

Leucemia Leucemia linfocítica crónica

Estudio para comparar la eficacia y seguridad de Obinituzumab + GDC-0199 versus Obinituzumab + Clorambucilo en pacientes con Leucemia Linfocítica Crónica.

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

Trial Status Activo, no seleccionando	Trial Runs In 21 Countries	Trial Identifier NCT02242942 2014-001810-24 BO25323
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La información se obtuvo directamente de sitios web de registros públicos, como ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., y no se ha editado.

Official Title:

Ensayo en fase III aleatorizado, multicéntrico, abierto, prospectivo para comparar la eficacia y la seguridad de un régimen combinado de obinutuzumab y GDC-0199 con obinutuzumab y clorambucilo en pacientes previamente no tratados con LLC con condiciones médicas coexistentes.

Trial Summary:

Este estudio de fase III, multicéntrico, aleatorio y abierto, está diseñado para comparar la eficacia y la seguridad de un régimen combinado de obinutuzumab y venetoclax frente a obinutuzumab + clorambucilo en participantes con leucemia linfocítica crónica (LLC) y afecciones médicas coexistentes. El tiempo previsto para el tratamiento en estudio será de aproximadamente un año y el período de seguimiento será de hasta 5 años.

Hoffmann-La Roche
Sponsor

Fase III
Phase

NCT02242942 2014-001810-24 BO25323
Trial Identifiers

Eligibility Criteria:

Gender
All

Age
#18 Years

Healthy Volunteers
No

1. Why is the CLL14 study needed?

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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:

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- 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?

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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:

- Tener LLC documentada no tratada previamente, conforme a los criterios IWCLL.
- LLC que requiere tratamiento conforme a los criterios IWCLL.
- Puntuación CIRS total > 6.
- Función medular adecuada, con independencia del apoyo con factores de crecimiento o transfusiones en las 2 semanas anteriores a la selección, salvo que la citopenia se deba a afectación medular de la LLC.
- Función hepática adecuada.
- Esperanza de vida >6 meses.
- Aceptación de utilizar métodos anticonceptivos altamente efectivos según protocolo.

Exclusion Criteria:

- Transformación de LLC a LNH de gran malignidad (transformación de Richter o leucemia prolinfocítica).
- Afectación conocida del sistema nervioso central.
- Pacientes con antecedentes de leucoencefalopatía multifocal progresiva (LMP) confirmada.
- Una puntuación de 4 en la afectación de aparatos, órganos o sistemas individuales evaluada mediante la definición de la escala CIRS que limita la capacidad de recibir el régimen de tratamiento de este ensayo con la excepción de ojos, oídos, nariz y garganta.
- Pacientes con anemia hemolítica autoinmunitaria o trombocitopenia inmunitaria no controladas.
- Función renal inadecuada.

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- Antecedentes de neoplasia maligna anterior, salvo las condiciones señaladas en el protocolo, si los pacientes se han recuperado de los efectos secundarios tras dosis únicas provocados por un tratamiento anterior.
- Pacientes con infecciones activas que requieren tratamiento i.v. (Grado 3 o 4) en los 2 meses anteriores a la inscripción.
- Antecedentes de reacciones anafilácticas o alérgicas graves a los anticuerpos monoclonales humanizados o murinos o sensibilidad o alergia conocidas a los productos murinos.
- Hipersensibilidad a clorambucilo, obinutuzumab, o venetoclax o a cualquiera de sus excipientes.
- Mujeres embarazadas o en período de lactancia.
- Resultados positivos en los análisis de la infección crónica por el VHB (definido como serología positiva para el HBsAg) y resultado positivo en el análisis de la hepatitis C (análisis de serología del anticuerpo contra el virus de la hepatitis C [VHC]).
- Pacientes con infección conocida por el virus de la inmunodeficiencia humana (VIH) o el virus de la leucemia de linfocitos T humana tipo I (HTLV-1).
- Requiere el uso de warfarina, marcumar o fenprocumón.
- Administración de los fármacos inhibidores potentes y moderados de la CYP3A4 en los 7 días anteriores a la primera dosis de fármaco del estudio.