LYMPHOME CANADA

Understanding clinical research trials

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Goals of this presentation

- Better understand clinical research trials
  - What are they?
  - What are they for?
  - As a patient
    - Why should I be interested?
    - Are they safe?

A clinical research trial

- Study conducted in humans
- Objectives
  - Improve the diagnosis, prevention and treatment of a medical condition
  - Improve the quality of life associated with a medical condition or its treatment
  - Expand understanding of this medical condition

https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics

Developing a clinical trial

- The starting point is a specific question
- Examples
  - Does a new product have an anti-cancer effect?
  - What is the optimal dosage of a new treatment?
  - Is the new anti-cancer treatment better than the one now being used?
    - In terms of efficacy?
    - In terms of tolerability?

Development of a clinical trial

- A clinical trial can be conducted of
  - A new therapy developed in the laboratory
  - A promising therapy in an animal model
  - A drug already used on humans but for a different disease, a different dosage or a different route of administration
  - A new combination of already known drugs

- A clinical trial
  - Ensures a rigorous/safe framework
  - Seeks accurate and precise results

Methodology

- The number of participants and their monitoring is defined by statistical calculations based on the study objectives, among others

- For example: a study that evaluates the safety of a new drug will require fewer participants than a study that compares the response time to two different therapies

Methodology

- Interim statistical analyses (before the study ends) may be planned to ensure the safety of the participants

- The best interest and the safety of the participants are in the forefront

Eligibility for a clinical trial

- Inclusion and exclusion criteria are predefined
  - No exception or deviation allowed!
  - This is related to the safety of the participants and the validity of the study!
- The inclusion and exclusion criteria may be related to
  - The participant's medical history
    - Cytopenia, kidney or liver function
    - Prior hepatitis B
    - Treatments received previously
  - The histology involved
    - A study of follicular lymphoma cannot include participants with a chronic lymphoid leukemia
- The recruiting time for a trial is limited
  - Even if you satisfy the criteria, if the study is closed, you cannot participate in it

Principal types of clinical research trials

- Phase 0
  - Analysis of human body reactions exposed to the drug
  - Rarely used and very few participants
- Phase I
  - Safety analysis and finding the optimal dose
- Phase II
  - Evaluate the effectiveness of a new treatment
- Phase III
  - Compare a new treatment with the standard treatment standard
- Phase IV
  - Find long-term side effects

Phase I

- Find the dose and optimal administration route
- Safety analysis
  - Phase I is often the first time that a particular drug (or combination) is used in humans
  - Phase I may also be the first time that a known drug is used for a new indication
    - Example: using a drug that is approved and effective with myeloma against lymphoma
  - Analyses of pharmacokinetics
  - Very close monitoring of side effects in small groups
  - Efficacy of a product explored in future phases

Phase II

- Focus on efficacy
- More participants than Phase I (often < 100)

Phase III

- Compares the efficacy of an innovative treatment to the current standard treatment
- Even more participants than in Phase II trials
  - Often > 100 to + 1,000 participants
  - Usually takes place at several sites, cities and/or countries

Phase III has the most impact

on medical practice

Cancer.ca

Phase III: randomization

- A randomized phase III study offers various therapeutic options and the participants are directed toward one of these options by chance
- Neither the principal investigator nor the patient can choose the treatment option

http://www.ger.ethique.gc.ca/fra/policy-politique/initiatives/tcps2-eptc2/chapter11-chapitre11/

Phase III: randomization

- Clinical equipoise
  - Basic principle justifying randomization
  - Ethical principle is that there is genuine uncertainty in the expert medical community about the best choice of treatment among the options studied
- If a study is randomized, it means that there is not enough information to determine which of the therapeutic options is best
- The objective of the study is thus to define the best option

http://www.ger.ethique.gc.ca/fra/policy-politique/initiatives/tcps2-eptc2/chapter11-chapitre11/

Phase III: study with placebo

- The use of the placebo must
  - Be described in the information and consent form
  - Be justified and accepted by the Ethics Committee

Phase III: study with placebo

- Example
  - Is the addition of oral treatment X to standard intravenous treatment Y beneficial?
  - The proposed study could have 2 treatment options
    1) Intravenous treatment Y + oral treatment X
    2) Intravenous treatment Y + placebo
  - The placebo makes it possible to truly isolate the additive effect of oral treatment X from the known benefit of intravenous treatment Y

Phase III: study with placebo

- The use of the placebo may be hidden from the participant +/- the principal investigator
  - Even if described in the information and consent form

	The participant knows if he is getting the placebo	The researcher knows if the participant is receiving the placebo
Single blind	No	Yes
Double blind	No	No

- If your state of health requires, it is always possible to find out if you are receiving the experimental drug or the placebo

Phase IV

- Seeks the benefits or delayed side effects that may occur once the drug is approved

Safety of clinical trials

- The trials are subject to strict regulations intended to avoid negligence or abuse of participants
  - Helsinki Declaration
  - *Good clinical practices* (international)
  - Health Canada *Division 5 Regulations*
  - Random external auditing/monitoring
    - Study sponsor
    - Health Canada
    - *Food and Drug Administration (FDA)*

Respect for the protocol is essential for the safety of participants in the clinical trial

Safety of clinical trials

- The Research Ethics Committee of the Institution is in the forefront of trial approval
- It consists of at least 5 persons
  - 2 members with scientific expertise
  - 1 member with knowledge of research ethics
  - 1 member with knowledge of the Canadian law applicable to the protocol
  - 1 member with expertise in a non-scientific field
  - 1 member of the community or 1 interested independent member

Safety of clinical trials

PARTICIPATION

MUST BE FREE AND INFORMED

Safety of clinical trials

- When a research protocol is proposed, the potential participant is given and information and consent form
- This form provides written documentation in clear language about such aspects as
  - The invitation to participate in the study, its purpose, the identity of the investigator and the sponsor of the trial
  - The nature and duration of participation
  - Potential benefits
  - All associated reasonably foreseeable risks

Safety of clinical trials

- The information and consent form also provides information about
  - Possible financial compensation
    - Example: parking fees for additional medical visits
  - The possibility of marketing the research results

Safety of clinical trials

- The principal investigator and team are available to answer your questions

- A reasonable amount of time is allowed to properly read the documentation and understand it
  - You are welcome to talk to your family about the trial if you want

Safety of clinical trials

- Participants can be withdrawn from the trial at any time
  - NO JUSTIFICATION REQUIRED
- Participants may also decide to have their data or biological materials withdrawn

Participating in a clinical trial?

- Potential risks
  - Ultimately, the experimental treatment may not be any better than the standard treatment standard
  - You could be randomized to the standard therapeutic option and not to the experimental therapeutic option
  - Unexpected side effects could occur
  - There may be more medical visits, tests and/or imaging

Participating in a clinical trial?

- Potential advantages
  - Have access to experimental therapies before their possible approval
  - Medical monitoring is sometimes more intense
  - You could contribute
    - To the advancement of knowledge about lymphoma
    - Potentially to the improvement of lymphoma treatment and prognosis

You are interested in participating in a clinical research trial

- Speak to your doctor
- http://www.lymphoma.ca/fr/lymphome/cheminement-du-patient/diagnostic/trouver-des-essais-cliniques

In conclusion

- Clinical research trial in lymphoma
  - Study conducted in humans
  - Intended to improve lymphoma management
  - Safe and rigorous framework
- Clinical trials are essential
  - Impossible without participants
    - Always free and informed participation
    - Pride from contributing to progress in modern medicine