ForPatients
by Roche

LeukemiaChronic Lymphocytic Leukemia

A clinical study to compare obinutuzumab in combination with venetoclax and obinutuzumab in combination with chlorambucil in people with previously untreated chronic lymphocytic leukaemia who have other medical conditions

A Study to Compare the Efficacy and Safety of Obinutuzumab + Venetoclax (GDC-0199) Versus Obinutuzumab + Chlorambucil in Participants With Chronic Lymphocytic Leukemia

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	21 Countries	NCT02242942 2014-001810-24 BO25323

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A prospective, open-label, multicenter, randomized phase III trial to compare the efficacy and safety of a combined regimen of obinutuzumab and venetoclax (GDC-0199/ABT-199) versus obinutuzumab and chlorambucil in previously untreated patients with CLL and coexisting medical conditions

Trial Summary:

This open-label, multicenter, randomized Phase III study is designed to compare the efficacy and safety of a combined regimen of obinutuzumab and venetoclax versus obinutuzumab + chlorambucil in participants with chronic lymphocytic leukemia (CLL) and coexisting medical conditions. The time on study treatment was approximately one year and the follow-up period will be up to 9 years

Hoffmann-La Roche Sponsor	**Phase 3** Phase

NCT02242942 2014-001810-24 BO25323
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the CLL14 study needed?

Chronic lymphocytic leukaemia (CLL) is a type of blood cancer in which the bone marrow makes too many B-cells (a type of white blood cell). The excess B-cells build up and stop the blood, bone marrow and lymph nodes from working correctly. CLL can be treated with a stem cell transplant, but for most people with CLL, age or other medical conditions prevent them from having this treatment. Standard first treatment includes chemotherapy, such as chlorambucil, given with a targeted therapy (a type of treatment that uses drugs to find and attack specific types of cancer cells with less harm to normal cells), such as obinutuzumab (which is known as 'immunotherapy' because it sticks to CLL cells and helps the body's immune system fight the cancer) or venetoclax (which works by blocking the action of a protein called BCL2 that helps keep CLL cells alive). Chemotherapy can be challenging for older people or people with other medical conditions.

This clinical study aimed to compare the effects, good or bad, of venetoclax in combination with obinutuzumab (a new, chemotherapy-free treatment) versus obinutuzumab in combination with chlorambucil in people with previously untreated CLL. When this study began, the combination of venetoclax and obinutuzumab was an experimental treatment - health authorities had not yet approved it for treating CLL.

Results from this study have led to venetoclax in combination with obinutuzumab being approved for the treatment of CLL by health authorities (U.S. Food and Drug Administration in 2019; European Medicines Agency in 2020). Researchers are not asking new people to join this study. Still, they are continuing to look at the effects of venetoclax in combination with obinutuzumab versus obinutuzumab in combination with chlorambucil over many years in people already taking part.

2. How does the CLL14 clinical study work?

This study recruited people with previously untreated CLL and with other medical conditions. People who took part in this study (participants) were given the study treatment venetoclax in combination with obinutuzumab OR obinutuzumab in combination with chlorambucil for 1 year, or until their CLL worsened, they had unacceptable side effects, or they left the study. The study doctor has seen and will continue to see them regularly for about 9 years after their last treatment dose. These checks are to see how the participants respond to the treatment and any side effects they have. The total time of participation in the study will be about 10 years. Participants can stop study treatment and leave the study at any time.

3. What are the main results measured in the CLL14 clinical study?

The main result measured in the study to see if the treatment worked is the length of time between the start of the study and participants' cancer getting worse.

The other key results include:

- The number of participants that show:
    - smaller tumours after 6 months and at the end of treatment
    - no cancer at the end of treatment
    - no cancer cells in blood or bone marrow after 6 months and at the end of treatment
    - no cancer, smaller tumours, tumours that stay the same, or cancer that worsened by the end of treatment
- How long participants live
- The amount of time between participants' cancer getting better from treatment and then getting worse
- The amount of time between the start of the study and participants' cancer getting worse
- The amount of time between the start of the study and participants starting a new treatment
- The number and seriousness of side effects
- The effect of treatment on participants' symptoms, quality of life, and their immune systems
- How the body processes venetoclax and obinutuzumab

4. Who took part in this clinical study?

The people who took part were at least 18 years old, had previously untreated CLL and other medical conditions that may have prevented them from being given high doses of chemotherapy. People could not take part if they had certain infections or other medical conditions, including CLL that affected the brain or spinal cord, previous cancer, kidney problems, or were pregnant or breastfeeding.

5. What treatment will participants be given in this clinical study?

Everyone who joined this study was split into 2 groups randomly (like flipping a coin) and given:

- Obinutuzumab, as an infusion (into the vein) once a week for 3 weeks in the first month, then once a month for the following 5 months, AND
- Venetoclax, as a pill every day from Week 3 for about 1 year, OR
- Chlorambucil, as a pill or pills (depending on body weight) once every 2 weeks for 1 year

Participants had an equal chance of being placed in either group. This is an open-label study, which means everyone involved, including the participant and the study doctor, know the study treatment the participant had been given.

6. Are there any risks or benefits in taking part in this clinical study?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the study. Most studies involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. Participants were told about any known risks and benefits of taking part in the clinical study, as well as any additional procedures, tests, or assessments they were asked to undergo. All of these were described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical study).

Risks associated with the study drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical study. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants are closely monitored during the clinical study; safety assessments are performed regularly. Participants are told about the known side effects of obinutuzumab, venetoclax and chlorambucil and possible side effects based on human and laboratory studies or knowledge of similar drugs. Participants were told about any known side effects of intravenous infusions and swallowing pills.

Potential benefits associated with the clinical study

Participants' health may or may not improve from participation in the clinical study. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Documented previously untreated CLL according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria
- CLL requiring treatment according to IWCLL criteria
- Total Cumulative Illness Rating Scale (CIRS score) greater than (>) 6
- Adequate marrow function independent of growth factor or transfusion support within 2 weeks of screening as per protocol, unless cytopenia is due to marrow involvement of CLL
- Adequate liver function
- Life expectancy > 6 months
- Agreement to use highly effective contraceptive methods per protocol

Exclusion Criteria:

- Transformation of CLL to aggressive Non-Hodgkin's lymphoma (Richter's transformation or pro-lymphocytic leukemia)
- Known central nervous system involvement
- Participants with a history of confirmed progressive multifocal leukoencephalopathy (PML)
- An individual organ/ system impairment score of 4 as assessed by the CIRS definition limiting the ability to receive the treatment regimen of this trial with the exception of eyes, ears, nose, throat organ system
- Participants with uncontrolled autoimmune hemolytic anemia or immune thrombocytopenia
- Inadequate renal function

- History of prior malignancy, except for conditions as listed in the protocol if participants have recovered from the acute side effects incurred as a result of previous therapy
- Use of investigational agents or concurrent anti-cancer treatment within the last 4 weeks of registration
- Participants with active bacterial, viral, or fungal infection requiring systemic treatment within the last two months prior to registration
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or known sensitivity or allergy to murine products
- Hypersensitivity to chlorambucil, obinutuzumab, or venetoclax or to any of the excipients
- Pregnant women and nursing mothers
- Positive test results for chronic hepatitis B virus (HBV) infection (defined as positive hepatitis B surface antigen [HBsAg] serology) or positive test result for hepatitis C (hepatitis C virus [HCV] antibody serology testing)
- Participants with known infection with human immunodeficiency virus (HIV) or human T-cell leukemia virus-1 (HTLV-1)
- Requires the use of warfarin, marcumar, or phenprocoumon
- Received agents known to be strong and moderate Cytochrome P450 3A inhibitors or inducers within 7 days prior to the first dose of study drug