

IF AT FIRST YOU DON'T SUCCEED: TRIAL, TRIAL AGAIN

Rena Buckstein MD FRCPC

Head Hematology Site Group Sunnybrook Odette Cancer Center (OCC)

Head of Hematology Clinical Trials Group at OCC

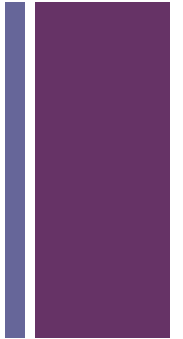
+ Outline



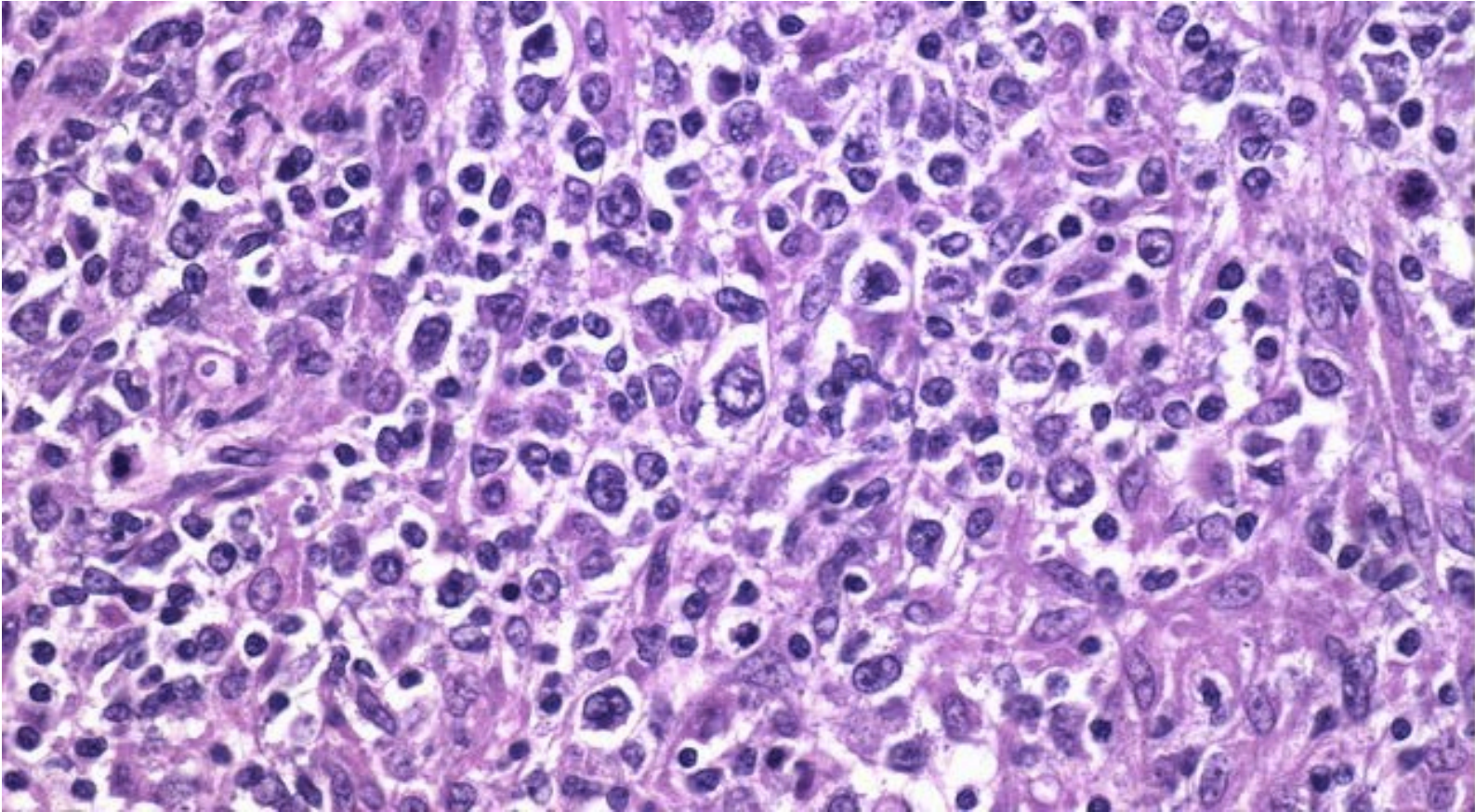
- Start with a case
- Why are clinical trials important?
- Types of trials
 - Advantages and disadvantages
- Who is eligible
- How to find out about trials

+ Case: The year is 2001

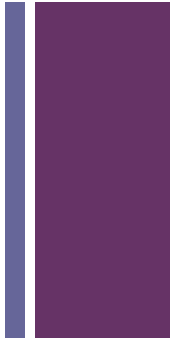
- 68 yo retired contractor is referred for enlarged lymph nodes in his neck
- He has no significant medical problems other than high blood pressure
- Non smoker, non drinker, married 2 kids
- Walks 45 mins every day
- On staging, he has enlarged lymph nodes above and below the diaphragm measuring 2-3 cm in size
- His bone marrow is negative
- Labs are normal



+ A lymph node biopsy is done: Its DLBCL



+ Stage 3A DLBCL in 67 yo man

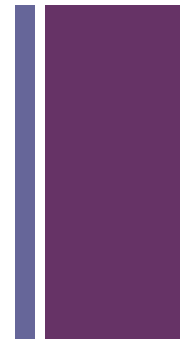


He is offered one of two options:

- 1. CHOP chemotherapy for 6 cycles or
- 2. participation in a phase III clinical trial comparing CHOP with CHOP + Rituximab in patients with large cell lymphoma between the age of 60-80

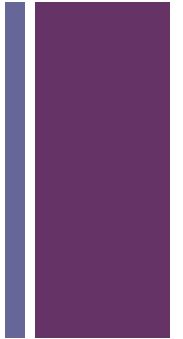


I just
drug in
stop



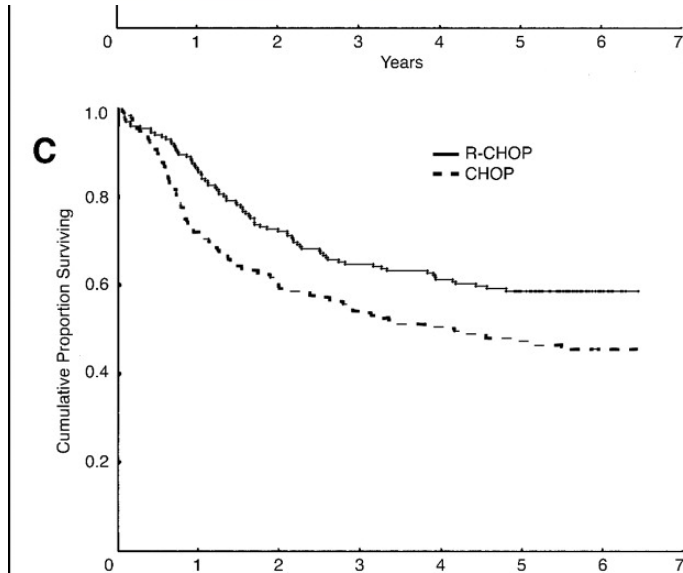
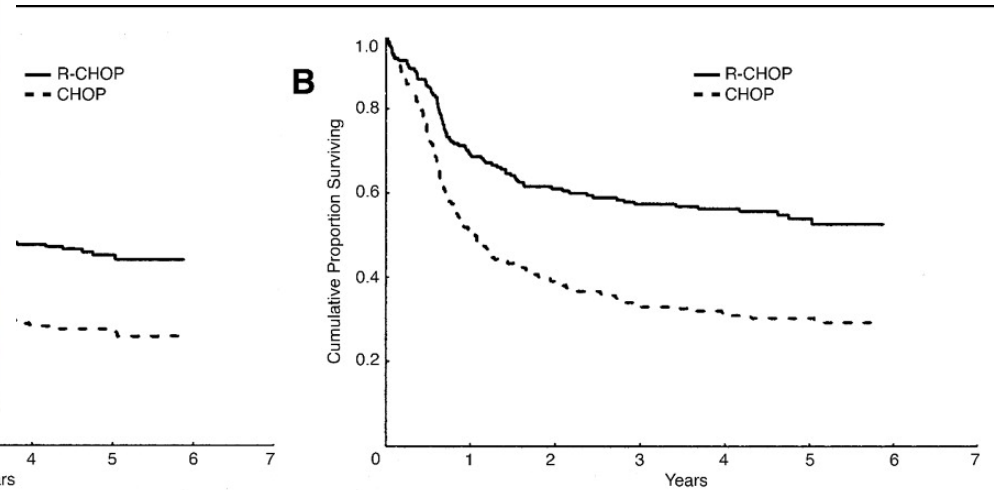
+ He decides to join the study....

- He gets randomized to the experimental arm of CHOP-Rituxan
- He tolerates his chemotherapy well and achieves a complete remission
- 5 years later, results from his clinical trial are published





gression-free survival, and (C) overall survival with a median
 ts treated with cyclophosphamide, doxorubicin, vincristine, and
 (CHOP), and rituximab plus CHOP (R-CHOP).

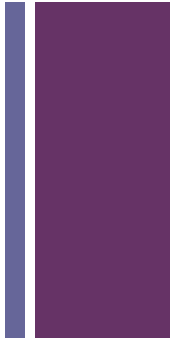


5 year survival 58% versus 45%

Feugier P et al. JCO 2005;23:4117-4126



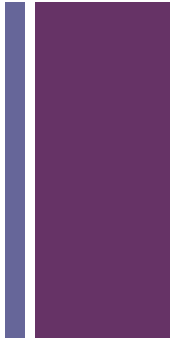
+ What are clinical trials?



- Research studies that involve people
- Final step in long ‘pre-clinical’ process
- Responsible for many treatments today
- In cancer, clinical trials are designed to answer questions about new ways to”
 - Treat cancer
 - Find and diagnose cancer
 - Prevent cancer
 - Manage symptoms of cancer or side effects from treatment

+ Sobering stats

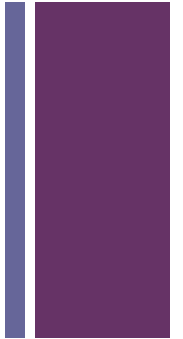
- < 3% of cancer patients go on clinical trials
- Of 500 NCI CTEP trials: 40% failed to achieve minimum enrolment and 3/5 randomized trials did not
- Barriers:
 - Fear of diminished QOL
 - Not wanting placebo
 - Side effects
 - Experimental drug may not be best option
 - Inconvenience
 - Not wanting randomization
 - **PHYSICIAN INFLUENCE**



Purpose	Number of people who take part
Phase I	
<ul style="list-style-type: none"> ▪ To find a safe dose ▪ To decide how the new treatment should be given ▪ To see how the new treatment affects the human body 	15-30 people
Phase II	
<ul style="list-style-type: none"> ▪ To determine if the new treatment has an effect on a certain cancer ▪ To see how the new treatment affects the human body 	Less than 100 people
Phase III	
<ul style="list-style-type: none"> ▪ To compare the new treatment (or new use of a treatment) with the current standard treatment 	From 100 to several thousand people
Phase IV	
<ul style="list-style-type: none"> ▪ To further assess the long-term safety and effectiveness of a new treatment 	Several hundred to several thousand people

+ Types of Trials

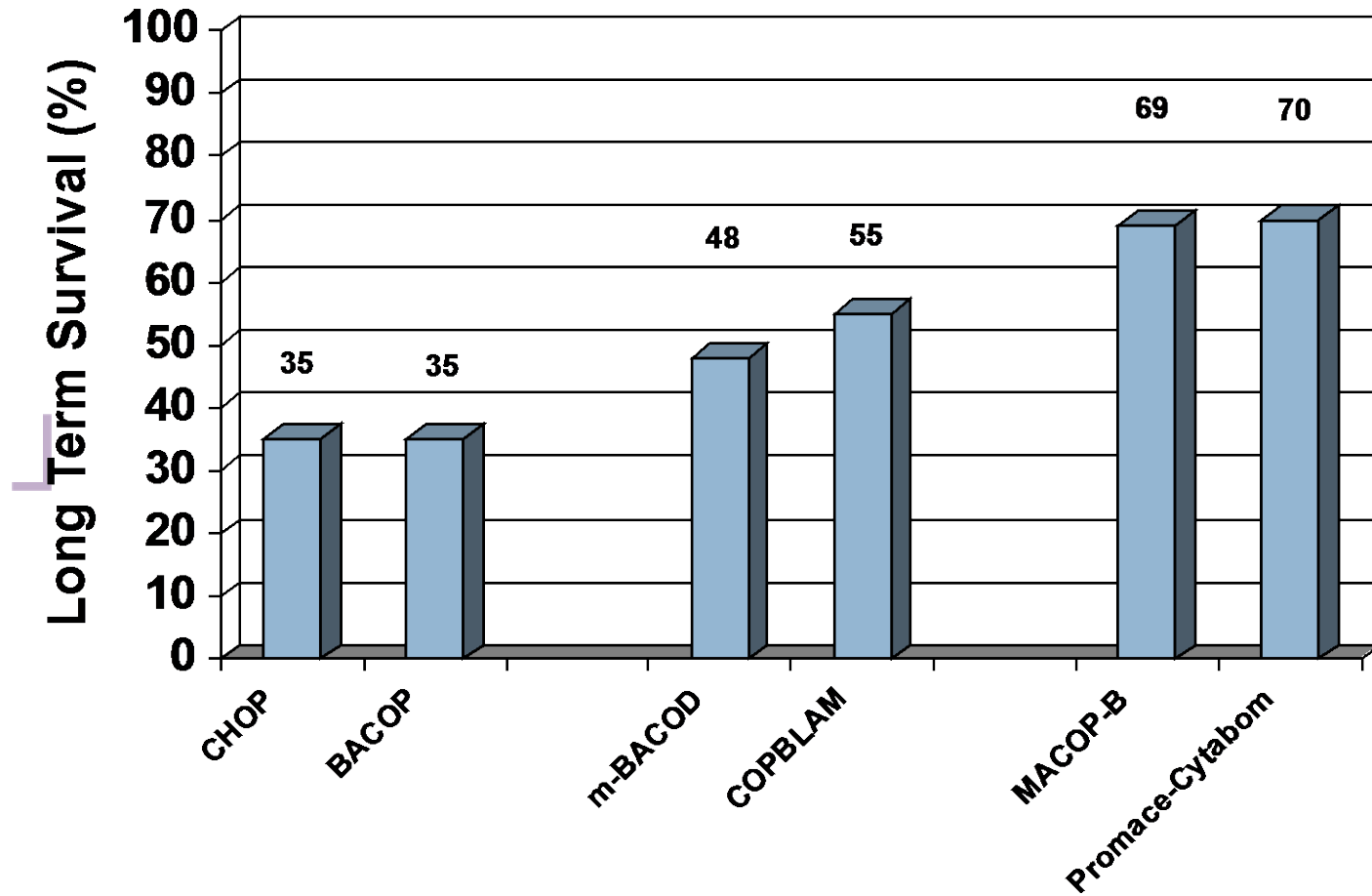
- Investigator initiated:
 - usually single or small # centers
 - sample sizes smaller
- Cooperative group: NCI (C), NCI, SWOG, ECOG, EORTC, CALGB
- Pharmaceutically driven



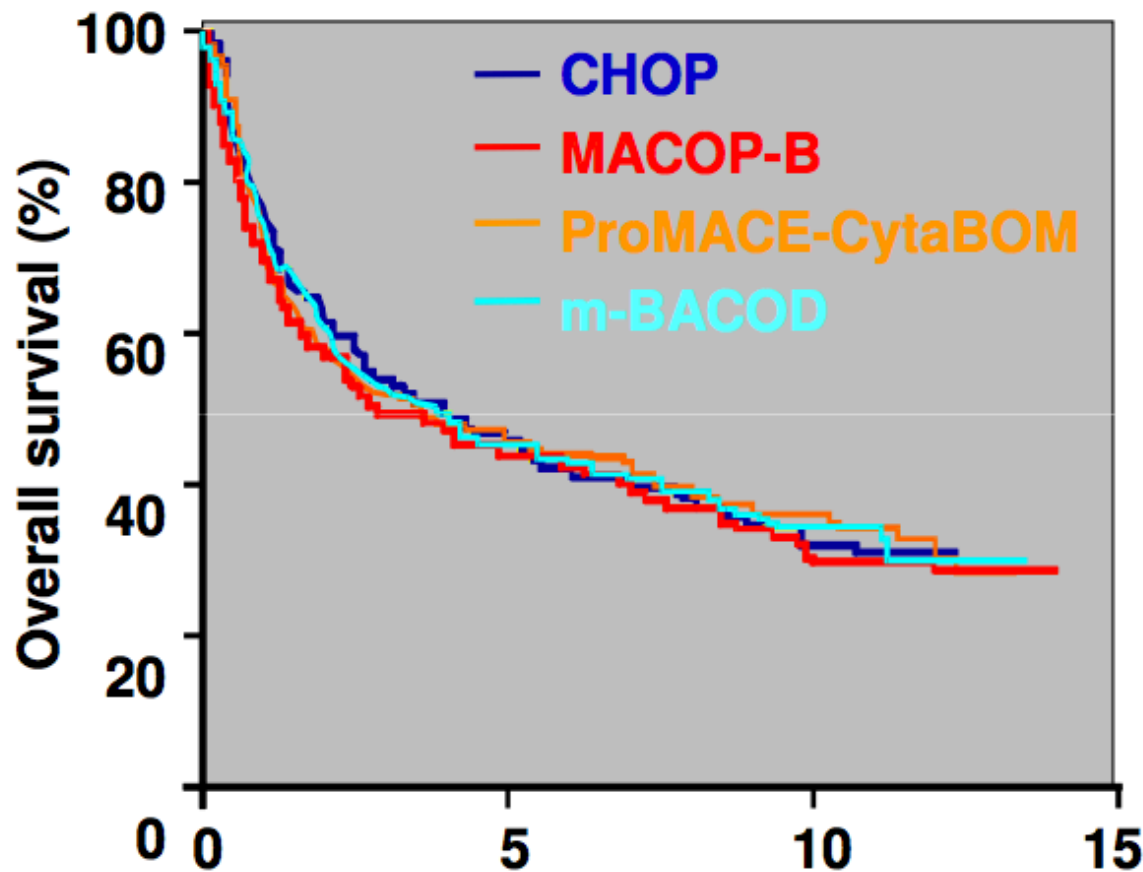
+ Why are phase 3 trials important?



Anthracycline-Based Chemotherapy Regimens

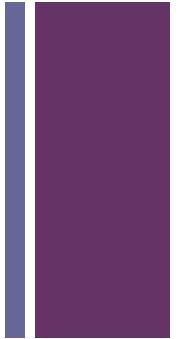


+ Comparison of 4 Anthracycline-Based Regimens in DLBCL





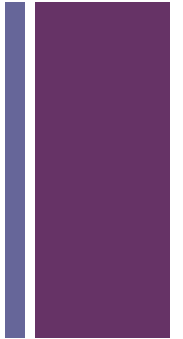
Clinical trials follow strict guidelines and protocol



- The reason for doing the study
 - The hypothesis
- Who can join the study and who cannot
- How many people are needed for the study
- Any drugs they will take, the dose, how often
- What medical tests they will have and how often
- What information will be gathered about them



Inclusion/Exclusion criteria



- Inclusion Criteria
 - Certain type of and stage of cancer
 - Certain kinds of therapy (or untreated)
 - Being a certain age group

- Exclusion criteria
 - Safety
 - Accurate and meaningful study results

+ Randomization

- Is used in all phase III and some phase II trials
 - Essential for getting drugs licensed
- If you are randomized to a control group: standard therapy
- If you are randomized to the investigational group, you will get the new treatment being tested
- Randomization is by chance
 - 1:1
 - 2:1
 - 3:1

**PLACEBOS ARE ALMOST
NEVER USED IN ONCOLOGY
TRIALS**

+

Really Good Clinical Trials

Double blind is
a curse when
you're the Dr.!

I hate
blinded
studies!

Is that
you, Liz?



+ PROS and CONS

PRO

- High quality cancer care: VIP
- If new treatment proven to work and you are receiving it, you may be the first to benefit
- Help others by furthering science
 - Tissue samples
- Free to you –
 - often parking covered or subsidized
- Active role in a decision that affects your life

CONS

- New treatment may not be better than SOC
- More visits and tests
- If randomized, you may not get the experimental agent/intervention
- May not work for you
- Worse or unexpected side effects

+ Side effects

The UQT-2 stopped my cancer but my skin turned blue and my foot fell off and uh, other stuff...

Is that a problem, sir?

Clinical Trial Headquarters



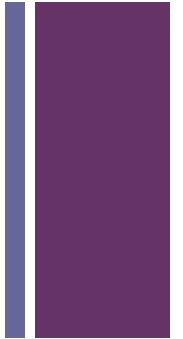
Uhhh, this sounds silly, but somehow you seem taller!

Oh that! New meds, minor side effect, that's all.





How can I be sure my safety is protected?



- Federal rules ensure that clinical trials are run in an ethical manner.
- Your rights and safety are protected by
 - Informed consent
 - Review by two panels:
 - Scientific review
 - IRB or REB
 - Ongoing monitoring by the
 - IRB
 - Data safety monitoring board
 - Your research team
 - Built in dose reductions, delays, discontinuation rules

+ How's this? "Contraindications exacerbate primordial apsrption at the microcellular level."

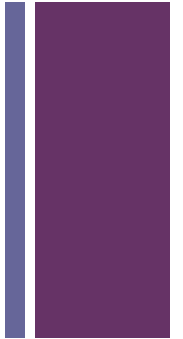
Totally confusing!
Good job! Print it!



Axman



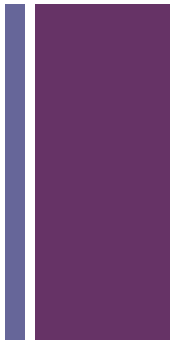
What about confidentiality?



- Clinical trials staff are governed by ICH GCP regulations and **Health Insurance Portability & Accountability Act (HIPAA)**
- Patient data is anonymized
- Regulatory bodies may have access to original charts
- Data stored in locked and password protected environments



Questions to ask your doctor



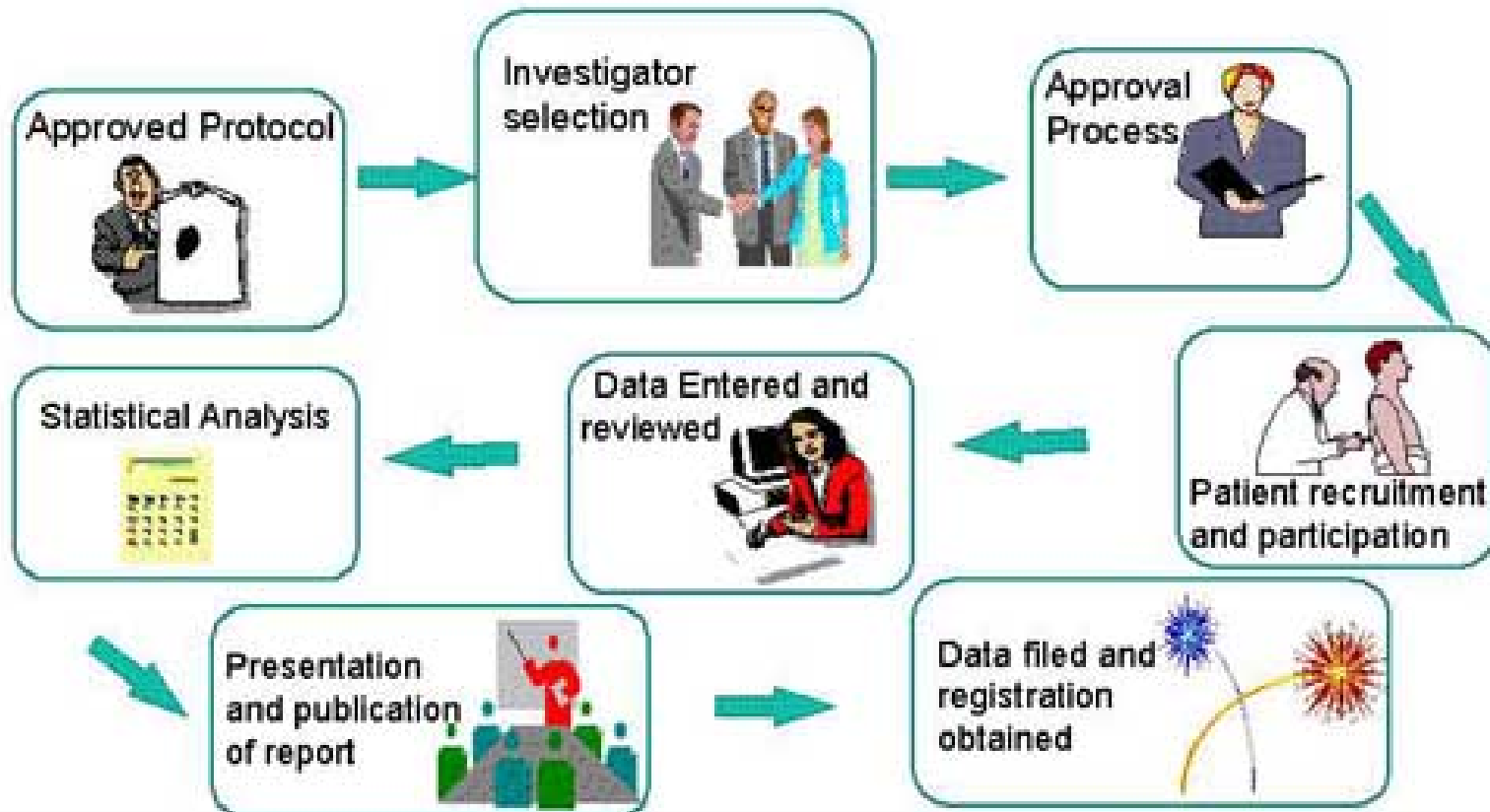
- Why is trial being done?
- How long will I be in the trial?
- What kinds of tests and treatments are involved?
- What are possible side effects and risks?
- What are possible benefits?
- How will I know the treatment is working?
- What will it cost me?
- How will it affect my daily life?
- What are other treatment options including standard treatments?
- Is this treatment curative?

+ What have clinical trials taught us in lymphoma?

- That rituximab added to most B cell lymphomas improves overall remission rates, depths of remissions, lengths of remission and overall survival
- That Rituximab added to FC chemotherapy for CLL has the same effect
- That some types of large cell lymphoma may be more responsive to bortezomib or lenalidomide
- That lower dose radiation added to 2 cycles of chemotherapy for good prognosis limited stage Hodgkin's is just as good as higher dose radiation and 4 cycles of chemotherapy
- That bendamustine is a very active drug in B cell lymphoma
- That ofatumumab is an antibody that works for CLL that relapses after or is refractory to fludarabine
- That PET scanning after therapy for Hodgkin's lymphoma is a good tool to help predict lower or higher risks of relapse
-To name but a few

+ How long does it take?

Clinical Trials in a Nut Shell





Where can I find clinical trials

- Ask your doctor first

Internet:

- **NCI PDQ**

- www.clinicaltrials.gov

- **OICR**

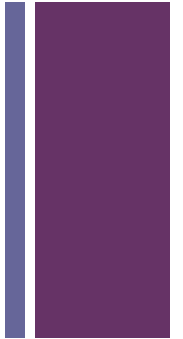
- <http://www.ontario.canadiancancertrials.ca>

- **Canadian Partnership Against Cancer**

- CanadianCancerTrials.ca

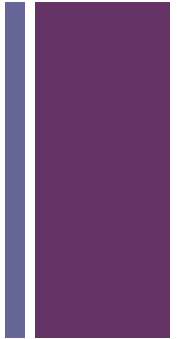
- **NCIC Clinical Trials Group**

- www.ctg.queensu.ca





In Summary: You should always ask about clinical trials



- Clinical trials are responsible for the innovations in therapy that change the natural history of disease
- They are as safe as they can be
- At the worst, you will get standard of care: placebos uncommon
- You can stop whenever you want
- You may personally benefit



+ THANK YOU!

