ForPatients
by Roche

Chronic Lymphocytic Leukemia

A clinical trial to compare venetoclax plus obinutuzumab with fludarabine, cyclophosphamide and rituximab or bendamustine and rituximab in people with chronic lymphocytic leukemia.

A Study to Compare the Efficacy and Safety of a Combined Regimen of Venetoclax and Obinutuzumab Versus Fludarabine, Cyclophosphamide, and Rituximab (FCR)/ Bendamustine And Rituximab (BR) in FIT Patients With Previously Untreated Chronic Lymphocytic Leukemia (CLL) Without DEL (17P) or TP53 Mutation

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	5 Countries	NCT04285567 2019-003327-37 2023-504036-17-00 CO41685

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 Study to Compare The Efficacy and Safety of A Combined Regimen of Venetoclax and Obinutuzumab Versus Fludarabine, Cyclophosphamide, and Rituximab (FCR)/Bendamustine and Rituximab (BR) in FIT Patients With Previously Untreated Chronic Lymphocytic Leukemia (CLL) Without DEL(17P) or TP53 Mutation

Trial Summary:

This study will evaluate the efficacy and safety of venetoclax and obinutuzumab (VEN + G) compared with fludarabine + cyclophosphamide + rituximab or bendamustine + rituximab (FCR/BR) in FIT participants (FIT is defined by a cumulative illness rating scale [CIRS]/ score of #6 and a normal creatinine clearance of #70 mL/min) with previously untreated CLL without DEL(17P) or TP53 mutation requiring treatment. Eligible participants will be randomly assigned in a 1:1 ratio to receive either VEN + G (Arm A) or FCR/BR (Arm B).

Hoffmann-La Roche
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Phase 3
Phase

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Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

All	#18 Years	No

How does the CRISTALLO clinical trial work?

This clinical trial is recruiting people who have a type of disease called chronic lymphocytic leukemia (CLL). In order to take part in this trial, patients must have CLL that they have not previously been treated for.

The purpose of this clinical trial is to compare the effects, good or bad, of different treatments for patients with CLL. In this clinical trial, you will get either venetoclax plus obinutuzumab, or fludarabine and cyclophosphamide plus rituximab, or bendamustine plus rituximab.

How do I take part in this clinical trial?
To be able to take part in this clinical trial, you must have CLL.

You must not have received previous treatment for CLL and you cannot join the trial if you are pregnant.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in the clinical trial, both men and women (if you are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will I be given if I join this clinical trial?
Everyone who joins this clinical trial will be split into 2 groups randomly (like flipping a coin) and given either:

- GROUP A: venetoclax, given as a tablet to swallow, plus obinutuzumab given as an infusion (a slow injection) into the vein

  - Patients in this group will receive 12 rounds of treatment; each round lasts for 28 days
  - Obinutuzumab is given every week for the first 3 weeks of Round 1, then once a month for Rounds 2–6
  - After the first 3 weeks of Round 1, venetoclax is given every day up until the end of the trial
- OR GROUP B: the clinical trial doctor will decide whether you receive fludarabine, cyclophosphamide and rituximab OR bendamustine and rituximab given as infusions (through a drip) into the vein
  - Patients in this group will receive 6 rounds of treatment; each round lasts for 28 days. Clinical trial doctors will decide which of the two treatments available in this group is best for you:
  - Treatment 1: patients will receive rituximab on the first day of each round and fludarabine and cyclophosphamide infusions will be given on the first 3 days of each round
  - Treatment 2: patients will receive rituximab on the first day of each round and bendamustine on the first 2 days of each round

You will have an equal chance of being placed in either Group A or Group B.

How often will I be seen in follow-up appointments and for how long? You will be given the clinical trial treatments venetoclax plus obinutuzumab for 12 months or fludarabine, cyclophosphamide and rituximab/bendamustine and rituximab for 6 months. You are free to stop this treatment at any time. After receiving treatment, you will be seen regularly by the clinical trial doctor. These visits will include checks to see how you are responding to the treatment and any side effects that you may be having.

What happens if I am unable to take part in this clinical trial? If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov

Trial-identifier: NCT04285567

Inclusion Criteria:

- Ability to comply with the study protocol, in the investigator's judgment
- Aged 18 years or older
- Have previously untreated documented Chronic Lymphocytic Leukemia (CLL) according to the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria
- CLL requiring treatment according to the iwCLL criteria

- Cumulative Illness Rating Scale (CIRS) score # 6 and creatinine clearance (CrCl) # 70 mL/min
- Hematology values within the following limits, unless cytopenia is caused by the underlying disease (i.e., no evidence of additional bone marrow (BM) dysfunction; e.g., myelodysplastic syndrome, hypoplastic BM):
- Absolute neutrophil count # 1.0 x 109/L, unless there is BM involvement * Platelet count # 75 x 109/L and more than 7 days since last transfusion, or # 30 x 109/L if there is BM involvement
- Adequate liver function as indicated by a total bilirubin, aspartate aminotransferase, and Alanine transaminase # 2 times the institutional upper limit of normal (ULN) value, unless directly attributable to the participant's CLL
- Life expectancy >6 months
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception and agreement to refrain from donating eggs
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods, and agreement to refrain from donating sperm

Exclusion Criteria:

- Transformation of CLL to aggressive Non-Hodgkin's Lymphoma (NHL)
- Participants with Small Lymphocyclic Lymphoma (SLL) only
- Known central nervous system involvement
- Participants with a history of confirmed progressive multifocal leukoencephalopathy (PML)
- Detected del(17p) or TP53 mutation (valid test within 6-months from screening is required for randomisation)
- An individual organ/system impairment score of 4 as assessed by the Cumulative Illness Rating Scale (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
- History of prior malignancy
- Participants with infections requiring IV treatment (Grade 3 or 4) within the last 8 weeks prior to enrollment
- Evidence of other clinically significant uncontrolled conditions including but not limited to active or uncontrolled systemic infection (e.g., viral, bacterial, or fungal)
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or known sensitivity or allergy to murine products
- Hypersensitivity to fludarabine, bendamustine, cyclophosphamide, rituximab, obinutuzumab, or venetoclax or to any of the excipients (e.g., trehalose)
- Pregnant women and nursing mothers
- Vaccination with a live vaccine # 28 days prior to randomization
- Prisoners or participants who are institutionalized by regulatory or court order or persons who are in dependence to the Sponsor or an investigator
- History of illicit drug or alcohol abuse within 12 months prior to screening, in the investigator's judgment
- Positive test results for chronic hepatitis B virus (HBV) infection (defined as positive hepatitis B surface antigen [HBsAg] serology)
- Positive test result for hepatitis C (hepatitis C virus [HCV] antibody serology testing)
- Participants with known infection with HIV or Human T-Cell Leukemia Virus 1 (HTLV-1)
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the participant's safe participation in and completion of the study
- Received any of the following agents within 28 days prior to the first dose of study treatment:
- Immunotherapy * Radiotherapy * Hormone therapy * Any therapies intended for the treatment of lymphoma/leukemia whether approved or experimental
- Participants who have received the following agents:

- Strong and moderate CYP3A inhibitors/inducers within 7 days prior to the initiation of study treatment * Steroid therapy for anti-neoplastic intent with the exception of inhaled steroids for asthma, topical steroids, or replacement/stress corticosteroids within 7 days prior to the first dose of study drug administration * Consumed grapefruit, grapefruit products, Seville oranges(including marmalade containing Seville oranges), or star fruit within 3 days prior to the first dose of study drug and throughout venetoclax administration
- Inability to swallow a large number of tablets.