Introduction

The Leukemia/Bone Marrow Transplant (BMT) Program of British Columbia (BC) is committed to advancing our knowledge of blood disorders and meeting the needs of patients for whom we provide care. The advancement of knowledge can be achieved through research. Research currently ongoing within the Leukemia/BMT Program includes translational research via the Hematology Cell Bank of British Columbia (BC) and clinical trials research through the Hematology Research and Clinical Trials Unit (HRCTU).

The purpose of this document is to help you understand more about how new treatments are developed, how to evaluate the benefits and risks of a clinical research trial for yourself and what questions to ask to decide if a clinical research trial is right for you.

Acknowledgement

The HRCTU and Leukemia/BMT Program of BC would like to acknowledge patients for their contribution to scientific knowledge and advancement in the treatment of blood disorders.
Frequently Asked Questions

What is clinical research?

Research is an incremental process that moves forward in small and carefully planned steps. Usually research begins as basic science in the lab and after years of testing in cells and tissues, testing is done on animal models using human cells. After treatments prove successful in animals, these treatments may be tested on people through clinical research trials.

New Drug Development

1. Discovery of new drug in lab
2. Drug tested in lab and on animals
3. Health Canada approves Investigational New Drug applications
4. The drug can now be tested on humans in a clinical trial
Research is an incremental process that moves forward in small and carefully planned steps.

What is a clinical research trial?

A clinical research trial is a research study designed to answer questions about the safety and effectiveness of a drug or treatment. These research trials follow a rigorous scientific process with built-in safeguards for patients who volunteer and are selected for research. Most clinical research involves the testing of a new drug in an orderly series of steps, called phases. The process starts with small trials testing the safety of a treatment and then moves towards progressively larger trials. The larger trials compare the safety and effectiveness of the new therapy to the currently accepted standard of care.

It is important to remember that in a clinical research trial, researchers do not know if the new treatment will be more effective than the current standard of care treatment.

Why carry out a clinical research trial?

In a clinical research trial, the focus of the research is to find out if:

- a new treatment is safe
- a new treatment is better, the same, or not as good as what is currently being offered.

Clinical research trials also help scientists and physicians to answer various questions about new therapies such as: What diseases should they be used for? What dose of a new drug is most effective? Which patients can benefit most?

When new treatments prove to be safe and effective, they are made available to the public.

What are the phases of a clinical research trial and what do they mean?

To participate in a clinical research trial, patients must first meet screening criteria. The tables on the following pages provide details on each phase of a clinical research trial.
### Phase I Trials

**Summary**
- Earliest trials in the life of a new drug or treatment
- Usually smaller trials; recruitment is low from 15 to 50 patients
- Since Phase I trials are usually the first time a drug is given to a patient, the first few patients, or cohorts, are given a small dose of the drug.
- The dose is then gradually increased with each group. The effect is monitored until the best dose is determined.
- Phase I trials require significant time commitment from patients because they involve frequent blood tests and side effects monitoring.
- Often patients with a cancer that lacks or does not respond to standard treatment participate.

**Objectives**
- To determine safe dose range
- To determine side effects
- To determine how the drug works in the body (pharmacologic behavior) and how the body copes with and excretes the drug (pharmacokinetic studies)
- To determine how well the drug works (efficacy)

**Benefits**
- Patients may not directly benefit from participating in the clinical research trial.

**Risks**
- Unpredictable side effects can occur.

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### Phase II Trials

**Summary**
- To evaluate the effectiveness in a larger population, usually less than 100 patients
- Often focus on cancers for which no effective treatment exists or that are most likely to show a response to therapy
- All patients receive the same dose.

**Objectives**
- To assess effectiveness of drug or therapy
- To assess for additional safety information

**Benefits**
- Patients may not directly benefit from participating in the clinical research trial.

**Risks**
- Unpredictable side effects may occur.
- Trials are often too short to determine long term benefits.
Phase III Trials

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<tr>
<th>Summary</th>
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<tr>
<td>• Large trials with 100+ patients</td>
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<td>• Multi-centre, often global</td>
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<td>• Survival time and quality of life measured</td>
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<td>• Subjects are ‘randomized’ to a group: the Study Group — receiving study therapy, or the Control Group — receiving standard of care.</td>
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<table>
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<tr>
<th>Objectives</th>
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<td>• To determine whether a new therapy or drug is more effective or has fewer side effects than standard of care</td>
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<th>Benefits</th>
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<td>• Patients may not directly benefit from participating in the clinical research trial.</td>
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<th>Risks</th>
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<td>• New treatments are not always better than or even as good as standard of care.</td>
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<td>• Side effects may be worse than those associated with standard of care.</td>
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<td>• Unexpected side effects may occur despite preceding Phase I and Phase II trials.</td>
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What types of research trials are being conducted by the Leukemia/BMT Program?

• Drug therapy: new chemotherapy drugs or a new combination of drugs
• Targeted drug therapy: drugs designed to interfere with cell functions of specific cancer cells, resulting in cancer cell death
• Stem cell transplantation procedures
• Supportive therapy: treatments to reduce disease or treatment-related side effects such as infection
• Translational research (see Hematology Cell Bank of British Columbia section on page 11)

What is it like to be treated in a clinical research trial?

The clinical research trial process depends on the kind of trial being conducted. The research team includes doctors, nurses and other health care professionals. They check the health of the patients at the beginning of the trial, give specific instructions for participating in the trial, monitor the patients carefully during the trial, and stay in touch after the trial is completed. Some research trials involve more tests and doctor visits than the patient would normally have for an illness or condition. For all types of trials, the patient works with a research team. Clinical research trial participation is most successful when the research protocol is carefully followed and there is frequent contact with the research staff.
How are research trial patients protected?

All research protocols in Canada are conducted according to Good Clinical Practice (GCP). GCP is an international ethical and scientific quality standard. It provides guidance for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical research trials. GCP provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Before a research protocol can be put into practice, it must obtain two levels of approval: Health Canada (national regulatory agency) and an independent Ethics Committee. Approval at these two levels ensures that the research protocol is scientifically sound, that it adheres to GCP and local regulations and that the safety of the patient is not jeopardized (i.e., the potential benefits outweigh the risks associated with the new drug). Ethics Committees are composed of an independent group of professionals designated to review and approve the research protocol, Informed Consent Forms, study advertisements, and patient brochures to ensure that the study is safe and effective for human participation.

In the Leukemia/BMT Program, a committee of nurses and doctors reviews all clinical research trials proposed by the Leukemia/BMT Program. The purpose of the Review Committee is to ensure that the research trials meet the needs of patients in the Leukemia/BMT Program. Once the research protocol has been accepted by the Leukemia/BMT Program Review Committee, the research protocol must then be approved by the Ethics Board. Before a trial can go ahead, the Ethics Board must be satisfied that the research trial addresses an important scientific question, is well-planned, is as safe as possible for the patients, and is ethically sound.

Before participating in any clinical research trial, patients must sign a consent form to ensure that they are fully informed and thoroughly understand the research protocol and the risks and benefits of their participation.
How is my confidentiality protected in a research trial?

What is PIPEDA?

The Personal Information Protection and Electronic Documents Act (PIPEDA) is part of the Canadian Privacy Law and establishes principles for the collection, use, and disclosure of personal and identifiable information that is part of commercial activity (e.g., physician practices, pharmacies, private labs, pharmaceutical companies, etc.). PIPEDA requires obtaining consent for the collection of personal and identifiable information, informing research patients of their privacy rights and providing them with an opportunity to know what personal information is being collected, for what purpose, how it will be used, disclosed, and protected.

Your medical information is confidential, but individuals involved in monitoring the conduct of the research and recording information on the treatments may need to access your records in the presence of hospital research personnel. These individuals may be representatives of the research sponsors, such as the National Cancer Institute of Canada (NCIC) or the drug company supplying the trial drug. They may also be representatives from regulatory bodies such as Health Canada’s Health Protection Branch.

Any forms or paperwork recording your information and results will identify you by a code number only, and your name will never appear in any publications resulting from the research.

What are my rights if I participate in a research trial?

You do not waive or sign away your legal rights by signing consent to a research trial. Taking part in research is voluntary. This means you may choose not to take part, or may withdraw your consent and leave the research trial at any time. If you withdraw from or decline a research trial, your doctor will discuss further treatments with you and continue to treat your disease with the best means available. If there are other clinical research trial opportunities relevant to you later in your treatment, these will be offered to you.

Am I eligible?

In addition to you deciding whether the research trial is right for you, your hematologist will have to make sure you are right for the research trial. All patients must meet the eligibility criteria as written in the research protocol. After the consent form is signed, tests to determine the status of your disease and other baseline tests, such as blood, urine, or heart tests may be necessary to determine your eligibility.
What questions should I ask the research staff?

- What treatment options are available to me?
- Why is this research being done? What other clinical research trials with this medication have been done?
- Will I get a placebo?
- What inconveniences would I face as part of participating in the trial?
- How much additional time is required to participate in this trial?
- How long is the research trial?
- Will I have responsibilities such as keeping a record or filling out forms about my health?
- What are the main side effects of the research medication?
- What are the possible risks to me, compared to standard treatment?
- What are the pros and cons of participating in this clinical research trial?
- Will there be reasonable reimbursement of the cost of my travel for research visits?
- What if I change my mind?
- What happens when the research is over?
- Can I take my regular medications while participating in this research?

Questions to Ask Yourself

- Do I feel comfortable receiving a treatment whose risks and benefits are somewhat unknown?
- Can I dedicate the time needed to participate in this research trial?
- Will I be able to manage if taking part in the research trial means I might miss more work?
- Am I satisfied that my decision is right for me, and not a decision that is being made to please someone else?
- Do I have supportive family, friends or caregivers who can help me if I experience special problems such as nausea, tiredness, headaches, diarrhea?
What questions should I ask myself to decide if entering a clinical research trial is right for me?

• Do I feel comfortable receiving a treatment whose risks and benefits are somewhat unknown?
• Can I dedicate the time needed to participate in this research trial?
• Will I be able to manage if taking part in the research trial means I might miss more work?
• Am I satisfied that my decision is right for me, and not a decision that is being made to please someone else?
• Do I have supportive family, friends or caregivers who can help me if I experience special problems such as nausea, tiredness, headaches, diarrhea?

Where can I find more information?

Additional information can be found on the following web sites:

• **BC Cancer Agency**
  www.bccancer.bc.ca

• **BC Cancer Agency Research Ethics Board**
  www.bccancer.bc.ca/RES/REB/default.htm

• **Health Canada – Drug & Health Products**
  www.hc-sc.gc.ca/dhp-mps/prodpharma/index_e.html

• **Canada Trials**
  www.canadatrials.com

• **Canadian Cancer Society**

• **Leukemia & Lymphoma Society: Fighting Blood Cancers**
  www.LLS.org

• **ICH Guidance E6: Good Clinical Practice: Consolidated Guidelines**

• **Dana-Farber Cancer Institute**
  www.dana-farber.org

• **Clinical research trials.gov**
  www.clinicaltrials.gov

• **Centerwatch**
  www.centerwatch.com

• **US Food & Drug Administration (FDA)**
  www.fda.gov/oashi/clinicaltrials/clintrialdoc.html
Hematology Cell Bank of British Columbia
What is the Hematology Cell Bank of BC?

The Hematology Cell Bank of BC is a bank that stores human specimens. These specimens may include samples of blood, bone marrow and other tissues. We call the bank a ‘Cell Bank’ because it is the cells within the blood and bone marrow that are stored and used by scientists for research purposes.

With your written consent, specimens are collected when a routine medical procedure, such as blood work, is performed. The specimens are stored in the Cell Bank for scientists to use for research. Specimens donated to the bank are not used for blood transfusions or for transplant purposes. These donated specimens are used solely for research purposes.

Scientists who wish to use specimens stored in the Cell Bank must meet the requirements of the BC Cancer Agency Research Ethics Board (an independent ethics board that reviews all scientific research projects that use human specimens). The researcher must also demonstrate to a scientific review committee that their work has scientific merit.

At the time of your admission to hospital or when you visit the medical clinic, you will have an opportunity to read the consent form for the Hematology Cell Bank of BC and decide if you would like to participate in this research. Your physician or a clinical research nurse will meet with you and answer any questions you may have. You are free to discuss this with your family or close friends. Whatever decision you make about donating specimens, your treatment will remain the same.

Donating research specimens is completely voluntary and you are free to decline.

Why is research in blood diseases and cancers necessary?

What can research tell us?

“Samples of bone marrow and blood cells from healthy donors and patients with malignant disease, like leukemia, are extremely important to researchers…. Obtaining new understanding about healthy and malignant blood cells and investigating their common and unique properties are key strategies to developing new and more effective ways of treating patients with blood disorders or malignancies.”

Dr. Connie Eaves, Senior Scientist, Terry Fox Lab

Every day the body normally produces billions of new white blood cells, red blood cells, and other cells. Occasionally, something goes wrong with the growth and behaviour of the blood cells and a blood disease or cancer develops. Currently, not much is known about how normal blood cells become diseased or turn
into cancers. Scientists research the development of disease and cancer in the blood to help understand how the blood cells grow and to help develop safer and more effective treatments.

**What is translational research?**

You may hear your physician or researchers in the media talk about ‘translational research’ or sometimes this may be referred to as ‘bench to bedside’ research. What does this mean? As defined by the National Cancer Institute, “Translational research is a term used to describe the process by which the results of research done in the laboratory are used to develop new ways to diagnose and treat disease.” Such discoveries typically begin at the ‘bench’ with basic research in the laboratory and then progresses to the clinical level, or the patient’s ‘bedside’ with new treatments. Scientists provide clinicians with new tools to help treat patients and clinicians provide scientists access to specimens and clinical data to help further research.

**Making a Decision**

You may be feeling very overwhelmed by your recent diagnosis and hospitalization. The physicians and nurses understand that this is a very difficult time for you and your family. You may be approached to make several decisions regarding treatment and research participation with very little time to consider either. Every effort will be made to respect your needs at this time. We encourage you to involve your family in discussions about treatment and research.

Sometimes, decisions about treatment or participation in research need to be decided in a very short period of time. Treatment may begin soon after you are admitted to hospital. You may be admitted to hospital with little warning or preparation. Specific tests may be required to further determine your eligibility to participate in research trials to treat your disease and researchers studying your disease may need specimens before you begin treatment. This may require that you make these decisions the day you are admitted to hospital or the day you have been given a diagnosis of your disease by your physician.
Feeling overwhelmed?

The physicians and clinical research nurses speaking with you about treatment and research participation understand that you may be feeling overwhelmed. Feel free to ask questions.

What kind of human specimens are collected?

**Samples from Patients**

You may have one type of specimen collected or several types. Specimens may be collected at different periods throughout your treatment with the L/BMT Program. These specimens may include:

- Blood samples
- Bone marrow material
  (from bone marrow biopsy procedures or bone marrow harvest)
- Peripheral blood stem cells
- Leukapheresis samples (Leukapheresis is a procedure to reduce the white blood cell count)

**Samples from Healthy Donors**

Specimens donated from healthy individuals help scientists understand how healthy blood cells compare to diseased blood cells. These specimens may be donated by your family member or an unrelated donor at the time they are donating for your transplant. With their consent, a specimen will be collected and stored in the Cell Bank for scientific research. Removing these specimens from the donation will not affect your transplant. These specimens may include:

- Blood samples
- Peripheral blood stem cells
Specimen Donation

What to Expect

With your consent, specimens of blood and bone marrow material will be collected at the time you are scheduled for blood collection, a bone marrow biopsy or bone marrow harvest. The physician or nurse collecting the specimen will concentrate on collecting specimens that are required for your treatment or diagnosis first, research specimens will be collected after these important specimens are obtained.

Specimens are collected at the time you are scheduled to have a pre-planned procedure so that only one needle poke will be required to collect these specimens.

If you are donating peripheral blood stem cells for a transplant, a sample will be taken from the collection bag. You may be asked to have one additional blood sample collected outside of a pre-planned procedure, but you will not be asked to have additional bone marrow biopsies or stem cell collection procedures. Sometimes you may require a procedure called leukapheresis to reduce your white blood cell count. The white blood cells collected from this procedure may also be donated to the Cell Bank.

If you sign the Hematology Cell Bank consent, it is important that you understand that you are agreeing to the collection of samples and clinical information for the entire time period you will be receiving treatment and follow-up (which may last several years depending on your situation).

What if I change my mind?

• Your participation is entirely voluntary.
• You may withdraw at any time.
• Your decision not to participate will not affect the treatment you receive as a patient of the L/BMT Program.
• No further specimens will be collected from you.
• Specimens already collected may be destroyed upon your request.
• Specimens already released to a scientist will not be destroyed.
Providing Personal Health Information

Why do I need to provide information from my health records?

There may be times when a scientist may need to know more about you. This information helps the scientist learn more about the disease and how it has affected you. The information a scientist may need may include:

- The date of your diagnosis
- Your diagnosis
- Your age
- Your gender
- Your general health history
- The treatment you have or will receive
- Your family health history

Privacy and Confidentiality

How will my privacy be protected?

Every effort will be made to protect your privacy. Each specimen donated by you will be given a code number. All information that identifies you will be removed. All scientists who require further health information about you sign a confidentiality agreement. No information identifying you will be released in publications or given at presentations describing the research work. All information that identifies you will be kept behind locked doors or in secure password protected computer files. All requests for clinical data will be closely protected under the oversight of the Hematology Cell Bank of BC.

Research records and medical records identifying you may be inspected in the presence of representatives of Health Canada and the BCCA Research Ethics Board for the purpose of monitoring the research.
Hematology Cell Bank Research

Can I decide what research my specimens will be used for?

You will not be able to decide the specific research your specimens will be used for, just as when you donate blood to a blood bank, you cannot decide which patient will receive that blood. The use of your specimens will be reviewed by a panel of research scientists and clinicians. They will review the scientist’s research proposal to determine the use of the specimens. All research proposals are approved by the BC Cancer Agency Research Ethics Board (an independent ethics board that reviews all scientific research projects that use human specimens).

Will I know the results of the research using my specimens?

Research using human specimens can take a long time. The results of the research may not be determined for many years. You will not be informed of the results of that research, but may hear of important discoveries through your physician. Recent research publications are posted on our website at www.leukemiabmtprogram.com.

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Cited with Permission

Some information in this booklet is cited with permission by:

• BC Cancer Agency
• www.canadatrials.com
• Dana-Farber Cancer Institute
• The Leukemia & Lymphoma Society (LLS)

Notes
Disclaimer:

Please note that the information contained in this manual is not intended to replace the advice of your health care team. Use this as a reference and education guide. Consult your health care team if you have any questions or concerns.