Evaluation of IL-2 Immunotherapy Against Acute Lymphocytic Leukemia

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Background

What Is Acute Lymphocytic Leukemia?

- Acute Lymphocytic Leukemia is a type of cancer of the blood and bone marrow that is a rapidly advancing type of cancer
- The disease causes the bone marrow to create immature blood cells instead of mature ones which is due to the rapidly spreading nature of the cancer
- This is caused when a bone marrow cell develops mutations in its genetic material
- The cells would normally grow and die at a set rate, however with the development of the leukemia, the mutations in the cells genes tell the bone marrow to continue to grow and divide causing blood cells production to be out of control
- The immature cells produced by the bone marrow are called lymphoblasts which are the leukemic white blood cells
- This cancer is most common in children and it is most often curable however in adult cases like the one we are dealing with, the chance of curing an adult is greatly reduced compared to a child

Background

Name of Clinical Trial:

- Evaluation of IL-2 Immunotherapy Against Acute lymphocytic Leukemia

Population Being Studied:

- Adults with later stages of Acute Lymphocytic Leukemia who have not responded to other treatments

Route of Administration:

Our route of administration to treat this leukemia would be to perform intraosseous infusion of the IL-2 drug directly into the bone marrow while the person receiving treatment is under anesthesia.

Cells the Treatment Will Target:

The treatment will target the white blood cells that are cancer causing due to the fact that they have mutations in their genetic material. The IL-2 will stimulate the function and production of T-cells, natural killer cells, and B- cells.

Background

What are any potential/known risks & symptoms of using Interleukin 2?

- Increased risk of infection & possibility of developing Capillary Leak Syndrome.
- Possibility of heart issues such as an irregular heartbeat or chest pain if given in high doses.
- May develop low blood pressure.
- Mild Symptoms:
  - Chills, fever, fatigue, nausea, vomiting, diarrhea, muscle aches, drowsiness, confusion, & swelling in legs or face.
- Less Common Symptoms:
  - Injection site reactions (itchiness, rashes, breathing difficulty), mouth sores, poor appetite, weight gain/loss.

What are potential benefits?

- Interleukin-2 helps increase production of several different components of the immune system found in the blood, including T lymphocytes and natural killer cells.
- If successful, we believe the amount of cancer cells in the body will decrease as clinical studies have been successful against melanomas.

Background

How will the IL-2 treatment will target these cells:

- The IL-2 will target the cancer cells since the leukemia originates in the mutation of white blood cells produced by the bone marrow, injecting the IL-2 directly into the bone marrow will stimulate the development of white blood cells that will attack the cancerous cells. The treatment does not have a way to target only the cancerous cells much like any other type of cancer treatment and with the conclusion of the treatment it may be in the patient's' best interest to receive a stem cell transplant to help produce healthy blood cells leading to a higher chance of completely eradicating the cancer.

How will the treatment will be released into the targeted tissue or cells:

- The treatment will be released via intraosseous infusion into the bone marrow where the white blood cells originate. The patient would would be under anesthesia for this procedure as any injection into the bone marrow is extremely painful.

Background

What the IL-2 treatment will do once inside the targeted tissue or cells:

- Once inside the bone marrow, the IL-2 will work by blocking the reproduction and spread of the cancerous cells. The IL-2 will also help to stimulate the development of white blood cells that attack cancer. The cancer cells that are produced will release chemicals that attract the cancer-killing immune cells to help destroy the cancer cells in the body.

How the IL-2 treatment will destroy cancer cells:

- The IL-2 treatment will destroy the cancer cells because the treatment itself is a group of proteins made by T-Lymphocytes which are part of the immune system that help to develop stem cells in the bone marrow helping to protect the body from infection and helping the body to fight cancer. The T-Lymphocytes produced from the treatment directly work to kill infected cells along with activating other immune cells and producing cytokines that help regulate immune response. The cytokines themselves are crucial in controlling the growth and development of immune system and blood cells. Overall the IL-2 helps to produce the right things in the body to work to kill the cancer cells.

Example of Success Using this Treatment for Another Cancer- Metastatic Melanoma

Example of a trial already being conducted using interleukins:
Interleukin-2 is *a therapy that is systematic. Meaning the treatment reaches the body in all parts through the bloodstream*

- The FDA approved IL-2 in 1998 in order to help treat patients with stage IV (metastatic) melanoma
- The patients have to receive IL-2 in a hospital, under a physician qualified to distribute IL-2 in order to be done safely and properly.

Patients will receive the drug intravenously, meaning (into a blood vein) through infusion in a treatment course of two cycles:

- Three times per day for five days
- Seven to 10 days of rest
- Three times per day for five days

Interleukin-2 works by:

- Blocking the reproduction and spread of cancer cells
- Stimulating the development of white blood cells that attack cancer
- Causing cancer cells to release chemicals that attract cancer-killing immune system cells

Trial Objectives & Purpose

Trial Objectives & Purpose

What are our goals for this clinical trial?

- Using interleukins to stimulate an immune response to eliminate a significant amount of cancer cells.
- To slow the progression of the growth & spread of Acute Lymphocytic Leukemia.
- To potentially cure adults with further progression of Acute Lymphocytic Leukemia.

Trial Objectives & Purpose

Our Hypothesis:

If you inject interleukin 2 into the femur, containing bone marrow, then the cancerous white blood cells will be killed from the route of where they start to grow because IL-2 will stimulate the function and production of T-cells, natural killer cells, and B- cells in turn killing the cancer cells and stopping the leukemia from spreading throughout the body.

Trial Objectives & Purpose

What is currently being used to treat Acute Lymphocytic Leukemia?

- Chemotherapy
- Radiation therapy
- Chemotherapy with stem cell transplant
- Targeted therapy

How is using Interleukin-2 better than the other treatments for Acute Lymphocytic Leukemia?

- Using Interleukin-2 would be better because the symptoms of using Interleukin-2 as not nearly as severe as the symptoms patients may experience using Chemotherapy or Radiation.
- This therapy has also shown extreme promise in trials against metastatic melanoma which is an extremely aggressive and rapidly growing cancer as well.

Trial Design

Trial Design

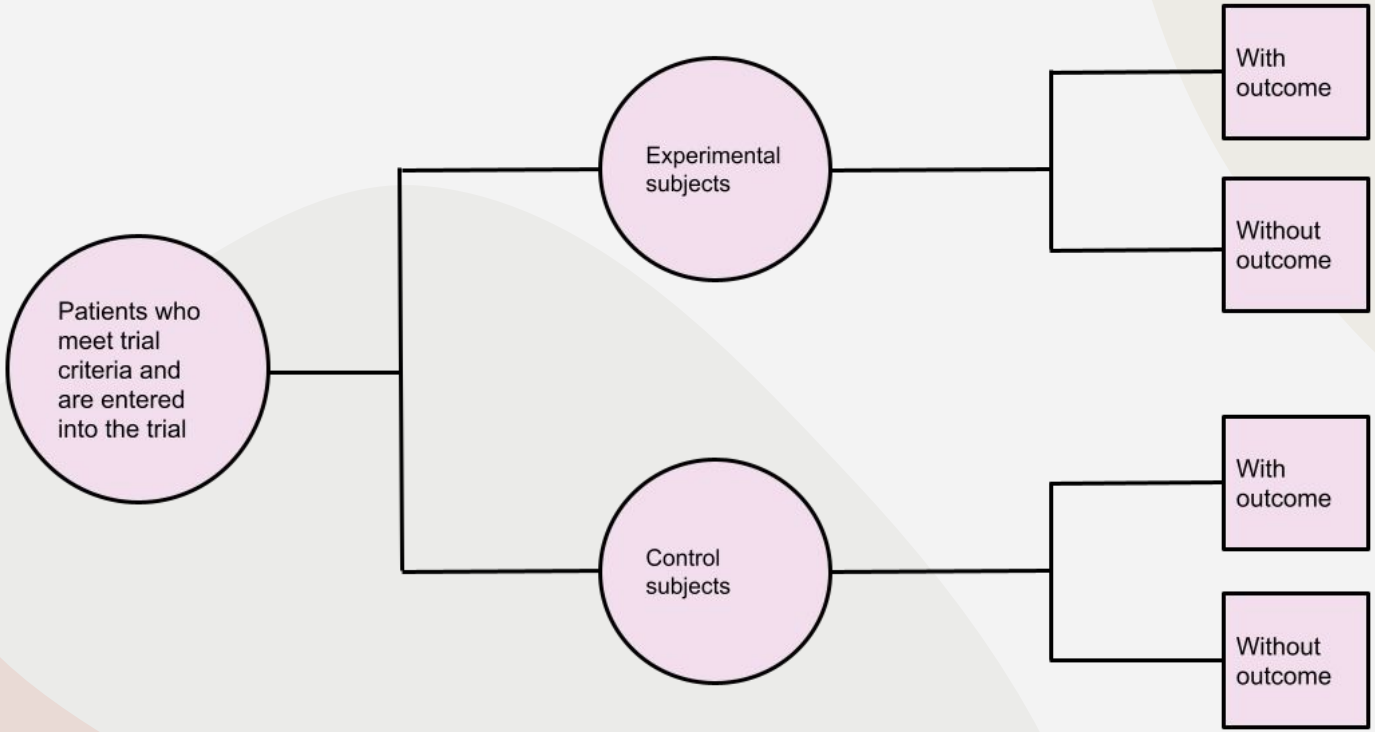
What type of Clinical Trial is it?

- Our Clinical Trial for the Evaluation of IL-2 Immunotherapy against Acute Lymphocytic Leukemia will be double blind placebo controlled.
- It is best for the trial to be double blind placebo controlled because there would be no bias in who is being selected to receive the placebo versus the IL-2, resulting in the trial being completely random.
- The randomization would result in better results because a variety of patients would be selected, so the results wouldn't be for a specific sample, but rather a larger population of people.

Trial Design Brief Overview

- Possible Candidate will undergo a series of diagnostic tests to determine eligibility for the trial.
- 150 candidates will be accepted into Phase 1 of the trial, if results are promising more will be later accepted.
- Trial will start with patients already at the hospital and being prepared to undergo anesthesia.
- Once under anesthesia, injection site will be sterilized and doctors will use an intraosseous infusion to inject interleukin directly into the bone marrow.
- Participants will remain in hospital during the entirety of the clinical trial in order to monitor the progress of the Interleukin-2 and monitor the patient if any problems arise as a result of the injection.
- There will be a rest period of about 7-10 days between each cycle which will last three to five days with one round per day to allow the Interleukin-2 to take into effect and allow the body rest between treatments.
- Throughout the course of the trial, participants will undergo several tests to monitor the progression of the cancer to identify whether or not the Interleukin-2 is working.

Schematic Diagram



Selection of Subjects & Safety

Selection of Subjects

Who is able to participate in this Clinical Trial and what criteria must they fit?

- Participants must be adults who are ages 30 and up and are at later stages of Acute Lymphocytic Leukemia and who have tried several other treatments and have not had a positive response to them.
- The trial is limited to ages 30 and up because as stated in an article on *Ash Publications* by Nicolas Boissel and André Baruchel, studies have proven that pediatric treatments performed on adolescents to age 20 have shown a high success rate of 70%.
- Patients with underlying health conditions such as a weak immune system will not be able to undergo this trial due to the need to limit confounding variables during the experiment.
- Participants must have also shown no improvement in other treatments because this is a last resort option due to it being a clinical trial that would be in its early stages and nothing has been proven to be effective yet.

Safety Procedures

- Before being allowed to participate in the trial, the patient(s) will undergo numerous tests and questioning to ensure they coincide with the guidelines for the trial
- Patients who have underlying health conditions besides the cancer will not be allowed to participate in the trial as to avoid further weakening of already weak immune systems as well as avoid the skewing of our results during the trial
- Patients will be continuously monitored and taken care of during the trial to ensure they are kept as healthy as possible
- Because of the volume of IL-2 a patient will be receiving per day, there will be seven to ten days of rest between each cycle which will last three to five days with one round per day because we are directly injecting the IL-2 into the bone marrow
- Due to the level of pain experienced with an infusion directly into the bone marrow patients will be sedated to keep them as comfortable as possible
- Before entering the trial, a patient must consult their doctor and care team to ensure they are eligible and ready to undergo a clinical trial along with the fact that they will be briefed about the entirety of the trial before deciding to enter as well

Safety Procedures

- The trial will be done in phases and as the trial looks more promising and is producing positive results, we can move into next phases that are within larger groups of people
- There will be written documents of safety protocols that patients and trial staff will be required to follow in order to make sure the trial is done safely and in a controlled environment
- There will also be a data and safety monitoring plan put in place to ensure the quality and safety of the trial at all times
- There will be strict rules provided by the Federal Government regarding the trial to ensure that participants are safe
- The trial has to be approved by the Institutional Review Board before beginning treatment on any patients
- The trial will be closely monitored by a safety and data monitoring committee who will monitor the results of the study along the way to see if the trial is having a positive or negative outcome
- The informed consent process is a large safety protocol as it informs the patient on anything that they may undergo while in the clinical trial

Sources

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