Study of the Infusion of ARI-0001 Cells in Patients With CD19 + Acute Lymphoid Leukemia Resistant or Refractory to Therapy

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	32
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico nacional	seguridad, eficacia	Terapia génica

Información

Identificador
2024-513601-31-00 (CTIS)

Cod. Protocolo
CART19-BE-02

Transicionado 2019-003038-17

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

Enfermedad investigada
Acute lymphoid leukemia

Título Científico
Phase 2 study of the infusion of differentiated autologous T-cells from peripheral blood, expanded and transduced with a lentivirus to express a chimeric antigen receptor with anti-CD19 specificity (A3B1) conjugated with the co-stimulatory regions 4-1BB and CD3z (ARI-0001 cells) in patients with CD19+ acute lymphoid leukemia resistant or refractory to therapy

Justificación

No aportado

Objetivo Principal

To assess the efficacy (in terms of response rate and duration) of the infusion of ARI-0001 cells (Adult differentiated autologous T-cells from peripheral blood, expanded and transducted with a lentivirus to express a chimeric antigen receptor with anti-CD19 specificity [A3B1] conjugated to the 4-aBB and CD3z co-stimulatory regions) in patients with resistant or refractory CD19+ acute lymphoid leukemia

Variables de Evaluación Primaria

Response rate with measurable residual disease negative by multiparametric flow cytometry 28 days after infusion of ARI-0001 cells.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Assess adverse events occurring at 3 months and per year
To assess overall survival after infusion of ARI-0001
To evaluate the duration of ARI-0001 cells in peripheral blood, bone marrow and CSF after administration

Variables de Evaluación Secundaria

Duration of response
Best response during the first 3 months of follow-up after administration of the first fractioned dose of ARI-0001
Progression-free survival at 6 months and 1 year of the infusion and after the signature of informed consent.
Overall Survival (OS) at 1 year of the infusion and after the informed consent form signature
Assessment of ARI-0001 cell toxicity considering special interest in the following adverse events: CRS (cytokine release syndrome), encephalopathy associated with CARs (ICANS) and cerebral edema. Mortality related to study procedures and adverse events grade 3-4 will be evaluated at month 3 and year 1. Intensity will be assessed using CTCAE version 5.0 scale. To evaluate CRS and neurotoxicity ASTCT criteria will be used.
In vivo survival of ARI-0001 cells in peripheral blood, bone narrow and cerebrospinal fluid, to be determined by flow cytometry and quantitative transgene PCR with monthly frequency in the first 6 months and thereafter quarterly up to 2 years of infusion

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Diagnoses of CD19+ acute lymphoid leukemia, with a life expectancy of less than 2 years that meet the following conditions: Relapsed/refractory not candidate for transplantation (due to associated diseases or absence of donor) or in allogenic post-transplant relapse.
Measurable disease understood as the presence of measurable residual disease by flow cytometry in bone marrow or peripheral blood
Age less than 70 years (from 18 to 70)
ECOG functional status from 0 to 2
Life expectancy of at least 3 months.
Adequate venous access to perform a lymphapheresis. Absence of contraindications for it
Signature of informed consent

Criterios de Exclusión

Treatment with any experimental or non-marketed substance within four weeks prior to recruitment, or actively participating in another therapeutic trial Positive serology for hepatitis B, defined as a positive test for HBsAg. In addition, if the patient is HBsAg negative but has anti-HBc antibodies it will be necessary to perform a DNA test of the hepatitis B virus, and if the result is positive the patient will be excluded Positive serology for hepatitis C, defined as a positive test for anti-VHC antibodies confirmed by RIBA Concurrent uncontrolled medical illnesses including cardiac, renal, hepatic, gastrointestinal, endocrine, pulmonary, neurological or psychiatric diseases that in the opinion of the investigator are potential risk factors to the patient Severe organ involvement, defined as cardiac ejection fraction <40%; DLCO <40%; calculated glomerular filtrate <30 ml/min; or bilirubin > 3 times the upper limit of normality (unless Gilbert syndrome) Pregnant or lactating women. Woman of childbearing potential should have a negative pregnancy test in the screening phase. Women of childbearing potential, including those whose last menstrual cycle was in the year prior to screening, who are unable or unwilling to use highly effective contraceptive methods* from the start of the study to the completion of the study. Men who cannot or do not wish to use highly effective contraceptive methods* from the beginning of the study until the end of the study Previous treatment with CART therapy (commercial or experimental) Diagnosis of another neoplasm, past or present. Patients may be included in complete remission for more than 3 years, or have a history of non-melanoma skin cancer or in-situ carcinoma resected completely. Relief of central nervous system (CNS-3) at the time of inclusion. Inclusion will be permitted in patients with a lower grade (CNS-2) or CNS-3 who have responded to intrathecal chemotherapy Isolated extramedullary involvement (i.e. in the absence of minimal residual disease in peripheral blood, bone marrow, or cerebrospinal fluid) Early relapse after transplantation (less than 3 months for mononuclear cell apheresis, less than 6 months for infusion of ARI-0001) Active immunosuppressive treatment for graft-versus-host disease and other diseases. The use of corticosteroids to control leukaemia at the time of inclusion should be limited as much as possible and should be discontinued prior to infusion of ARI-0001 cells. Active infection requiring systemic medical treatment such as chronic kidney infection, chronic lung infection or tuberculosis. HIV infection

Calendario

(Última actualización: 24/10/2024)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
18/09/2020	11/05/2021	19/05/2021	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
No aportado	No aportado	No aportado	No aportado	No aportado

Promotor

Fundacio De Recerca Clinic Barcelona-Institut D¿Investigacions Biomediques August Pi I Sunyer Spain

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Monetary support: N/A

Tipo de promotor: Comercial

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Centros

Activo (18/01/2022)

CLINICA UNIVERSIDAD DE NAVARRA

Pamplona/Iruña

NAVARRA

Activo (28/01/2022)

Complejo Asistencial Universitario De Salamanca

Salamanca

SALAMANCA

Activo (11/05/2021)

HOSPITAL CLINIC DE BARCELONA

Barcelona

BARCELONA

Activo (21/12/2021)

HOSPITAL CLINICO UNIVERSITARIO VIRGEN DE LA ARRIXACA

Murcia

MURCIA

Activo (07/03/2022)

HOSPITAL UNIVERSITARI GERMANS TRIAS I PUJOL DE BADALONA

Badalona

BARCELONA

Activo (28/01/2022)

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

Madrid

MADRID

Medicamentos

PARACETAMOL
CAPSULE, HARD
ORAL

-

Principios Activos: N/A

Experimental

FLUDARABINE
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

Varnimcabtagene autoleucel
DISPERSION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

CYCLOPHOSPHAMIDE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

DEXCHLORPHENIRAMINE
TABLET
ORAL

-

Principios Activos: N/A

Experimental

BENDAMUSTINE
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

TOCILIZUMAB
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

ALLOPURINOL
TABLET
ORAL

-

Principios Activos: N/A

Experimental

Sin resultados

Study of the Infusion of ARI-0001 Cells in Patients With CD19 + Acute Lymphoid Leukemia Resistant or Refractory to Therapy

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	32
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
National multicenter	safety, effectiveness	Gene therapy

Information

Identifier
2024-513601-31-00 (CTIS)

Protocol Code
CART19-BE-02

Transitioned 2019-003038-17

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

Investigated Disease
Acute lymphoid leukemia

Scientific Title
Phase 2 study of the infusion of differentiated autologous T-cells from peripheral blood, expanded and transduced with a lentivirus to express a chimeric antigen receptor with anti-CD19 specificity (A3B1) conjugated with the co-stimulatory regions 4-1BB and CD3z (ARI-0001 cells) in patients with CD19+ acute lymphoid leukemia resistant or refractory to therapy

Rationale

Not provided

Main Objective

To assess the efficacy (in terms of response rate and duration) of the infusion of ARI-0001 cells (Adult differentiated autologous T-cells from peripheral blood, expanded and transducted with a lentivirus to express a chimeric antigen receptor with anti-CD19 specificity [A3B1] conjugated to the 4-aBB and CD3z co-stimulatory regions) in patients with resistant or refractory CD19+ acute lymphoid leukemia

Primary Endpoints

Response rate with measurable residual disease negative by multiparametric flow cytometry 28 days after infusion of ARI-0001 cells.

Temporary moments of secondary assessment

Not provided

Secondary Objective

Assess adverse events occurring at 3 months and per year
To assess overall survival after infusion of ARI-0001
To evaluate the duration of ARI-0001 cells in peripheral blood, bone marrow and CSF after administration

Secondary Endpoints

Duration of response
Best response during the first 3 months of follow-up after administration of the first fractioned dose of ARI-0001
Progression-free survival at 6 months and 1 year of the infusion and after the signature of informed consent.
Overall Survival (OS) at 1 year of the infusion and after the informed consent form signature
Assessment of ARI-0001 cell toxicity considering special interest in the following adverse events: CRS (cytokine release syndrome), encephalopathy associated with CARs (ICANS) and cerebral edema. Mortality related to study procedures and adverse events grade 3-4 will be evaluated at month 3 and year 1. Intensity will be assessed using CTCAE version 5.0 scale. To evaluate CRS and neurotoxicity ASTCT criteria will be used.
In vivo survival of ARI-0001 cells in peripheral blood, bone narrow and cerebrospinal fluid, to be determined by flow cytometry and quantitative transgene PCR with monthly frequency in the first 6 months and thereafter quarterly up to 2 years of infusion

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Diagnoses of CD19+ acute lymphoid leukemia, with a life expectancy of less than 2 years that meet the following conditions: Relapsed/refractory not candidate for transplantation (due to associated diseases or absence of donor) or in allogenic post-transplant relapse.
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Calendar

(Last Update: 24/10/2024)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
18/09/2020	11/05/2021	19/05/2021	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
Not aported	Not aported	Not aported	Not aported	Not aported

Sponsor

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Monetary support: N/A

Sponsor type: Commercial

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Sites

Active (18/01/2022)

CLINICA UNIVERSIDAD DE NAVARRA

Pamplona/Iruña

NAVARRA

Active (28/01/2022)

Complejo Asistencial Universitario De Salamanca

Salamanca

SALAMANCA

Active (11/05/2021)

HOSPITAL CLINIC DE BARCELONA

Barcelona

BARCELONA

Active (21/12/2021)

HOSPITAL CLINICO UNIVERSITARIO VIRGEN DE LA ARRIXACA

Murcia

MURCIA

Active (07/03/2022)

HOSPITAL UNIVERSITARI GERMANS TRIAS I PUJOL DE BADALONA

Badalona

BARCELONA

Active (28/01/2022)

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

Madrid

MADRID

Medication

PARACETAMOL
CAPSULE, HARD
ORAL

-
Active Principles: N/A
Experimental

FLUDARABINE
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A
Experimental

Varnimcabtagene autoleucel
DISPERSION FOR INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A
Experimental

CYCLOPHOSPHAMIDE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A
Experimental

DEXCHLORPHENIRAMINE
TABLET
ORAL

-
Active Principles: N/A
Experimental

BENDAMUSTINE
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A
Experimental

TOCILIZUMAB
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-
Active Principles: N/A
Experimental

ALLOPURINOL
TABLET
ORAL

-
Active Principles: N/A
Experimental

No results