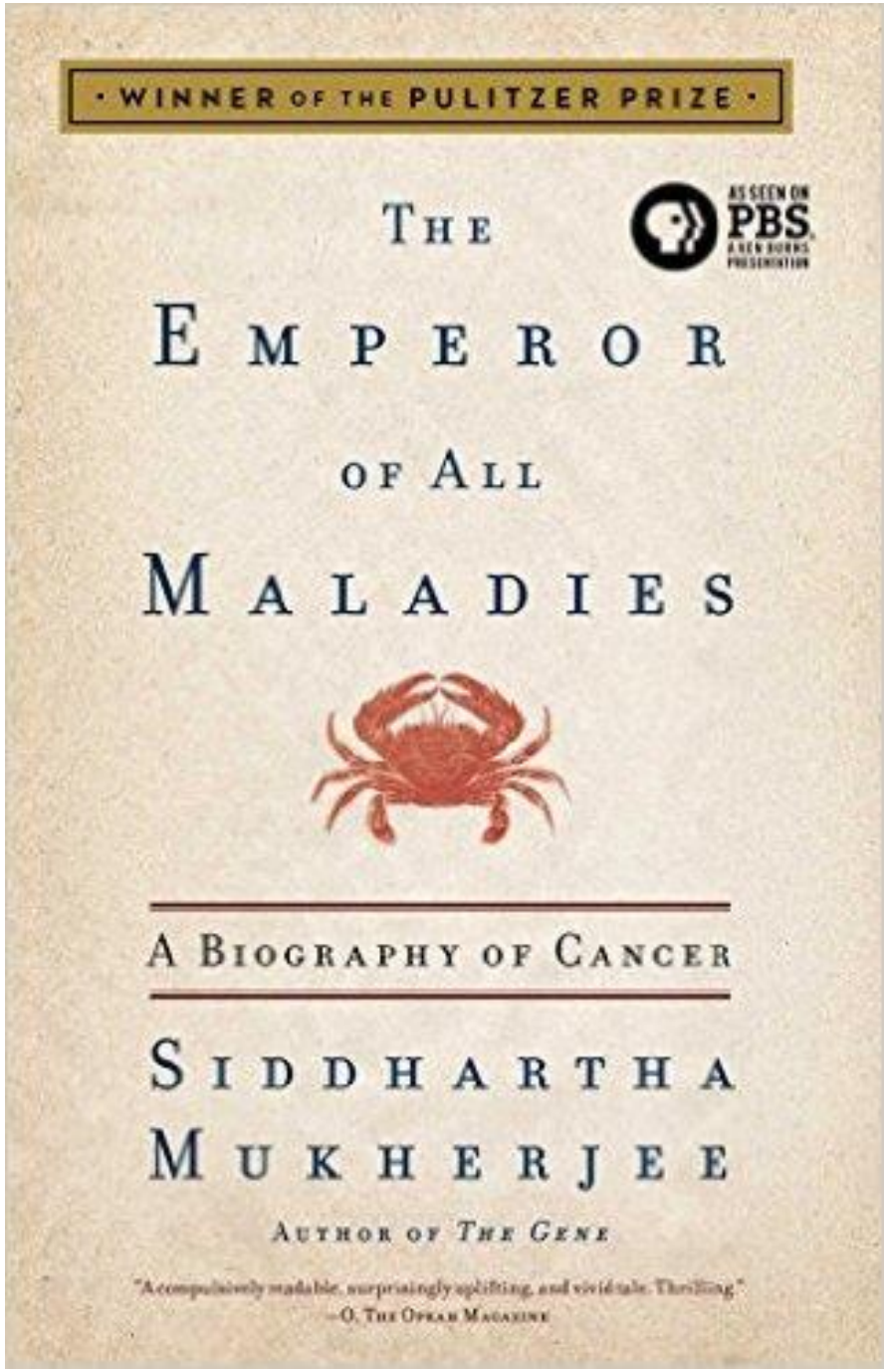
A mathematic model for relating the drug sensitivity of tumors to their spontaneous mutation rate.

Goldie JH, Coldman AJ.

Then - at home….
(1982)

In the beginning …..

- Cancer has been documented in humans for millennia
- One of first documented cases of breast cancer, Persian Queen Atossa "….daughter of Cyrus and wife of Dareios had a tumour upon her breast, which afterwards burst and then was spreading further…":



Early Treatments of Cancer

- Limited benefits from any sort of treatment until late 19th /early 20th century:
  - Surgery was enabled by anesthesia and sterilisation
  - Radiation was discovered – but not used therapeutically until mid-20th century
- Many cancers had metastasized at time of or shortly after surgery and with no effective treatment available most died within months-years.
- ***1947:*** ***The National Cancer Institute of Canada (NCIC) was established by the Canadian Cancer Society.***
  NCIC was a non-governmental charitable organization.
  5-year survival rates for all cancers was then 33%

Cancer Treatment 1940s to 1980s

- Therapeutic radiation became possible with better understanding of physics, radiation dosing and safety.
- New imaging technologies (CT scanners) made it possible to stage cancers and thus plan treatment (surgery/radiation)
- First “Chemotherapy” drugs had been discovered, many through the US National Cancer Institute Screening program
  - Nitrogen Mustard (alkylating agents) derivatives
  - Plant alkaloids: e.g. vincristine (from Madagascar periwinkle)
  - Anti-tumour antibiotics

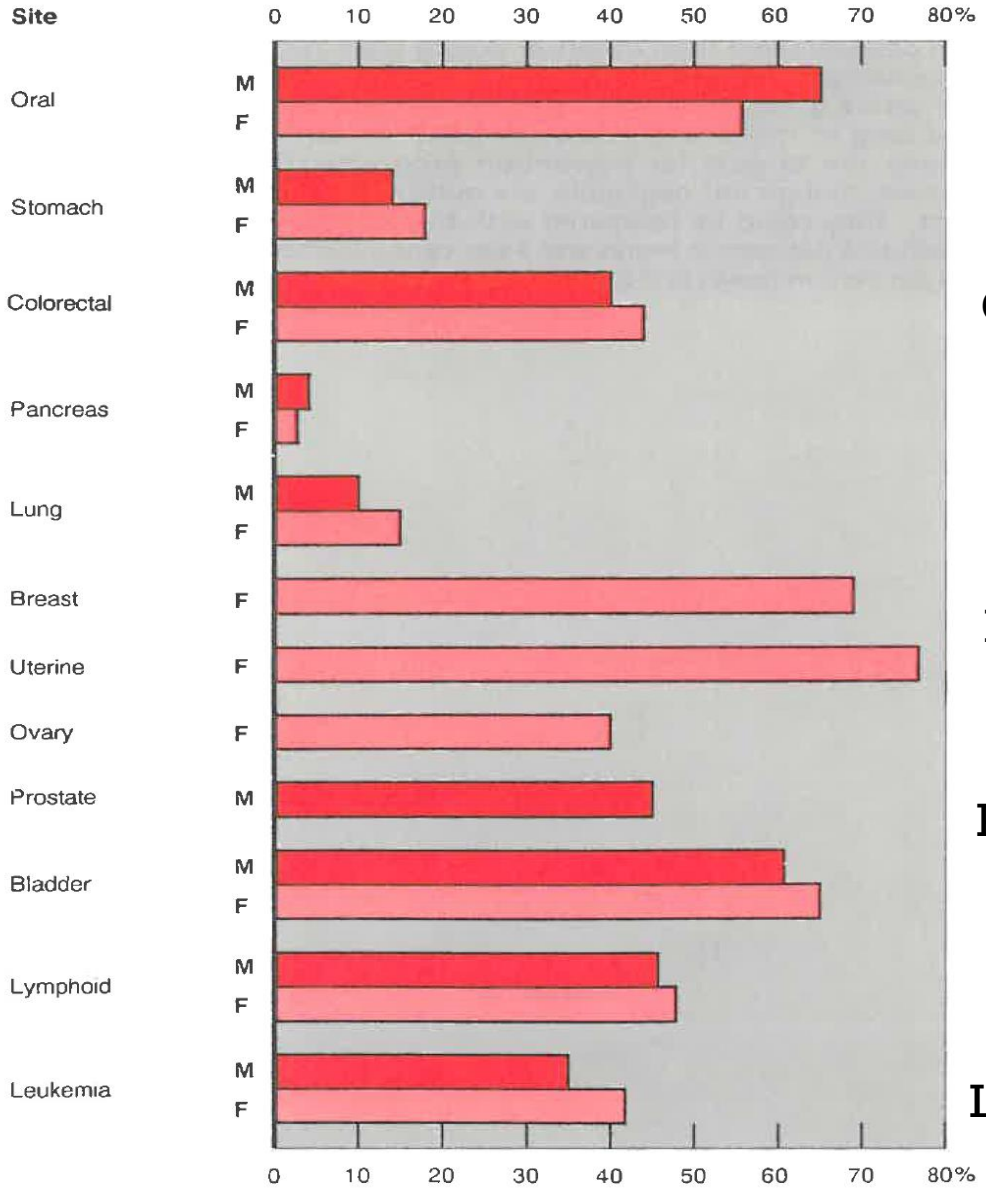
Madagascar periwinkle

By 1987

(earliest year of online data!)

5-year Net Survival

Figure 5
Five Year Cancer Survival Rates for Selected Sites by Sex – Cases Diagnosed, 1974-1978



Colon ~45%

Lung ~15%

Breast ~70%

Prostate ~48%

Leukemia ~40%

The 1980s – Cancer Biology and Clinical Trials

Big changes in cancer research afoot:

- In the laboratory:
  New technologies, techniques and cancer models began to unmask the fundamental biological changes in cancer cells that foreshadowed new avenues for treatment 2 decades later
- In the clinic:
  Canada, and many other nations, created ***cancer clinical trials cooperative groups or "networks"*** that could conduct academic driven research studies to accelerate the pace of development of new, effective cancer treatments.

NCIC CTG – now the CCTG

- 1980 - National Cancer Institute of Canada (NCIC) founded a clinical trials group (the “NCIC CTG”) to coordinate/ conduct multicenter cooperative clinical trials to improve cancer outcomes.
- The first Director of the NCIC CTG was Dr. Joseph Pater – an oncologist /scientist at Queen’s University
- 1982 - I joined NCIC CTG as the inaugural Director of the Investigational New Drug Program

Mission of the NCIC CTG

- To develop and conduct clinical trials aimed at improving the treatment (and prevention) of cancer with the goal of ***reducing morbidity and mortality from cancer.***

- To do this:
  - ***Scientific/Clinical leaders*** came together to develop to generate the research questions
  - ***A national network of cancer centres and hospitals*** (where these leaders were based) which carried out the research
  - ***Central statistical office*** to coordinate, develop, and report on the research results (at Queen's University)

In 2016, the NCIC CTG was renamed: ***The Canadian Cancer Trials Group***

IND Program – its beginnings

- In 1970s-80s –MOST new cancer drugs were identified and developed by the **US National Cancer Institute** drug discovery and cancer therapy evaluation programs (*Pharma didn't see cancer as a good area to invest in!)*
- Canadian investigators (and patients) wanted opportunity to be part of early phase trials – awarded based on letters of intent to US NCI
- 1981 - NCIC CTG established an Investigational New Drug Committee chaired by **Dr. Brian Weinerman** . They soon realized an in-house MD would be needed to help identify new drugs in US NCI pipeline so we could be more competitive in getting new drugs for study in Canada.
- **In 1982 – Investigational New Drug Program founded …**

My Qualifications at that time to Lead National Investigational Cancer Treatment Program?

- I had completed training in Hematology specialty program
- I was once enrolled as a *subject* on a clinical trial (a longer story…)
- I played violin in orchestra so knew a bit about team work

- But pretty much nothing else in terms of training except I was keen and wanted to do clinical trials
- *On the other hand – at that time in Canada few had any experience and training in this area*

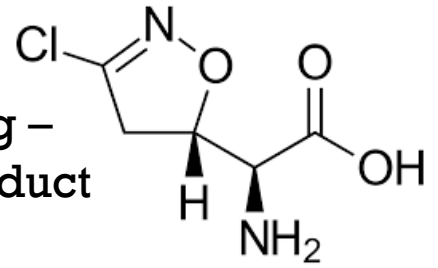
LESSON 1: Expanding your horizons to do things in which you do not (yet) have expertise can lead you to interesting places!

IND Program – Early Years

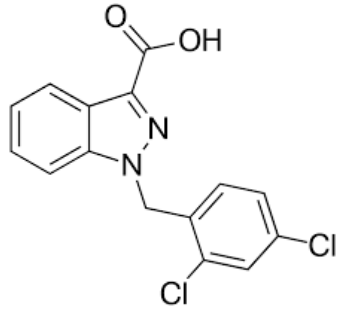
- IND program began by focusing on **phase II studies**
- Despite discovery of the first oncogenes in cancer in 1970s and what that would mean for future research – MOST new drugs were cytotoxic agents coming from huge screening platforms at US NCI and /or through analog development
- A few “lemons” in first years of program …. But then some exciting results

ID Sort	Study Title
I1C	NCIC CTG Phase II Study of Acivicin (AT125) in Colorectal Cancer + Read More
I2L	NCIC CTG Phase II Study of Acivicin (AT125) in Patients With Metastatic Non-Small Cell Lung + Read More
I3	NCIC CTG Phase II Study of Spirogermanium in Poor Prognosis Non-Hodgkin's Lymphoma + Read More
I4	NCIC CTG Phase II Study of Lonidamine in Hypernephroma + Read More
I4B	NCIC CTG Phase II Study of Lonidamine in Breast Cancer + Read More
I5	NCIC CTG Phase II Study of Spirogermanium in Melanoma + Read More

Acivicin
Glutamine analog – fermentation product



Spirogermanium



Lonidamine

inhibits aerobic glycolysis in cancer cells.

I12 NCIC CTG Phase II Study of CBDCA in Ovary

+ Read More

I13 NCIC CTG Phase II Study of N-methylformamide in Glioma

+ Read More

I14 NCIC CTG Phase II Study of N-methylformamide in Melanoma

+ Read More

I20 NCIC CTG Phase II Study of Menogaril in Lymphoma

+ Read More

I21 NCIC CTG Phase II Study of Menogaril in Melanoma

+ Read More

I22 NCIC CTG Phase II Study of Deoxycoformycin in Hairy Cell

+ Read More

IND.12

Cancer Treat Rep. 1986 Oct;70(10):1195-8

One of first studies of Carboplatin in recurrent OVCA

28% RR – lower dose recommended for future studies

IND.22

J Natl Cancer Inst. 1988 Jul 20;80(10):765-9.

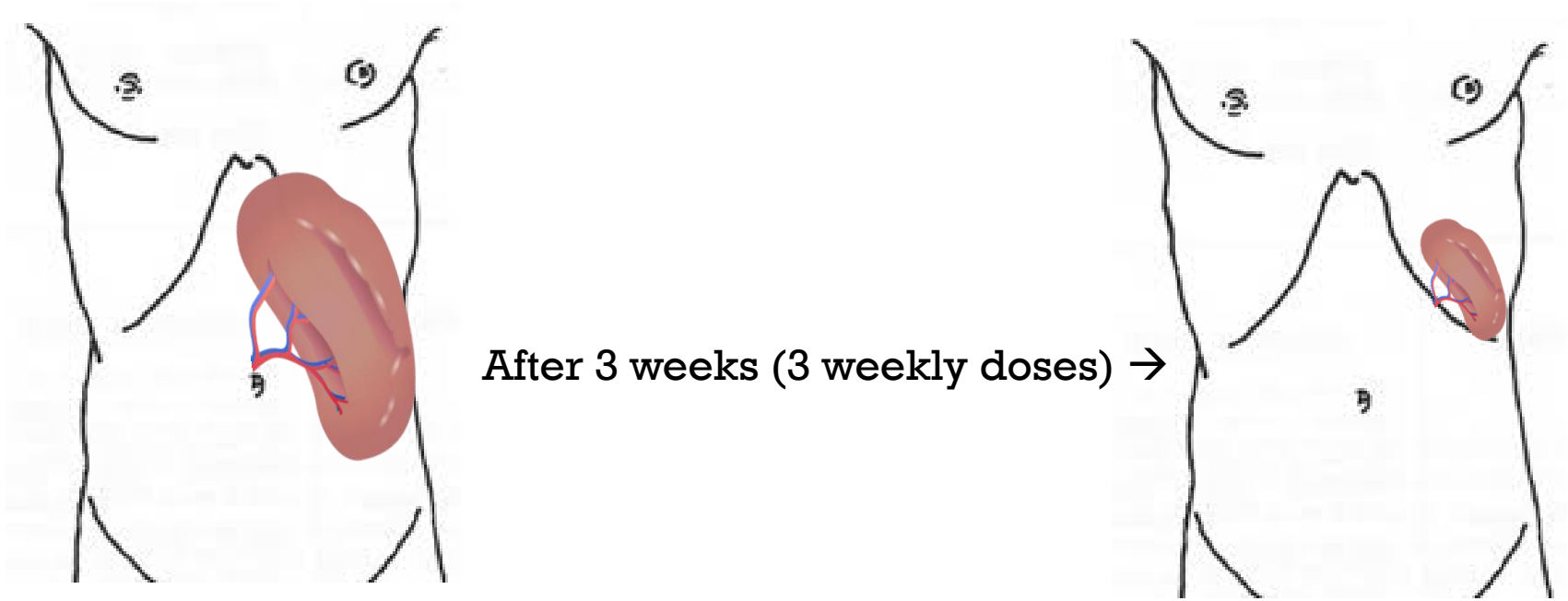
First study of DCF in Hairy Cell Leukemia. Based on lab work by Dr. James Johnston, Winnipeg.

RR 100% (89% CR)

DCF later compared to IFN in intergroup trial. DCF eventually replaced by cladribine for 1st line

Participating in IND.22

- First patient enrolled was KK-01 – by E Eisenhauer (!!)
- Massive spleen filling LUQ and below umbilicus



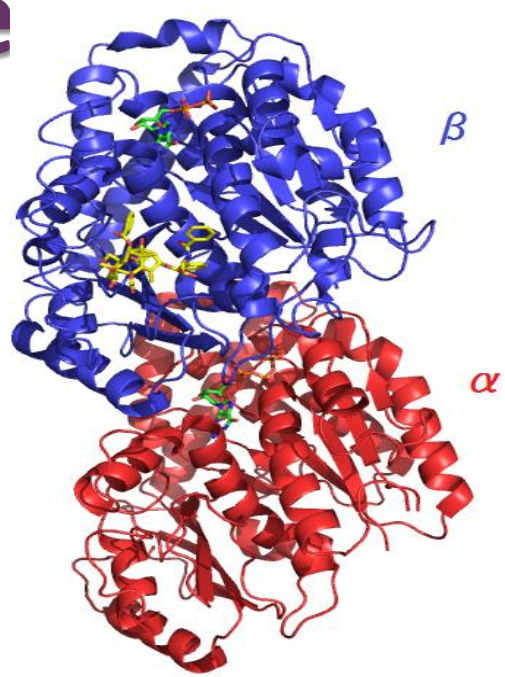
LESSON 2: There is nothing more exciting than participating in research that has a dramatic impact on a patient's life

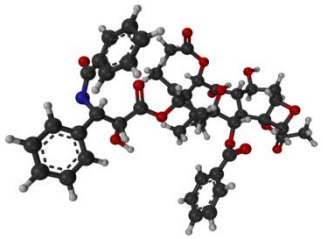
Speaking of Patients

- By late 1980s, my "limited" clinical practice included breast cancer, chronic leukemias, melanoma and sarcoma
- One day in clinic, a woman undergoing adjuvant breast cancer Rx told me she was having trouble with short term memory and asked if it could be her chemotherapy. My response: *"I've never heard of chemotherapy doing that so it much be something else…."*.
- A few weeks later at the 1987 OCTRF Couchiching Conference, work of Dr. Peter Maguire from UK was presented – some of first work showing cognitive effects of chemotherapy (later dubbed chemo-brain).

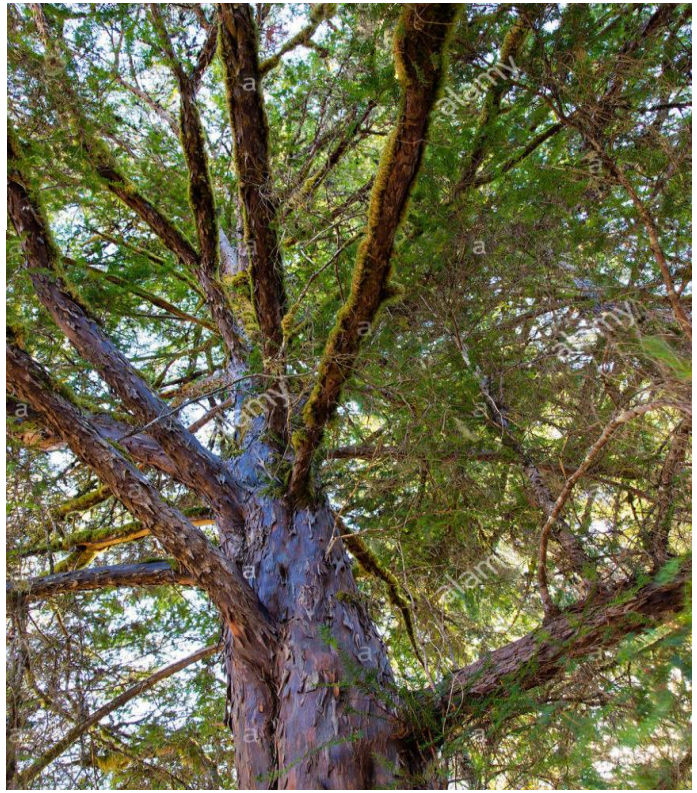
LESSON 3. Listen to what patients say. They ALWAYS teach you new things. This opened my mind to experiential aspects of cancer.

1990s - Taxane decade





- Taxol (later: paclitaxel; Taxol), an extract from bark of western yew – found active in NCI Screens in 1960s—but only of interest when “novel” mechanism (stabilization of microtubules) identified by Susan Horwitz in 1970s.
- Clinical trials 1980s - cardiac, hypersensitivities – but responses in ovarian cancer
- This led to OV.9 - my first foray into ovarian cancer trials



OV.9 – CCTG-led International randomized trial of 2 doses and schedules of paclitaxel in relapsed OVCA

- SHORTER infusion (3 hr vs 24 hr) was safer and effective – and outcomes better with HIGHER dose (175 vs 135 mg/m2)
- This not only changed practice but also was first CCTG trial of international collaboration in OVCA. ***It led to OV.10 frontline trial ….and to creation of Gynecologic Cancer Intergroup (GCIG).*** CCTG was a founding member

European-Canadian Randomized Trial of Paclitaxel in Relapsed Ovarian Cancer: High-Dose Versus Low-Dose and Long Versus Short Infusion

By Elizabeth A. Eisenhauer, Wim W. ten Bokkel Huinink, Kenneth D. Swenerton, Luca Gianni, James Myles, Maria E.L. van der Burg, Ian Kerr, Jan B. Vermorken, Katharina Buser, Nicoletta Colombo, Monica Bacon, Pedro Santabárbara, Nicole Onetto, Benjamin Winograd, and Renzo Canetta

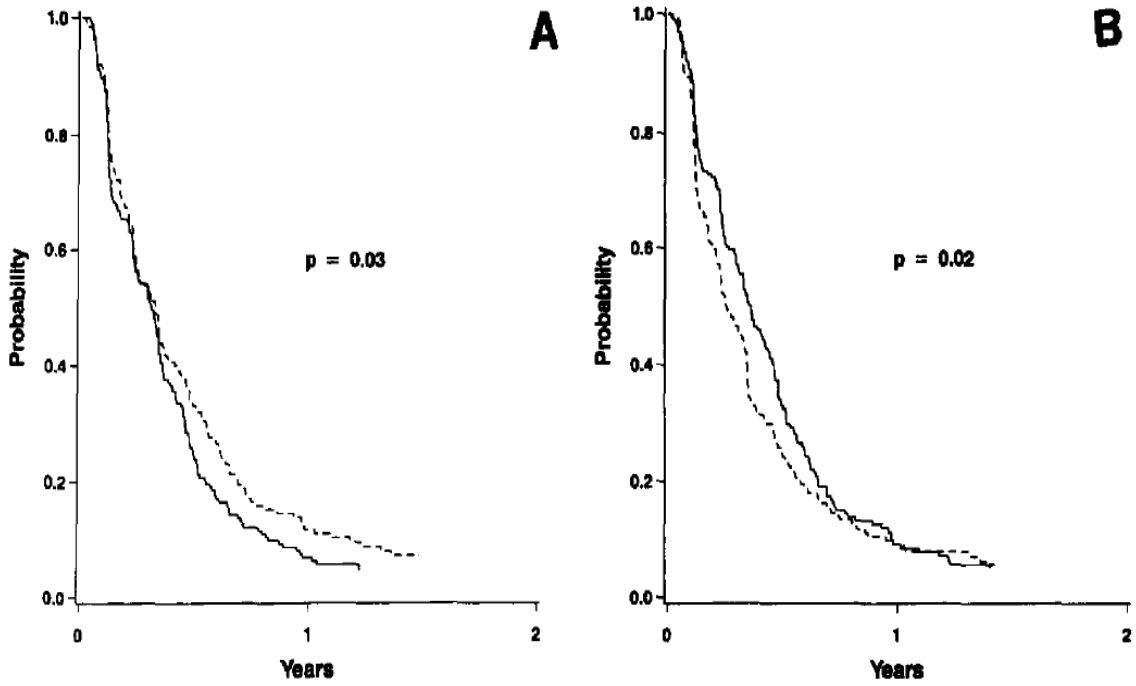
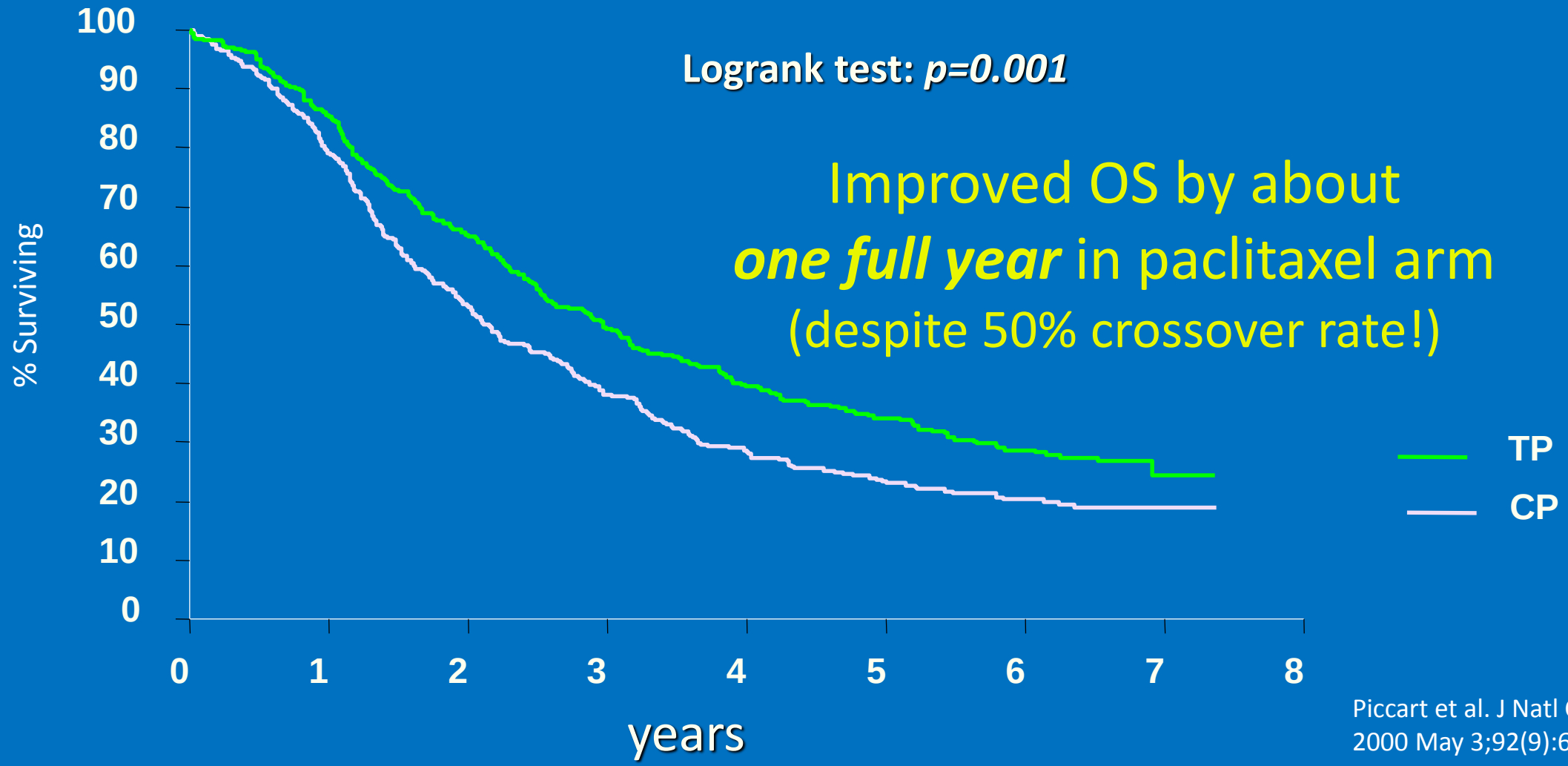


Fig 1. Progression-free survival of the (A) 24-hour (——) v 3-hour (– – –) infusion groups and (B) 175-mg/m² (——) v 135-mg/m² (– – –) groups. *P* values are adjusted for significant prognostic factors.

OV.10 Intergroup Ovarian Cancer Trial

OVERALL SURVIVAL



Improved OS by about
one full year in paclitaxel arm
(despite 50% crossover rate!)

Piccart et al. J Natl Cancer Inst. 2000 May 3;92(9):699-708.

GCIG Group representatives in 2004: *Baden-Baden consensus conference*

1993 Helsingor Denmark Ovarian Consensus Conference EE with Martine Piccart

LESSON 4: Collaborations across borders and oceans not only speeds clinical research, but creates life-long friendships

1990s – Taxanes everywhere

- With success of paclitaxel in OVCA -- ***dozens*** of trials ongoing in almost all solid tumours (and some hematological ones)
- In addition, the first "analogue" – docetaxel (Taxotere) started phase I trials. A theoretical advantage – no premeds needed since no cremophor
- Because of OV.9 success, NCIC CTG obtained this new agent for 5 phase II studies, including breast cancer.
- By the 10th patient enrolled we knew two things with certainty:
  - Drug was active: **7/10 PRs**
  - Pre-meds needed! **Most pts had HSR**

Docetaxel in Patients With Metastatic Breast Cancer: A Phase II Study of the National Cancer Institute of Canada-Clinical Trials Group

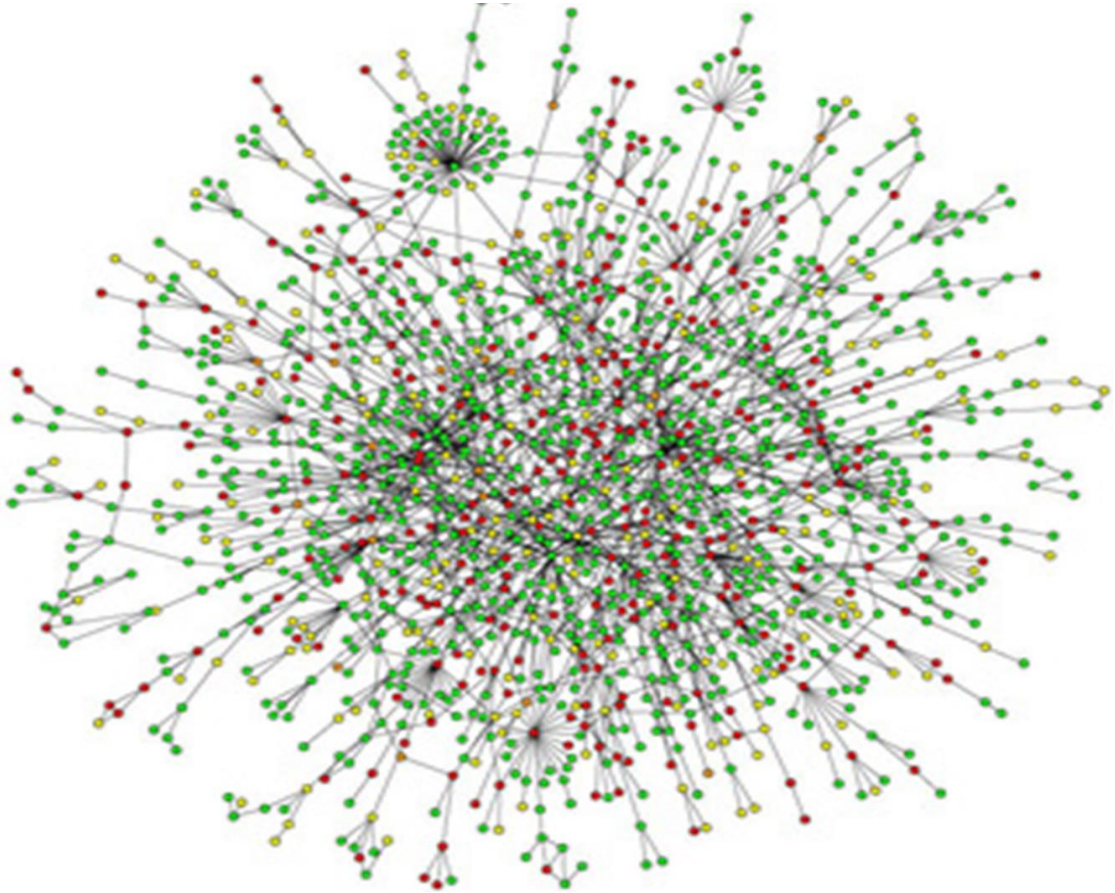
By Maureen E. Trudeau, Elizabeth A. Eisenhauer, Brian P. Higgins, Francois Letendre, Wycliffe S. Lofters, Brian D. Norris, Theodore A. Vandenberg, Fernand Delorme, and Alison M. Muldal

Late 1990s – change is in the air

1. Targeted drugs emerging
2. New endpoints and trial design
3. Professionally - Growing Involvement in Cancer Research and Oncology Professional Organizations

The New Wave – the First Targeted Drugs

- While ALL cytotoxic chemotherapy agents have molecular targets the "new wave" focused on agents targeted to signaling molecules and receptors
  - Antibodies
  - Small molecules
  - Anti-sense oligonucleotides



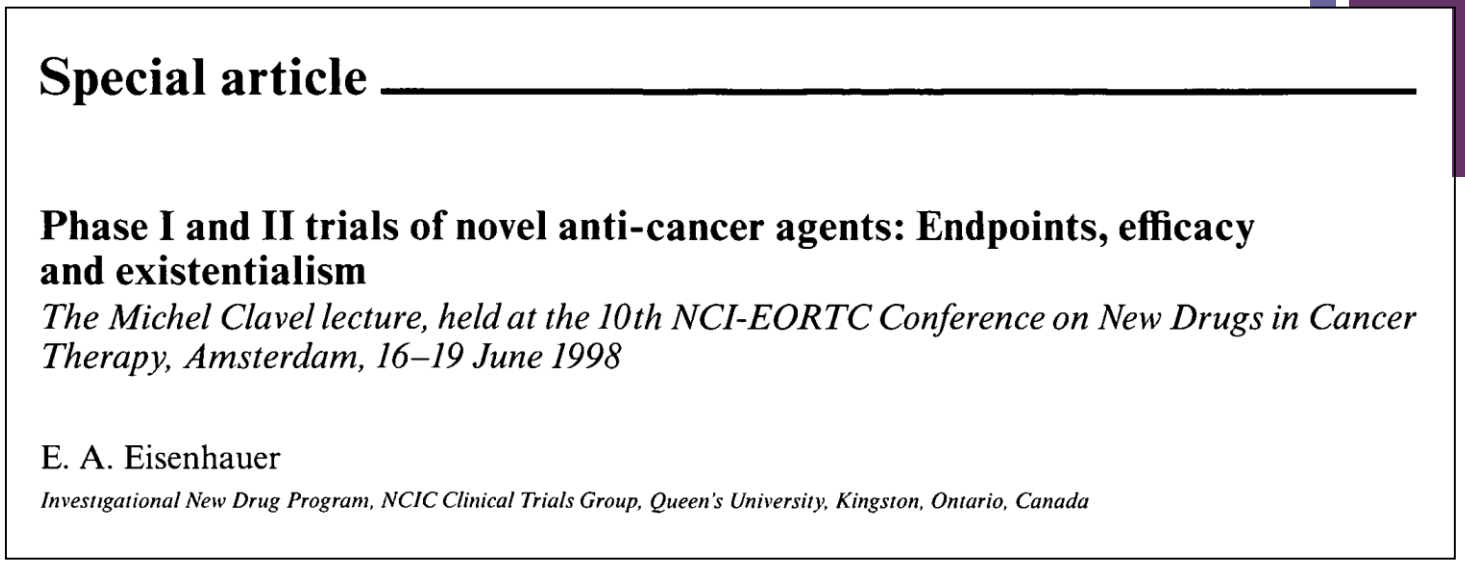
- These signaling networks were much more complex than initially thought!
- Nonetheless, many new agents emerged – some with stunning success

The New Wave – the First Targeted Drugs

- *The prevailing views at end of the 1990s about clinical development of these new, targeted agents*:
  - They HAD to be highly **specific**
  - They HAD to be given **continuously** to work
  - They would **NOT cause tumour regression**
  - They would be **NON-TOXIC** and change cancer into a chronic disease
  - **Biomarkers** would be needed and easy to define….

New Endpoints and Trial Designs

- In 1998 – a talk I gave in Amsterdam examined these ideas and predicted a number of ways drug development would need to change



Special article

Phase I and II trials of novel anti-cancer agents: Endpoints, efficacy and existentialism

The Michel Clavel lecture, held at the 10th NCI-EORTC Conference on New Drugs in Cancer Therapy, Amsterdam, 16–19 June 1998

E. A. Eisenhauer

Investigational New Drug Program, NCIC Clinical Trials Group, Queen's University, Kingston, Ontario, Canada

- Phase I endpoint –my 1998 prediction:
  dosing will be based on optimal target inhibition; toxicity avoided
- Phase II endpoint – my 1998 prediction:
  Targeted drugs will not cause tumour regression, thus need other measures (SD, PFS) – and thus randomized designs

1998-2005 – Targeted Drugs Everywhere….

CCTG IND program - we began a number of phase I and II trials of molecular targeted therapeutics. For example….

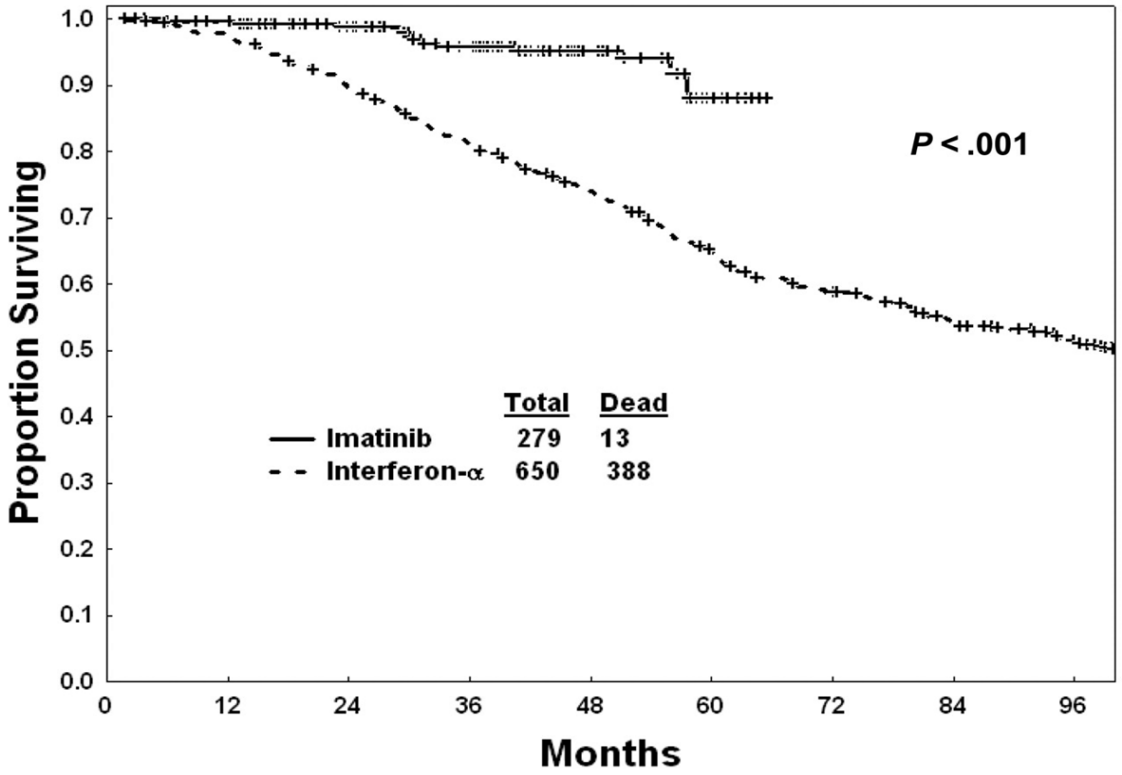
- Matrix metalloproteinase inhibitors (BAY 12-9566, BB-2516)
- EGFR inhibitors (gefitinib, erlotinib)
- Non-specific PKC inhibitors (flavopiridol)
- RAF inhibitors (sorafenib, ISIS 5132)
- PKC inhibitors (ISI3521, bryostatin)
- Farnesyltransferase inhibitor (SCH66336)
- CDK inhibitor (flavopiridol)
- Proteosome inhibitor (bortezomib)
- DNA methyltransferase inhibitor

- Most IND trials were negative except:
  - Bortezomib (MCL – 46% RR (A. Belch Chair); Waldenstroms – 26% (C. Chen Chair))
  - Sorafenib (AML – phase I saw a CR in pt with Flt3 ITD (M. Crump Chair))
- NCIC CTG (CCTG) – led **phase III trials** showing improved survival in CRC (CO.17) and NSCLC (BR.21)

By 2005: Targeted Therapy Trials a "Mixed Response"

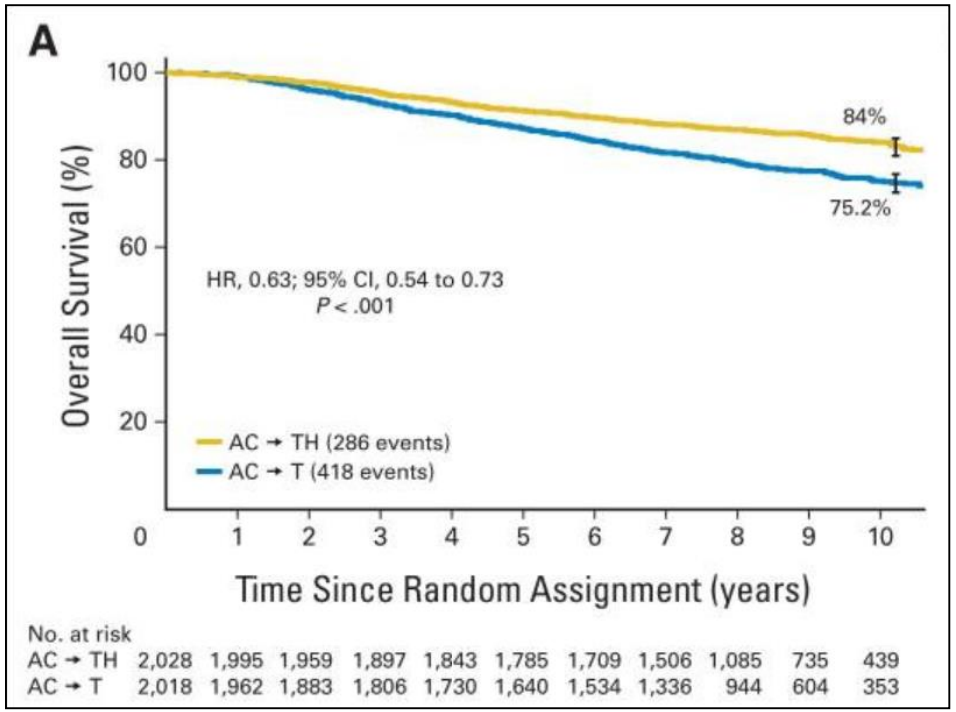
- Some striking and game changing
- Some less dramatic but important and practice changing

Imatinib CML -Survival



Blood 2006 108:1835-1840

Trastuzumab Adjuvant Breast

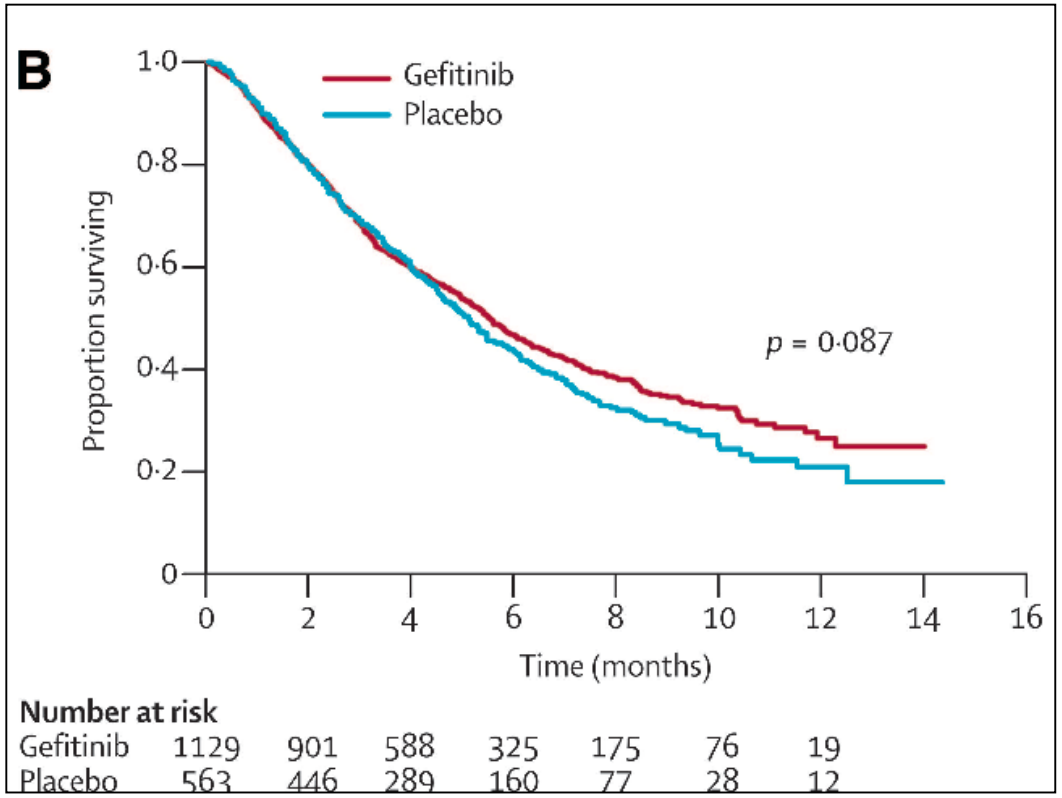


J Clin Oncol. 2014 32: 3744–3752.

By 2005: Targeted Therapy Trials a "Mixed Response"

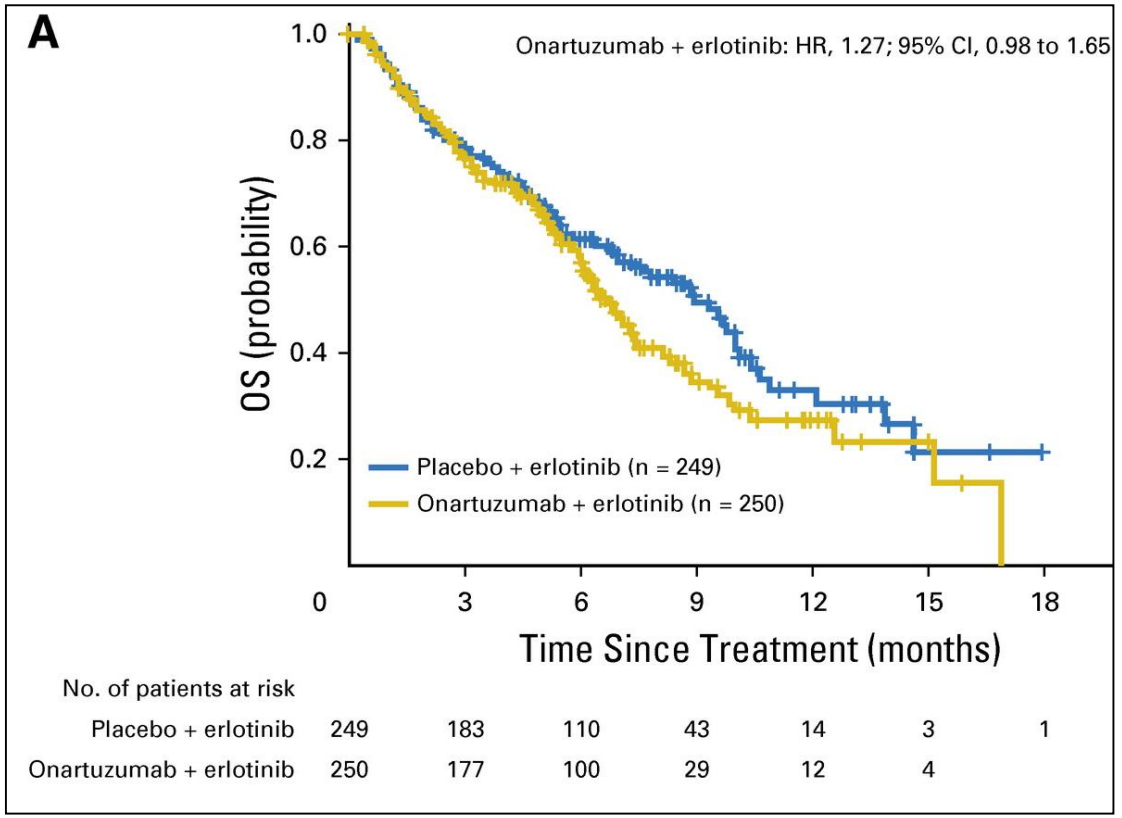
- Many negative ---or worse

Gefitinib vs Placebo NSCLC



Lancet 2005;366:1527-1537

Met inhibitor + erlotinib in NSCLC



J Clin Oncol. 2017 Feb;35(4):412-420

By 2005 – Bloom on Rose of Targeted Therapy Fading

- Not everything was going to be an imatinib in CML (or GIST).
- My 1998 predictions were not so good:
  - Targeted drugs WERE toxic
  - Dosing based only on target inhibition – might give too LOW a dose (e.g. gefitinib)
  - Targeted Drugs DID CAUSE tumour shrinkage – and without it much less likely to "make it" in phase III
  - Biomarkers were important but NOT EASY

VOLUME 26 · NUMBER 8 · MARCH 10 2008

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Review of Phase II Trial Designs Used in Studies of Molecular Targeted Agents: Outcomes and Predictors of Success in Phase III

Robert H. El-Maraghi and Elizabeth A. Eisenhauer

LESSON 5: HUMBLING - Predictions based on (imperfect) knowledge of biology may be wrong. Be open-minded and focus on effects seen in clinical trials

By 2005 – Bloom on Rose of Targeted Therapy Fading

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LESSON 6: LOTS of interesting research can be done with keen fellows
I've been lucky to work with many: Rob El-Maraghi, Janet Dancey, Rahima Jamal, Rachel Goodwin, Sarit Assouline, Annette Hay…… (to name but a few)

As this lesson being learned –

I was becoming involved in leadership, and teaching cancer research in Canada, US and Europe

American Society of Clinical Oncology

- 1994-1997 Board of Directors

FECS ASCO ACCR Workshop
American Society of Clinical Oncology

- 2000-2003 Co-Chair - Methods in Clinical Cancer Research" (Flims Switzerland)

National Cancer Institute of Canada
Canadian Cancer Society

- 2002- 2009 Member, NCIC Board of Directors
- 2006- 2009 President
  National Cancer Institute of Canada

Why get involved?

- Clinicians need to be part of discussions about cancer research directions – learning about where basic science is going, integrating disciplines, ensuring questions relevant to patients being addressed
- Clinicians need to be actively engaged in solving health system problems – we must serve not just patients, but society

Why get involved?

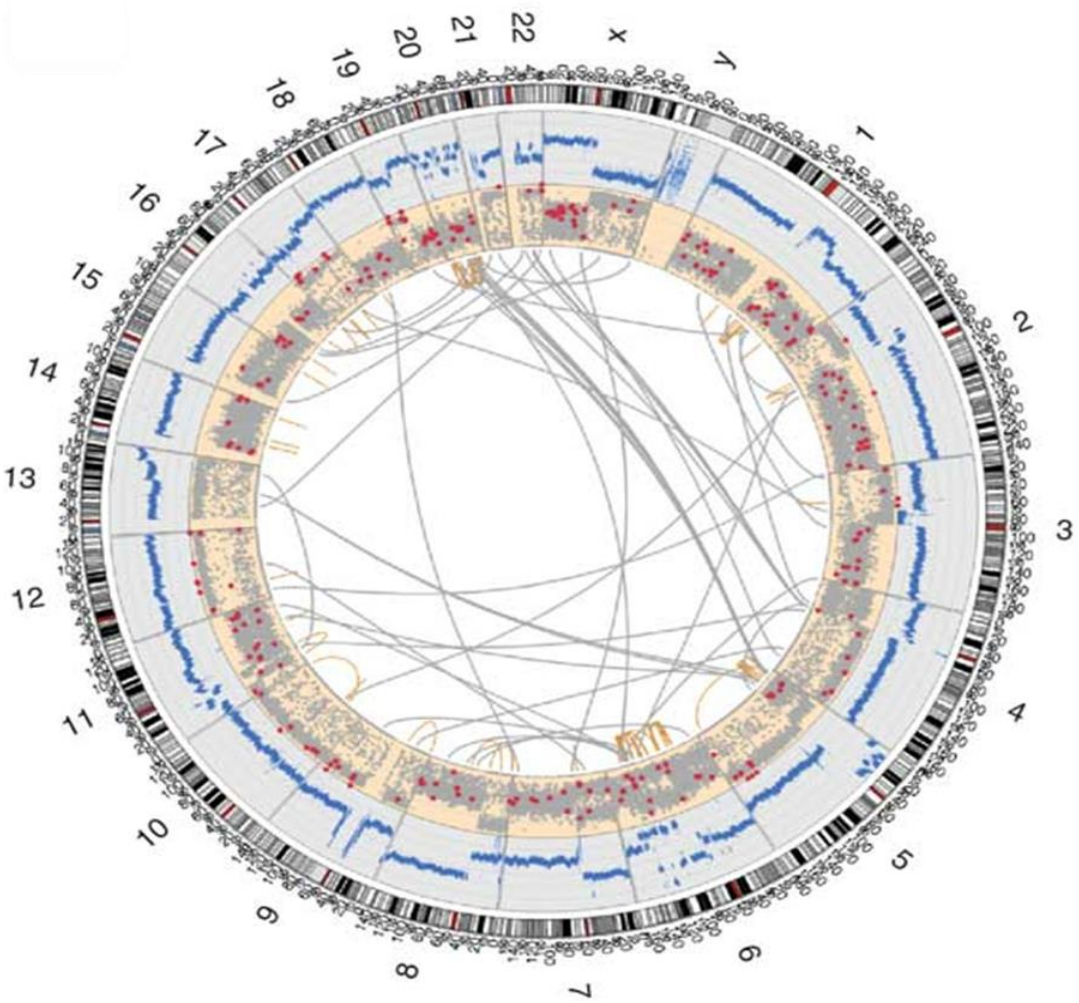
- ***We must find ways to give back:***
  - Reaching next generation
  - Supporting and growing organizations that support research
- FINALLY – because it is fulfilling, fun and even more new friends made …..

"Flims" Faculty and Trainees ~ 2003

EE, Margaret Tempero, Martine Piccart

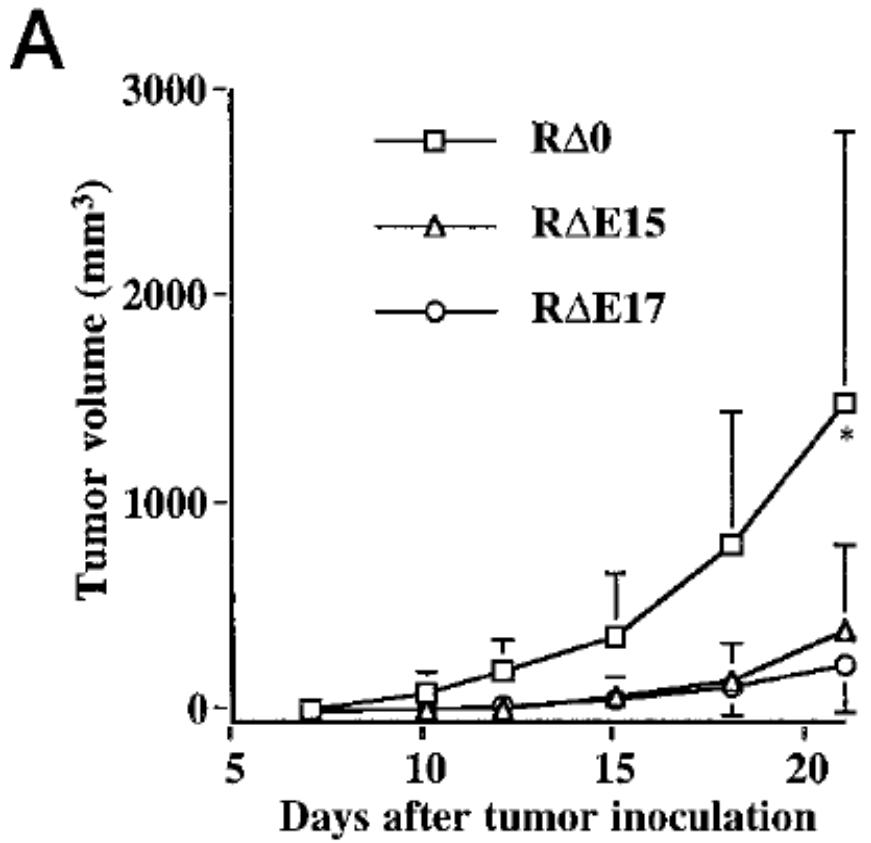
2005-2010

1. Therapy: many targets and drugs:
   - ***Genomic revolution and rise of precision medicine mantra***
   - ***Anti-angiogenesis drugs emerging***
2. Trial endpoint “regression”
3. Professionally –
   Moving from Cancer Research to Cancer Control and Policy



Anti-Angiogenesis Therapies

- Dr. Judah Folkman led the way to describing the role of angiogenesis in promoting/sustaining tumour growth and in identifying inhibitors of this process.
- Expectations were high when one of the first of these drugs, ***endostatin***, went into clinic trials that cancer "cure" was finally in sight



NCIC CTG IND Program 2005-2010

- Several phase I/II trials (and CCTG RCTs): ZD 6474, AZD 2171 (cediranib), were two agents studied – latter led to CCTG RCTs in lung and ovary
- ***Anti-Angiogenesis "wave" of trials*** became largest ever seen – ***more than 1000 trials with VEGF inhibitor bevacizumab alone***
- Despite this, it is infrequent that angiogenesis inhibitors have had a *meaningful* impact on cancer survival. *Preclinical models (which rely on dramatic tumour growth rates and thus angiogenesis) misled us.*

LESSON 7. When a drug or drug class has limited activity, you cannot make it become active by doing 100s or 1000s of trials.

Trial Endpoint "Regression"

- As noted the 1998 predictions I made about targeted drugs were largely proven **false**
- Nonetheless, primary endpoints in trials had (and remain) shifted: "tumour control rate" or PFS in phase II; PFS (not OS) in phase III.
- It seemed to me ***we were asking LESS of drugs in terms of impact – and these were costing MORE to give.***
- The "bar" for new drugs seemed to be "***regressing…***."
- Arising from this: personal work on PFS meaning – and Value Based Frameworks for cancer drug assessment/pricing

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COMMENTS AND CONTROVERSIES

Progression-Free Survival: Meaningful or Simply Measurable?

Christopher M. Booth and Elizabeth A. Eisenhauer, *NCIC Clinical Trials Group, Queen's University, Kingston, Ontario, Canada*

Dr. Chris Booth

- This work has continued under leadership of Chris Booth, Mike Brundage, Andrew Robinson, and others…
- Do patients understand <u>what PFS is?</u> If a new treatment can prolong PFS in *absence* of QoL, symptom or overall survival benefits, would they choose to take it? *Research in patients now ongoing to ask these questions.*
- This could have big implications on
  - Clinical trial endpoints
  - Regulatory and reimbursement approval decisions

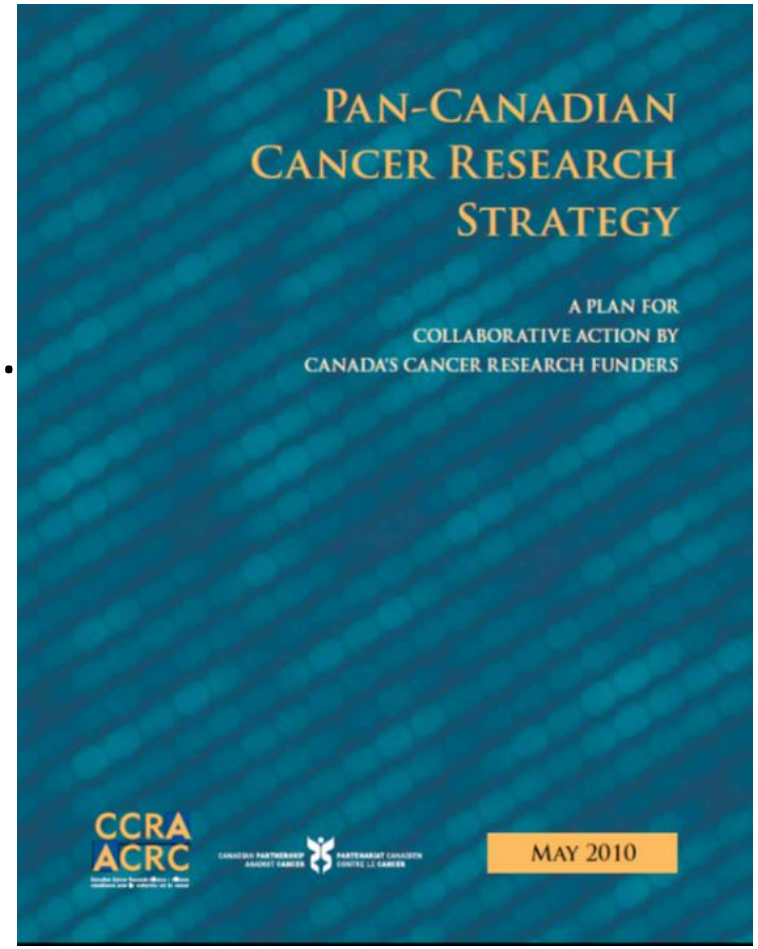
Dr. Andrew Robinson

Dr. Michael Brundage

From Cancer Research to Cancer Control and Policy

Creating a Pan-Canadian Research Strategy

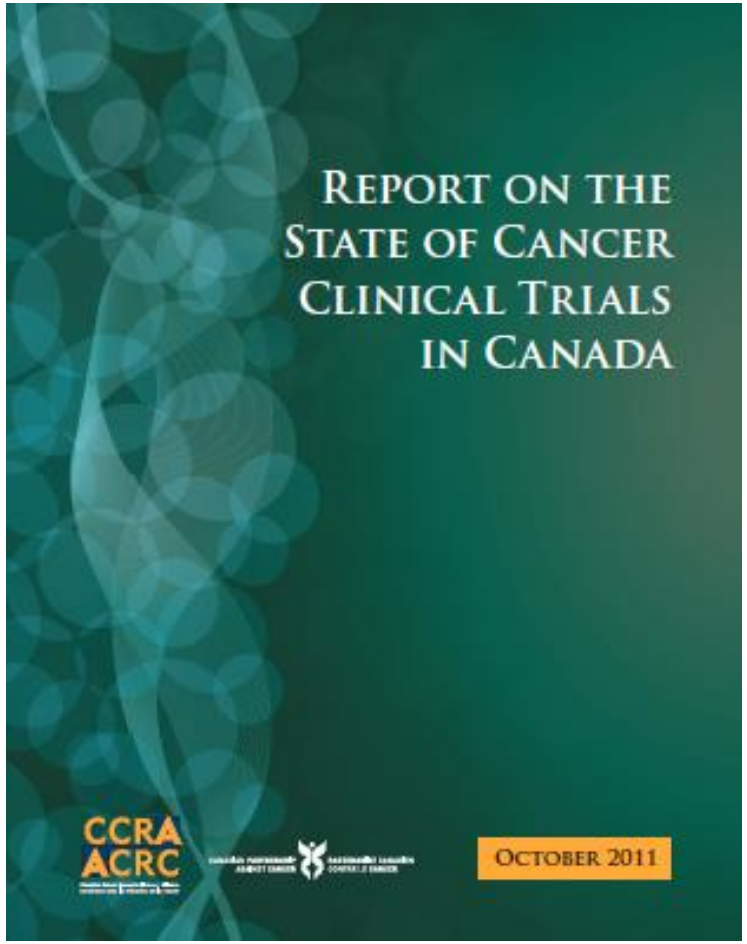
- 2007: Canadian Federal government created the **Canadian Partnership Against Cancer (CPAC)** to implement the Canadian Strategy for Cancer Control
- CPAC began hosting the executive office the **Canadian Cancer Research Alliance** which I began chairing in 2006.
- CCRA:
  - 2007 - ~20 cancer research funding organizations collectively funding >$250 M/yr in research (today: 34 orgs investing >$450M/yr in cancer research in Canada)
  - ***How do we best collaborate and make greater impact?***
  - Launch of 1st Pan-Canadian Cancer Research Strategy -- 2010



https://www.ccra-acrc.ca/wp-content/uploads/2019/06/Pan-Canadian_Strategy_2010_EN.pdf

From First Pan Canadian Cancer Research Strategy:

Action Item 11 – Report and make recommendations on *academic* cancer clinical trials in Canada



Findings:

- Trial accrual ↓
- Time to open/accrue ↑
- Trial costs and complexity ↑
- Administrative work ↑
- Institutional support ↓
- Change in trials being done

4 recommendations – the most NB:

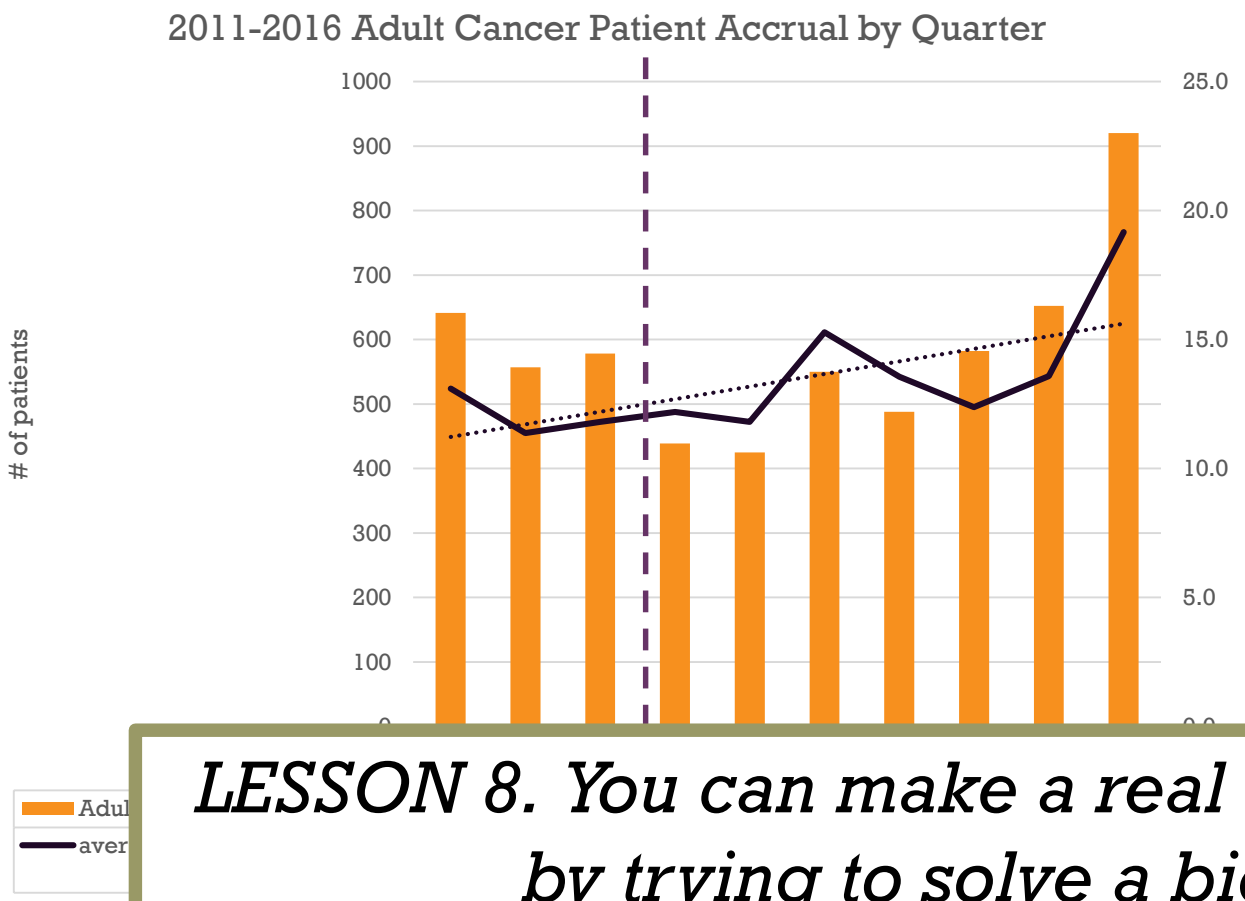
- ***Create a Pan-Canadian Infrastructure Program that Supports Academic Cancer Trials***

Canadian Cancer Clinical Trials Network (3CTN)

- Formed as result of the Clinical Trials Working Group report – the key recommendation for stable infrastructure support led to a CPAC-issued RFP for a coordinating centre.
- International peer review led to selection of OICR; Scientific Director - Dr. Janet Dancey
- Funders: 11 provincial, 2 national, 1 industry (project). The Canadian Partnership Against Cancer was a lead funder of this network

Canadian Cancer Clinical Trials Network

Recruitment improved since 2015 – Adult sites In 2018 - 3CTN successfully renewed funding



- By end of 2018:

↑53% PATIENTS RECRUITED ABOVE THE BASELINE FOR ADULT SITES IN Y4

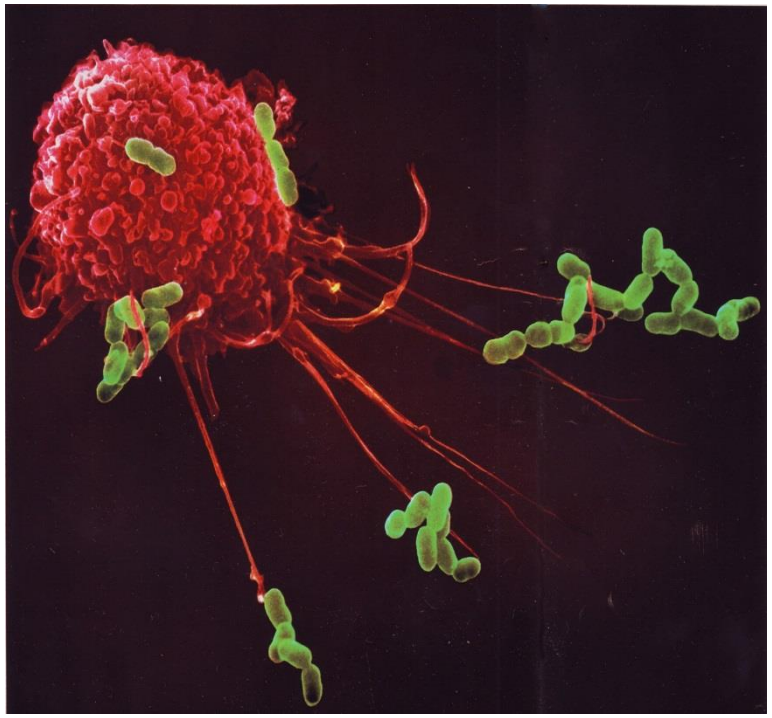
12,054 PATIENTS RECRUITED

559 TRIALS ON PORTFOLIO

LESSON 8. You can make a real difference to enable research by trying to solve a big problem together.

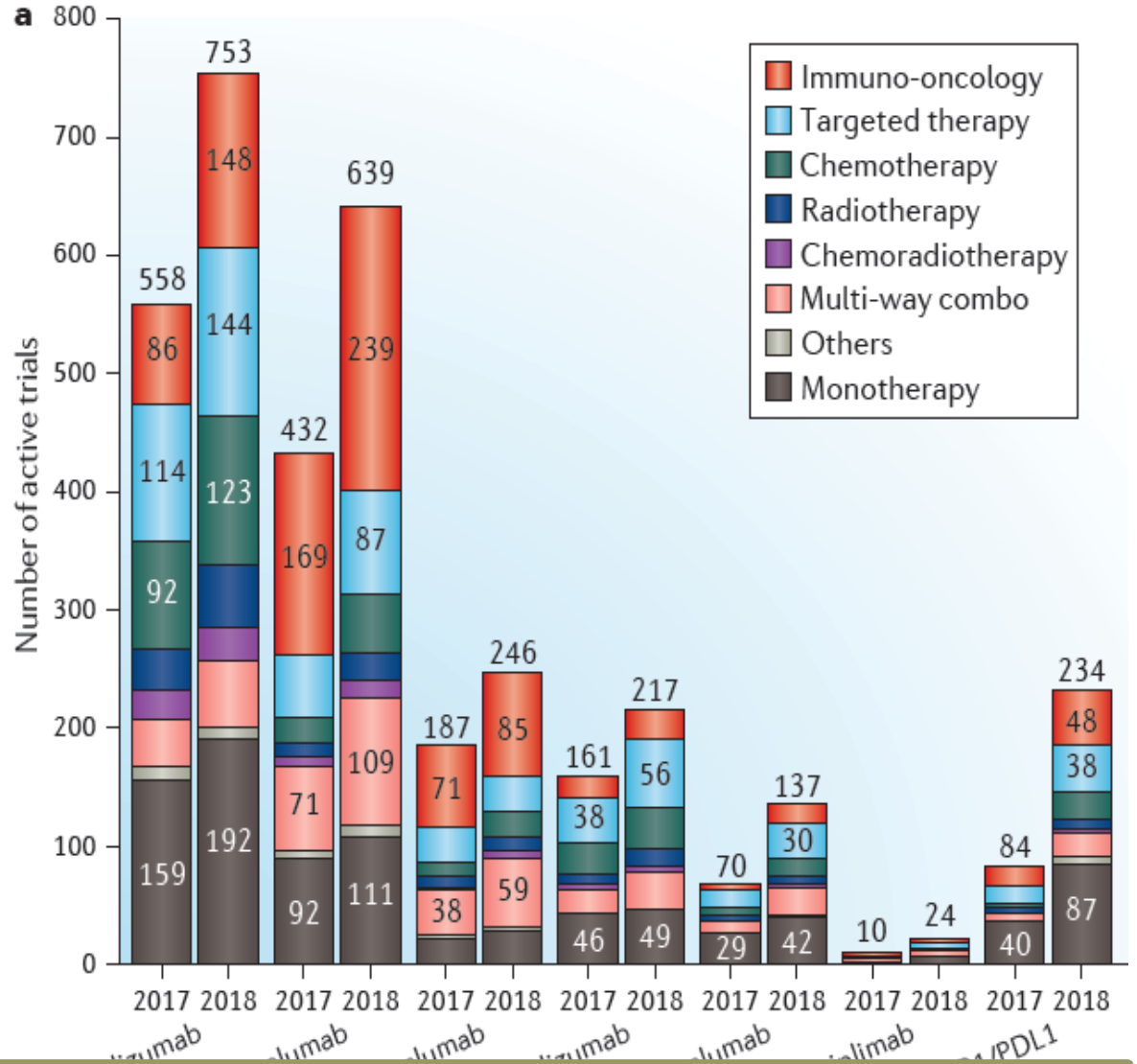
2011- today

1. **Immune oncology** revolution
2. Professionally I was….
   - Seeing the impact of cancer research on outcomes
   - Moving from CCTG to University leadership (then retirement!!!)
   - Interest moving from treatment research to prevention and palliation
3. All grown up



+ Immune therapy ~~wave~~ tsunami

- CTLA4 and PD1/PDL1 inhibitors
  - Transformative to melanoma
  - FDA Accelerated or Full Approvals alone or in combo with benefits in a number of diseases.
- CAR-T cells
  - Hematological malignancies – and likely solid tumours

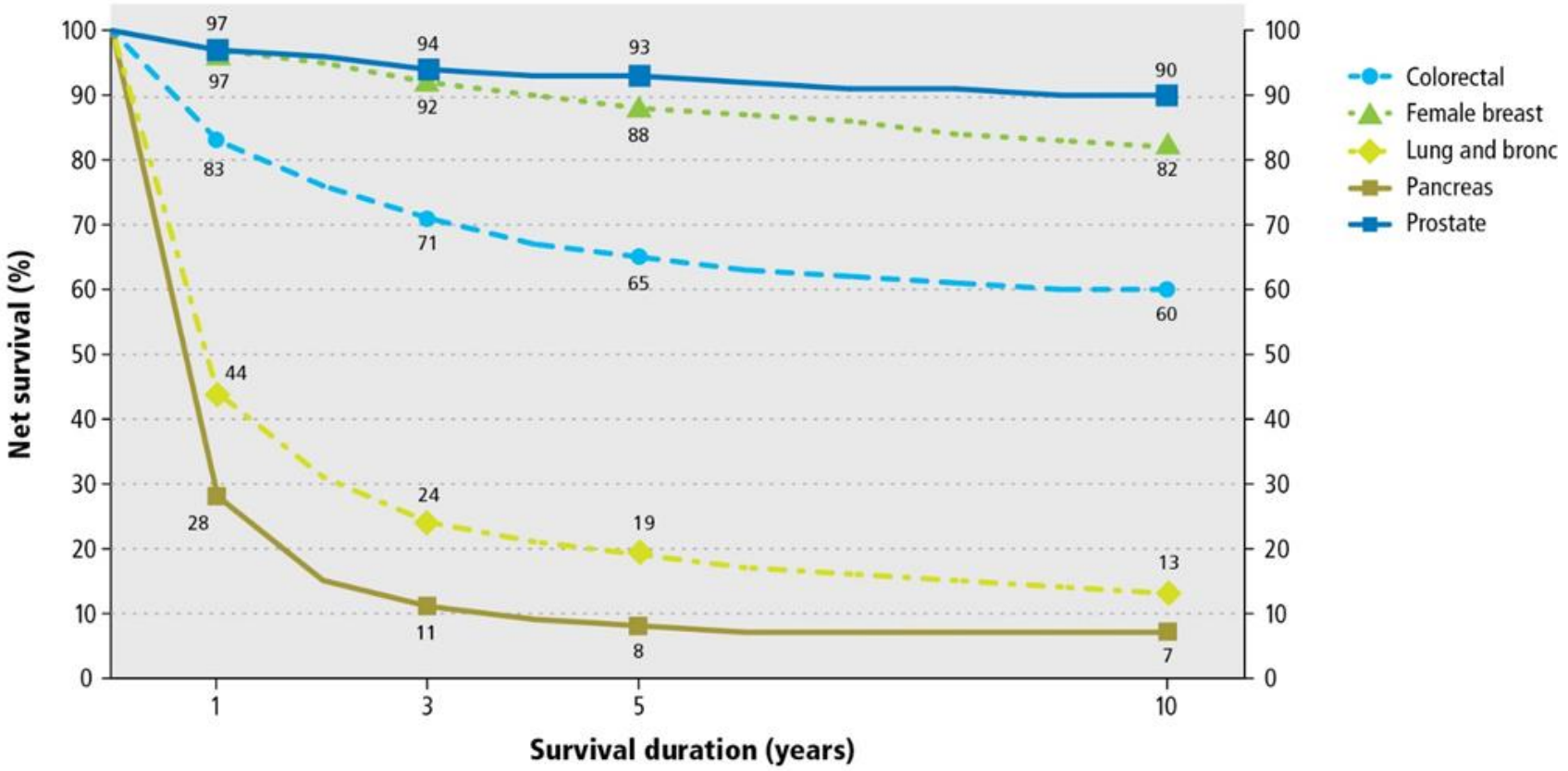


COMMENT. I am concerned about this - multiple trials addressing variants of the SAME questions may duplicate failure, waste resource and increase costs, and give false positive results!

So what have we achieved in 30+ years?

5-year Net Survival overall ~63%
(patients diagnosed 2012-14)

FIGURE 3.1 Predicted net survival for leading causes of cancer death by survival duration, ages 15–99, Canada (excluding Quebec*), 2012–2014



5-year Net Survival

Prostate 93%

Breast 88%

Colon 65%

Lung 19%

30 years of Progress in Cancer Survival Impact of Treatment (and Screening)

Cancer Type	1987 Statistics 5-year Net Survival	2019 Statistics 5-year Net Survival
Colon	45%	65%
Breast	70%	88%
Prostate	48%	93%
Lung	15%	19%

Age Standardized Mortality Trends 1984-2019

FIGURE 2.9 Age-standardized mortality rates (ASMR) for selected* cancers, females, Canada, 1984–2019

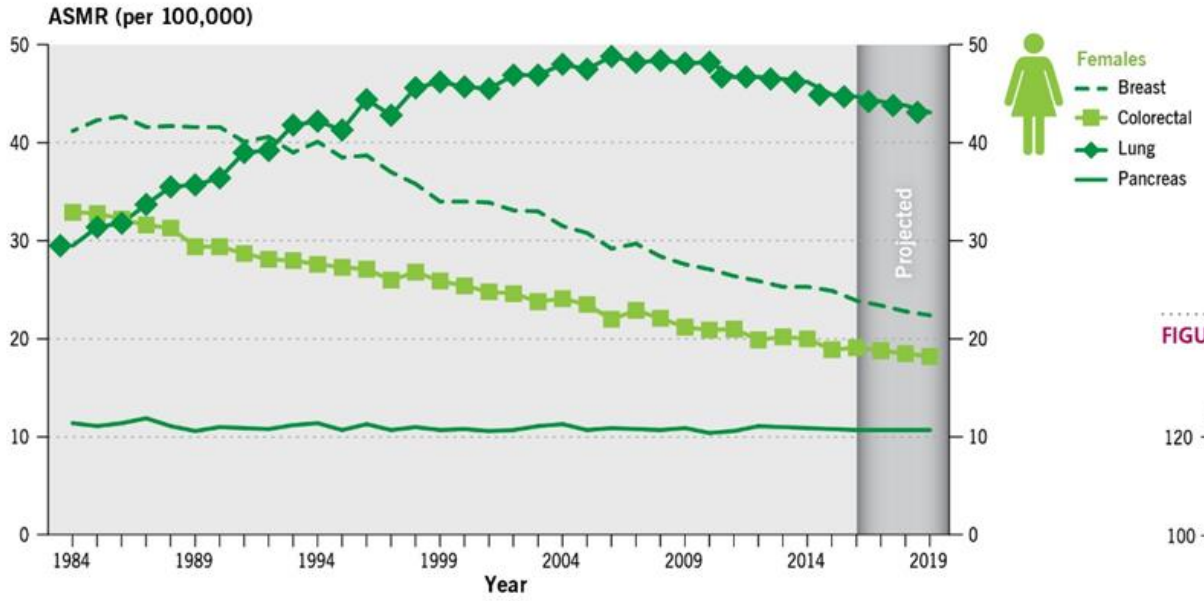
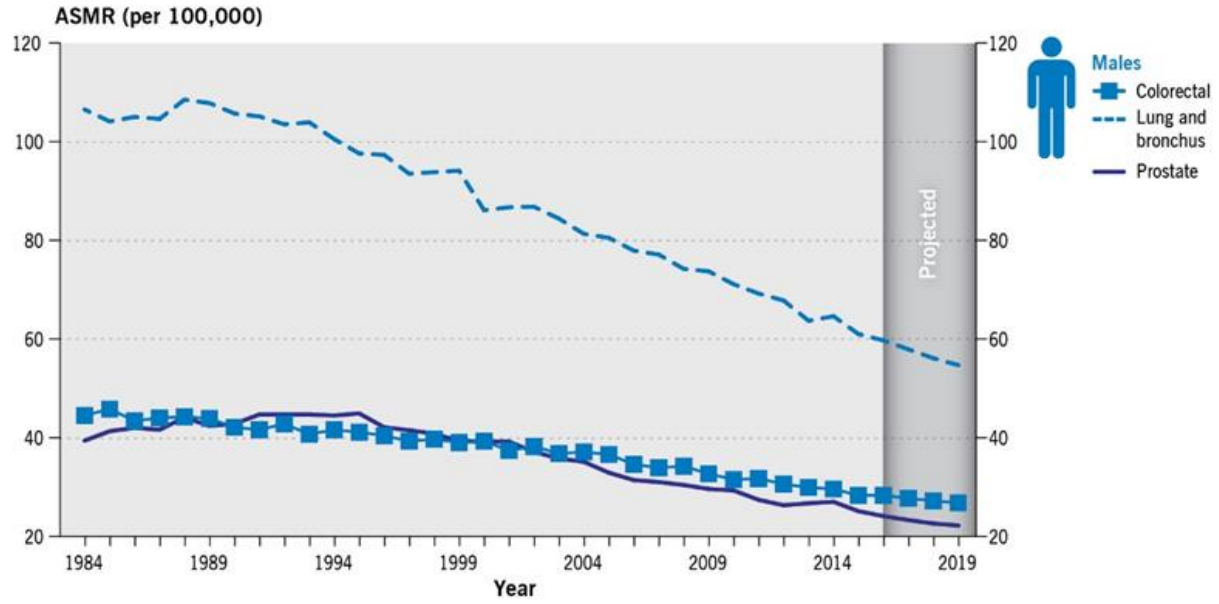


FIGURE 2.8 Age-standardized mortality rates (ASMR) for selected* cancers, males, Canada, 1984–2019



2012 – thinking differently

- Statistics show – Gains in survival; and reduction in mortality for **some** cancers -- But still a long way to go for some
- In 2012 – 3 events changed how I was thinking
  - Became Head of Department of Oncology at Queen's.
    I was not immersed daily in treatment research and this opened my eyes to the reality of cancer system challenges
  - Participated 2012 UICC World Cancer Congress
  - Participated in World Oncology forum

2012 World Cancer Congress (UICC meeting)

- Dr. Christopher Wild, then Director of IARC (International Agency for Research on Cancer) in Lyon, France

"The Global Cancer burden is/will become so large that ***we will not be able to treat our way out of the cancer problem***"

2012 World Oncology Forum

European School of Oncology
Learning to care
30 years

WORLD ONCOLOGY FORUM®

Are we winning the war on cancer?
1 Question • 100 Experts • 1 Answer

26-27 Octob
Grand Hotel Villa Castagnol

Ten-Point Action Plan….

Prevent preventable cancers:

1. **Wage war on tobacco, by far the biggest cause of cancer death across the globe. Extend to all countries the anti-tobacco measures already found to be effective and tax the profits made from tobacco.**

2. Give people the knowledge they need to understand which cancers threaten them most, and how to reduce their risk; develop and implement scientifically sound strategies, including vaccines, to protect against cancers caused by infections.

Treat treatable cancers:

3. Develop early detection programmes tailored to local needs and resources, which target cancers that are the most detectable and treatable and have the greatest social impact…….

2012 World Oncology Forum

European School of Oncology
Learning to care
30 years

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26-27 Octob
Grand Hotel Villa Castagnol

Ten-Point Action Plan….
Prevent preventable cancers:

1. **Reduce smoking rates to 0% --- *what we should have said!***

2. Give people the knowledge they need to understand which cancers threaten them most, and how to reduce their risk; develop and implement scientifically sound strategies, including vaccines, to protect against cancers caused by infections.

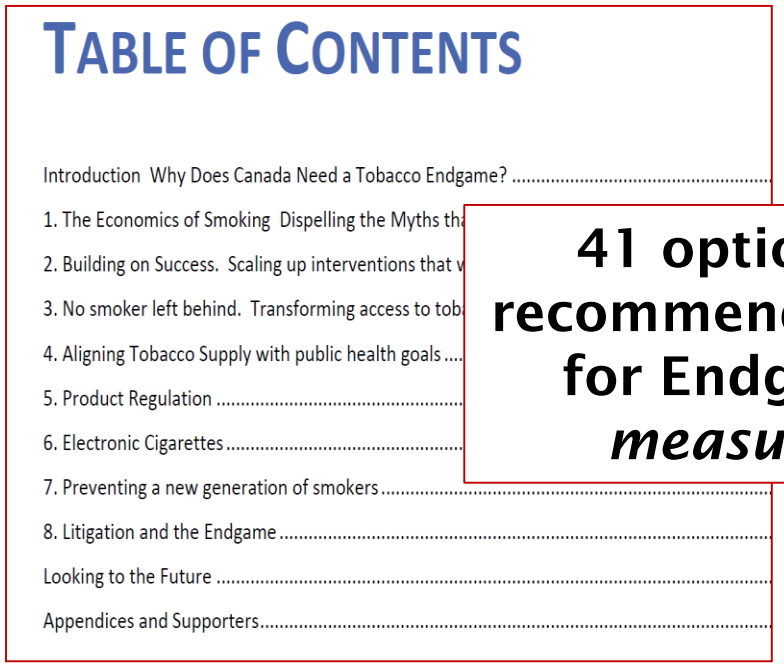
Treat treatable cancers:

3. Develop early detection programmes tailored to local needs and resources, which target cancers that are the most detectable and treatable and have the greatest social impact…….

Tobacco:
Single most common preventable cause of cancers.

So why aren't I (oncologists) DOING something?

- These thoughts started me on path to gathering relevant experts, developing extensive background papers culminating in a **National Summit on *Creation of a Tobacco Endgame for Canada* in 2016**
- Endgame Goal: ***to achieve <5% tobacco use by 2035***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2. Building on Success. Scaling up interventions that w
3. No smoker left behind. Transforming access to toba
4. Aligning Tobacco Supply with public health goals ....
5. Product Regulation .....
6. Electronic Cigarettes .....
7. Preventing a new generation of smokers .....
8. Litigation and the Endgame .....
Looking to the Future .....
Appendices and Supporters.....

41 options/ recommendations for Endgame *measures*

September 30 - October 1, 2016

Participants – Summit on Creation of a Tobacco Endgame for Canada

Summit Outcomes

- ***Agreed on need to develop Endgame Strategy for Commercial Tobacco to achieve <5 by '35***
- Strategy development must engage multiple groups including Indigenous Peoples
- Agreed to move this "volunteer" effort forward by creation of an Endgame "Cabinet" comprised of committed individuals and organizations

In 2017, Health Canada identified <5 by '35 as their Goal for new comprehensive tobacco control strategy

LESSON 9. Applying learnings from leadership in research, you can effect change in other areas important to you

Palliative Care

- Oncologists, especially those of my "vintage" have considerable experience with need for optimal palliative care.
- Despite this – challenging to ensure palliative care well integrated and available to all patients (with cancer or other chronic diseases!)
- Are there better models of care?
- "Familial" connections made this even more of a topic of interest to me!

Dr. Danielle Kain; Dr. Brian Kain
(my daughter and husband)
CFPC Family Medicine Forum, 2011

CURRENT ONCOLOGY
A Canadian Cancer Research Journal

COMMENTARY

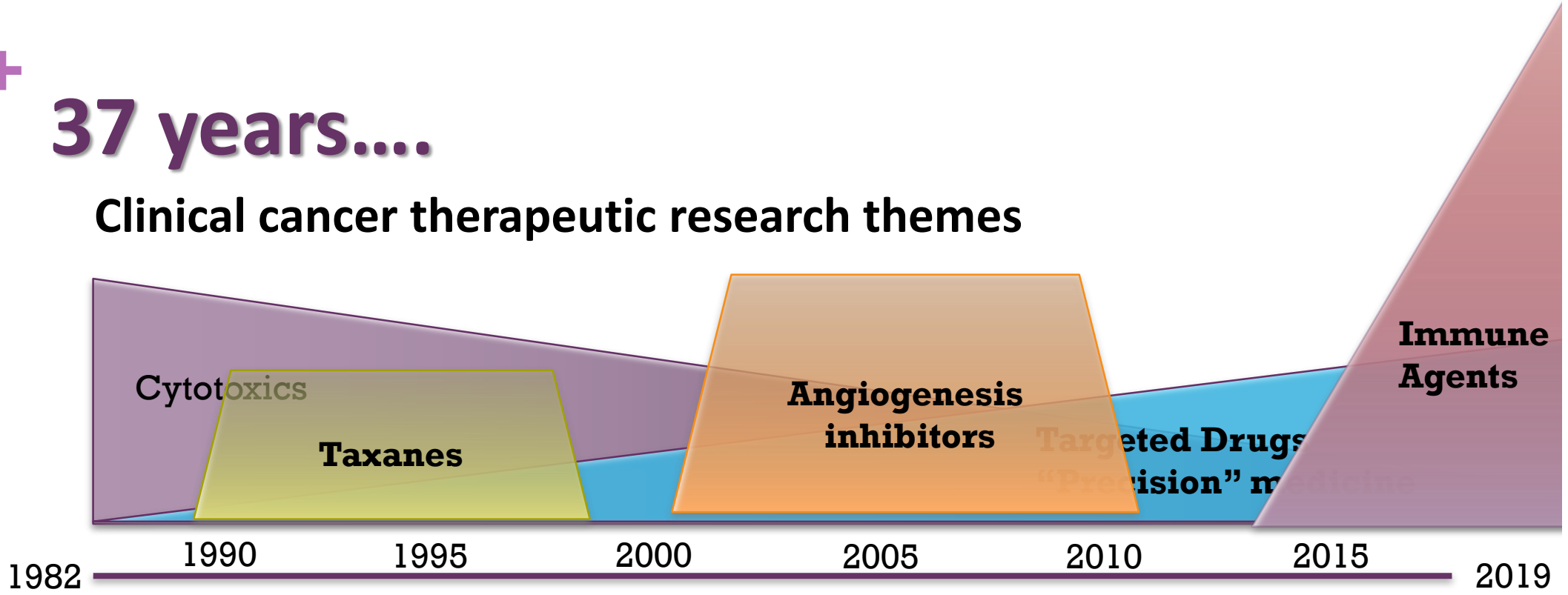
Early integration of palliative care into standard oncology care: evidence and overcoming barriers to implementation

D.A. Kain MA MD* and E.A. Eisenhauer MD†

(a mother-daughter publication!)

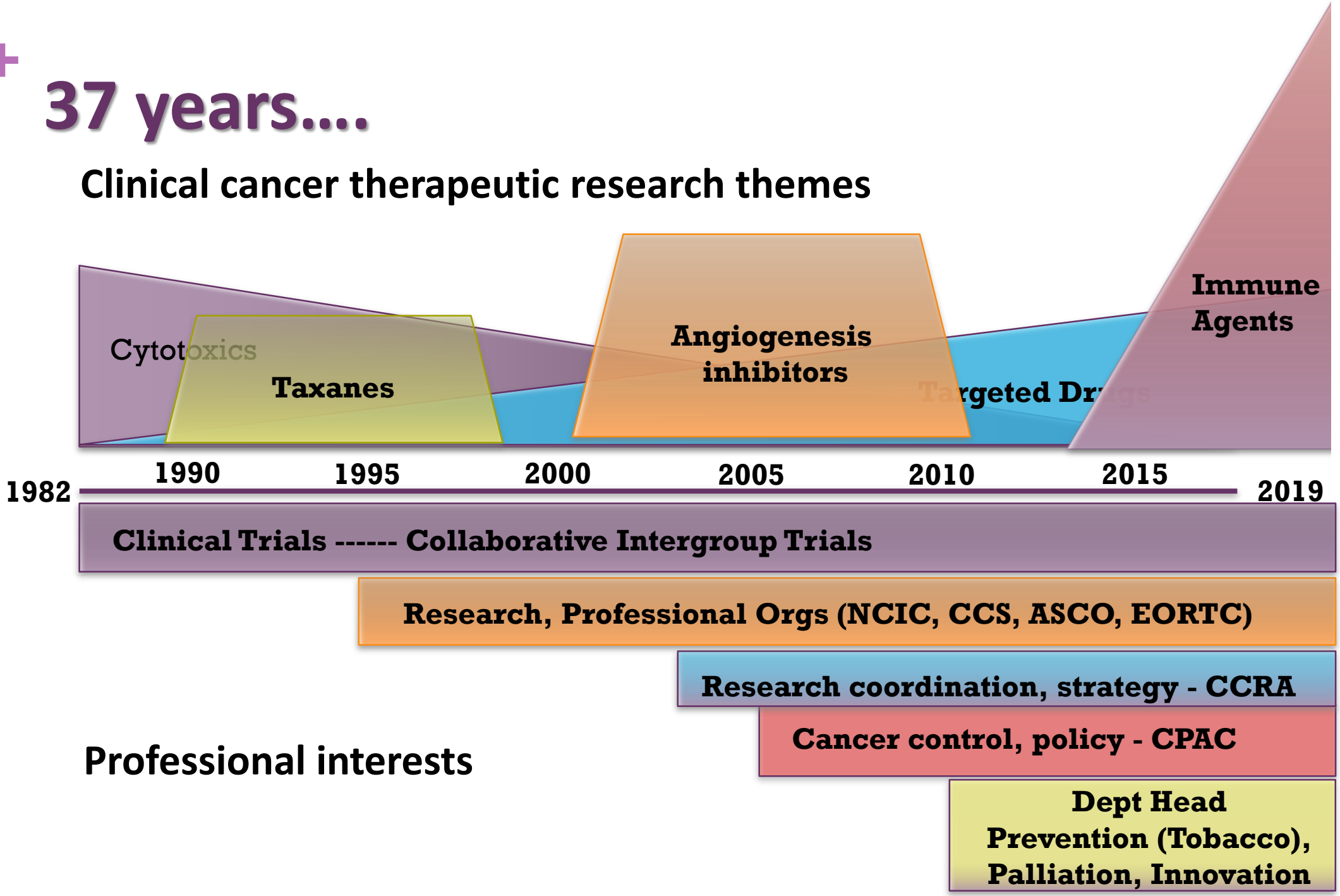
37 years….

Clinical cancer therapeutic research themes



37 years….

Clinical cancer therapeutic research themes



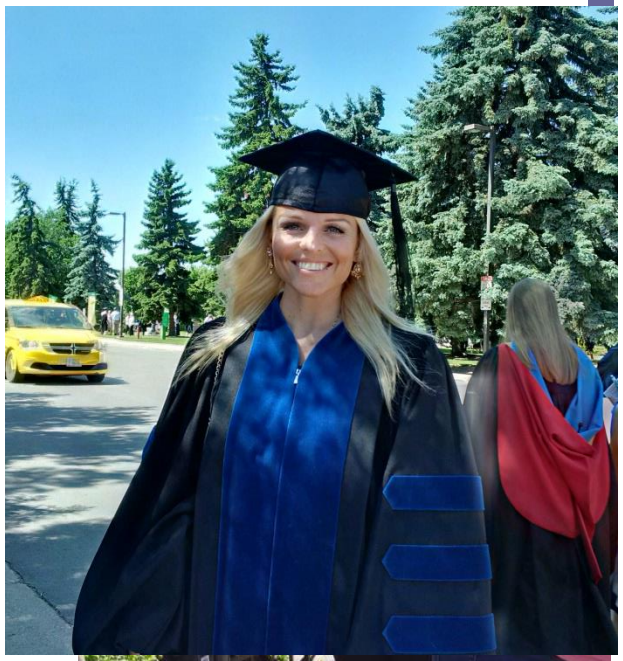
Professional interests

All Grown Up – 37 years later

- Thanks due to not only the many organizations (CCS, CIHR, NCI US, and many pharma companies who funded the research of the CCTG
- Also to mentors, colleagues, trainees, AND thousands of patient volunteers

All Grown Up – 37 years later

- Thanks especially to my family – who are indeed *grown older, grown up and grown larger!*



All Grown Up – 37 years later

- So much has changed since 1982 – I hope you get a sense of the “times” I have been privileged to live and work in.
- In addition to living through this time where we saw big impacts on cancer outcomes, I experienced a personal journey that was never really planned (or expected). It has brought lifelong friendships, fantastic shared experiences and meaning.
- ***Our work is far from done***. As oncologists we must think beyond treatment to cancer’s beginning and its ending – prevention and palliation deserve our action and advocacy,
- ***We have promises to keep. And miles to go before we sleep.***

Acknowledgement - Robert Frost

Stopping By Woods on a Snowy Evening

Whose woods these are I think I know.
His house is in the village though;
He will not see me stopping here
To watch his woods fill up with snow.

My little horse must think it queer
To stop without a farmhouse near
Between the woods and frozen lake
The darkest evening of the year.

He gives his harness bells a shake
To ask if there is some mistake.
The only other sound's the sweep
Of easy wind and downy flake.

The woods are lovely, dark and deep.
But I have promises to keep,
And miles to go before I sleep,
And miles to go before I sleep.

- written in New Hampshire, 1923