Efficacy and safety of tisagenlecleucel in adult patients with refractory or relapsed follicular lymphoma

Estado	**Tipo de Participantes**	**Rangos de Edad**
EC Finalizado	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	97
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Tiene resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica	Terapia génica

Información

Identificador
2023-508127-13-00 (CTIS)

Cod. Protocolo
CCTL019E2202

Transicionado 2017-004385-94

Área terapéutica
Enfermedades [C] - Cáncer [C04]|

Enfermedad investigada
Adult patients with refractory or relapsed follicular lymphoma

Título Científico
A Phase II, single arm, multicenter open label trial to determine the efficacy and safety of tisagenlecleucel (CTL019) in adult patients with refractory or relapsed follicular lymphoma

Justificación

No aportado

Objetivo Principal

Evaluate the efficacy of tisagenlecleucel therapy as measured by CRR determined by IRC

Variables de Evaluación Primaria

1. Complete response rate (CRR) determined by an Independent Review Committee (IRC) in the efficacy analysis set (EAS) based on Lugano 2014 classification response criteria (Cheson et al 2014).

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

1. Evaluate the efficacy of tisagenlecleucel as measured by additional efficacy measures, including ORR, DOR, PFS and OS
2. Evaluate safety of tisagenlecleucel
3. Characterize the in vivo cellular kinetics (levels, expansion, persistence) of tisagenlecleucel transduced cells into target tissues (blood, bone marrow, and other tissues if available) and CD3+ tisagenlecleucel cells in peripheral blood, summarized by clinical response
4. Characterize the incidence and prevalence of tisagenlecleucel immunogenicity (humoral and cellular)
5. Characterize the impact of pre-existing and treatment induced immunogenicity (cellular and humoral) on cellular kinetics, efficacy and safety
6. Describe the effect of tisagenlecleucel therapy on Patient reported outcomes (PRO)

Variables de Evaluación Secundaria

ORR, including complete response (CR) and partial response (PR) determined by IRC in the FAS based on Lugano 2014 classification. DOR, defined as time from CR/PR to relapse or death due to FL, based on IRC DOR for CR only, defined as time from CR to relapse or death due to FL, based on IRC. PFS, defined as time from tisagenlecleucel infusion to first documented disease progression or death due to any cause, based on IRC.OS, defined as time from tisagenlecleucel infusion to death due to any cause
Type, frequency and severity of adverse events and laboratory abnormalities
Summary of: -qPCR detected tisagenlecleucel transgene concentrations in peripheral blood, bone marrow and other tissues by time point and clinical response status. -cellular kinetic parameters: Cmax, Tmax, AUC0-28 and AUC0-84d, T1/2, and/or other relevant parameters in peripheral blood; bone marrow and other tissues by clinical response as appropriate -exposure and cellular kinetic parameters of CD3+ tisagenlecleucel cells in peripheral blood detected by flow cytometry
Summary of pre-existing and treatment induced immunogenicity (cellular and humoral) of tisagenlecleucel

Levels of pre-existing and treatment induced immunogenicity Cellular kinetic parameters (Cmax, AUCs, Tlast), concentration-time profile tisagenlecleucel by immunogenicity category (positive/negative) Efficacy (ORR, DOR, PFS) Safety (B-cell levels, CRS grades, neurologic events)
Summary scores of PRO measured by SF-36 version 2, EQ-5D-3L and FACT-Lym quality of life questionnaires

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

1. Written informed consent prior to any screening procedures 2. 18 years of age at the time of ICF signature 3. FL (Grade 1, 2, 3A) confirmed histologically by central pathology review before tisagenlecleucel infusion. 4. FL meeting one of the following criteria: Refractory to a second line or later line of systemic therapy (including an anti-CD20 antibody and an alkylating agent) or relapsed within 6 months after completion of a second line or later line of systemic therapy Relapsed during anti-CD20 antibody maintenance (following at least two lines of therapies as above) or within 6 months after maintenance completion Relapsed after autologous HSCT 5. Radiographically measurable disease at screening defined as: At least one nodal lesion greater than 20 mm in the long axis, regardless of the length of the short axis AND/OR Extranodal lesions (outside lymph node or nodal mass, including liver and spleen) greater than 10 mm in long AND short axis 6. ECOG performance status that is either 0 or 1 at screening 7. Patients must meet the following laboratory values without transfusion at screening: Absolute neutrophil count (ANC) 1,000/mm3 (1×109/L) Absolute lymphocyte count (ALC) > 300/mm3 (> 0.3×109/L) Absolute number of CD3+ T cells > 150/mm3 (> 0.15×109/L) Platelets 50 000/mm3 (50×109/L) Hemoglobin 8.0 g/dl (4.9 mmol/L) A serum creatinine of 1.5 times ULN or eGFR 60 mL/min/1.73 m2 Alanine aminotransferase (ALT)/ Aspartate aminotransferase (AST) 5 times the Upper Limit of Normal (ULN) Total bilirubin (TBIL) 1.5 times ULN (with the exception of patients with Gilberts syndrome. Patients with Gilberts syndrome may be included if their total bilirubin is 3.0 times ULN and direct bilirubin 1.5 times ULN 8. Adequate pulmonary function defined as: No or mild dyspnea (Grade 1) Oxygen saturation measured by pulse oximetry > 90% on room air 9. Must have a leukapheresis product of non-mobilized cells accepted for manufacturing

Criterios de Exclusión

1. Evidence of histologic transformation 10. Presence of active or prior hepatitis B or C as indicated by serology. Serology must be repeated, if the interval between testing prior to lymphodepletion and tisagenlecleucel infusion exceeds 8 weeks 11. Presence of HIV antibody. Serology must be repeated, if the interval between testing prior to lymphodepletion and tisagenlecleucel infusion exceeds 8 weeks 12. Uncontrolled acute life threatening bacterial, viral or fungal infection (e.g. blood culture positive 72 hours prior to tisagenlecleucel infusion) 13. Cardiac or cardiac repolarization abnormality, including any of the following: History of myocardial infarction (MI), angina pectoris, or coronary artery bypass graft (CABG) within 6 months prior to starting study treatment Clinically significant cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third degree AV block) LVEF <45% as determined by ECHO or MRA or MUGA NYHA functional class III or IV 14. Previous or concurrent malignancy with the following exceptions: a. Adequately treated basal cell or squamous cell carcinoma (adequate wound healing is required prior to enrollment) b. In situ carcinoma of the cervix or breast, treated curatively and without evidence of recurrence for at least 3 years prior to enrollment c. A primary malignancy which has been completely resected and in complete remission for 3 years at the time of enrollment 15. Pregnant or nursing (lactating) women NOTE: female study participants of reproductive potential must have a negative serum or urine pregnancy test performed within 24 hours before leukapheresis, lymphodepletion and prior to tisagenlecleucel infusion. 16. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception while taking study

treatment and for at least 12 months after the tisagenlecleucel infusion and until CAR T-cells are no longer present by qPCR on two consecutive tests. Highly effective contraception methods include: Total abstinence (when this is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy), total hysterectomy, or tubal ligation at least six weeks before taking study treatment. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment Male sterilization (at least 6 months prior to screening). For female patients on the study, the vasectomized male partner should be the sole partner for that patient Use of oral, (estrogen and progesterone), injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS), or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception. In case of use of oral contraception women should have been stable on the same pill for a minimum of 3 months before taking study treatment. 17. Sexually active males must use a condom during intercourse while taking study treatment and for at least 12 months after the tisagenlecleucel infusion and until CAR T-cells are no longer present by qPCR on two consecutive tests. A condom is required for all sexually active male participants to prevent them from fathering a child AND to prevent delivery of study treatment via seminal fluid to their partner. In addition, male participants must not donate sperm for the time period specified above. 18. Intolerance to the excipients of the tisagenlecleucel cell product. 2. Follicular Lymphoma Grade 3B 3. Prior anti-CD19 therapy 4. Prior gene therapy 5. Prior adoptive T cell therapy 6. Prior allogeneic hematopoietic stem cell transplant 7. Active CNS involvement by malignancy 8. Active neurological autoimmune or inflammatory disorders (e.g. Guillain-Barre syndrome, Amyotrophic Lateral Sclerosis) 9. Investigational medicinal product within the last 30 days or five half-lives (whichever is longer) prior to screening

Calendario

(Última actualización: 09/07/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
22/08/2018	01/04/2019	01/04/2019	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
30/03/2020	No aportado	No aportado	27/03/2025	28/05/2025

Promotor

Novartis Pharma AG Switzerland

Lichtstrasse 35

Contact Person

Novartis Pharma Arzneimittel GmbH

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Monetary support: N/A

Tipo de promotor: Comercial

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Centros

Activo (08/03/2019)

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

Madrid

MADRID

Hematología

Cerrado (02/07/2025)

HOSPITAL VIRGEN DEL ROCÍO

Sevilla

SEVILLA

Oncología

Medicamentos

TISAGENLECLEUCEL
DISPERSION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Huérfano **Experimental**

Tiene resultados

Efficacy and safety of tisagenlecleucel in adult patients with refractory or relapsed follicular lymphoma

State	Type of participants	Age Ranges
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	97
Results	**Low level of intervention**	**Rare disease**
Has results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics	Gene therapy

Information

Identifier
2023-508127-13-00 (CTIS)

Protocol Code
CCTL019E2202

Transitioned 2017-004385-94

Therapeutic area
Diseases [C] - Cancer [C04]|

Investigated Disease
Adult patients with refractory or relapsed follicular lymphoma

Scientific Title
A Phase II, single arm, multicenter open label trial to determine the efficacy and safety of tisagenlecleucel (CTL019) in adult patients with refractory or relapsed follicular lymphoma

Rationale

Not provided

Main Objective

Evaluate the efficacy of tisagenlecleucel therapy as measured by CRR determined by IRC

Primary Endpoints

1. Complete response rate (CRR) determined by an Independent Review Committee (IRC) in the efficacy analysis set (EAS) based on Lugano 2014 classification response criteria (Cheson et al 2014).

Temporary moments of secondary assessment

Not provided

Secondary Objective

1. Evaluate the efficacy of tisagenlecleucel as measured by additional efficacy measures, including ORR, DOR, PFS and OS
2. Evaluate safety of tisagenlecleucel
3. Characterize the in vivo cellular kinetics (levels, expansion, persistence) of tisagenlecleucel transduced cells into target tissues (blood, bone marrow, and other tissues if available) and CD3+ tisagenlecleucel cells in peripheral blood, summarized by clinical response
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5. Characterize the impact of pre-existing and treatment induced immunogenicity (cellular and humoral) on cellular kinetics, efficacy and safety
6. Describe the effect of tisagenlecleucel therapy on Patient reported outcomes (PRO)

Secondary Endpoints

ORR, including complete response (CR) and partial response (PR) determined by IRC in the FAS based on Lugano 2014 classification. DOR, defined as time from CR/PR to relapse or death due to FL, based on IRC DOR for CR only, defined as time from CR to relapse or death due to FL, based on IRC. PFS, defined as time from tisagenlecleucel infusion to first documented disease progression or death due to any cause, based on IRC.OS, defined as time from tisagenlecleucel infusion to death due to any cause
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Summary scores of PRO measured by SF-36 version 2, EQ-5D-3L and FACT-Lym quality of life questionnaires

Temporary moments of secondary assessment

Not provided

Inclusion criteria

1. Written informed consent prior to any screening procedures 2. 18 years of age at the time of ICF signature 3. FL (Grade 1, 2, 3A) confirmed histologically by central pathology review before tisagenlecleucel infusion. 4. FL meeting one of the following criteria: Refractory to a second line or later line of systemic therapy (including an anti-CD20 antibody and an alkylating agent) or relapsed within 6 months after completion of a second line or later line of systemic therapy Relapsed during anti-CD20 antibody maintenance (following at least two lines of therapies as above) or within 6 months after maintenance completion Relapsed after autologous HSCT 5. Radiographically measurable disease at screening defined as: At least one nodal lesion greater than 20 mm in the long axis, regardless of the length of the short axis AND/OR Extranodal lesions (outside lymph node or nodal mass, including liver and spleen) greater than 10 mm in long AND short axis 6. ECOG performance status that is either 0 or 1 at screening 7. Patients must meet the following laboratory values without transfusion at screening: Absolute neutrophil count (ANC) 1,000/mm3 (1×109/L) Absolute lymphocyte count (ALC) > 300/mm3 (> 0.3×109/L) Absolute number of CD3+ T cells > 150/mm3 (> 0.15×109/L) Platelets 50 000/mm3 (50×109/L) Hemoglobin 8.0 g/dl (4.9 mmol/L) A serum creatinine of 1.5 times ULN or eGFR 60 mL/min/1.73 m2 Alanine aminotransferase (ALT)/ Aspartate aminotransferase (AST) 5 times the Upper Limit of Normal (ULN) Total bilirubin (TBIL) 1.5 times ULN (with the exception of patients with Gilberts syndrome. Patients with Gilberts syndrome may be included if their total bilirubin is 3.0 times ULN and direct bilirubin 1.5 times ULN 8. Adequate pulmonary function defined as: No or mild dyspnea (Grade 1) Oxygen saturation measured by pulse oximetry > 90% on room air 9. Must have a leukapheresis product of non-mobilized cells accepted for manufacturing

Exclusion criteria

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Calendar

(Last Update: 09/07/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
22/08/2018	01/04/2019	01/04/2019	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
30/03/2020	Not aported	Not aported	27/03/2025	28/05/2025

Sponsor

Novartis Pharma AG Switzerland

Lichtstrasse 35

Contact Person

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Monetary support: N/A

Sponsor type: Commercial

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Sites

Active (08/03/2019)

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

Madrid

MADRID

Hematología

Closed (02/07/2025)

HOSPITAL VIRGEN DEL ROCÍO

Sevilla

SEVILLA

Oncología

Medication

TISAGENLECLEUCEL

DISPERSION FOR INFUSION

INTRAVENOUS INFUSION

-

Active Principles: N/A

Orphan **Experimental**

Has results