Preparation for bone marrow transplant through the combined use of chemo and radiotherapy (intensive or myeloablative: eliminates stem cells)

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	49
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Unicéntrico nacional	tratamiento, seguridad, eficacia	NO

Información

Identificador
2024-514484-25-00 (CTIS)

Cod. Protocolo
TMLI-MA

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

Enfermedad investigada
High-Risk Myelodisplastic Syndrome or Acute Myeloid Leukemia

Título Científico
PHASE II STUDY OF TOTAL MARROW AND LYMPHOID IRRADIATION (TMLI) ADMINISTERED IN COMBINATION WITH A MYELOABLATIVE REGIMEN BASED ON CYCLOPHOSPHAMIDE AND ETOPOSIDE AS A CONDITIONING FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (AHSCT) IN PATIENTS WITH HIGH-RISK MYELODYSPLASTIC SYNDROME OR ACUTE MYELOID LEUKEMIA

Justificación

No aportado

Objetivo Principal

The antitumor activity of the conditioning regimen with TMLI, cyclophosphamide and etoposide followed by AHSCT will be evaluated by means of the progression-free survival (PFS) at 2 years after a safety-lead phase.

Variables de Evaluación Primaria

Toxicity, which will be graded on both the Bearman Scale and the NCI CTCAE Scale v5.0
The evaluation of 2-year PFS. PFS will be defined as time from the start of treatment to the ate of death, disease relapse/progression, or date of last follow-up, and estimated using the Kaplan-Meier method

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To determine the complete remission (CR) rate at day 30 post-transplant
To estimate overall survival (OS), cumulative incidence (CI) of recurrence/progression, and non-relapse mortality (NRM) at 100 days, 1 year, and 2 years
MRD monitoring at 30, 90, 180, 270, 360, 575 days and 720 days post-transplant
To assess early and late toxicities/complications by organ and severity, as well as dose/dose-volume toxicity characterization across organs, including acute/chronic GVHD, infection, and long-term complications

Variables de Evaluación Secundaria

Overall survival (OS): patients are considered a failure for this endpoint if they die, regardless of the cause. The time to this event is the time from the start of protocol therapy to death, or the last follow-up, whichever comes first
Cumulative incidence (CI) of recurrence/progression: The event is relapse/progression either extramedullary (EM) or at bone marrow (BM) (date and place). The time to this event is measured from the start of therapy. Death without relapse/progression is considered a competing risk. Surviving patients with no history of relapse/progression are censored at the time of last follow-up
Complete remission (CR) rate at day 30 post-transplant: The event is whether or not the patient has a documented CR on day 30
Non-relapse mortality (NRM2. NRM is measured from the start of therapy until non-disease-related death, or the last follow-up, whichever comes first
Measurable residual disease (MRD): MRD monitoring assessed by multiparameter flow cytometry at 30, 90, 180, 360, 575 days, and 2 years post-transplant
Incidence of infection: Microbiologically documented infections will be reported by site of illness, date of onset, severity, and resolution, if applicable. This data will be captured through the case report form and will be collected

from day 0 to 100 days after transplantation
Toxicities/Adverse Events: The Bearman Scale (non-hematologic) and CTCAE v. 5.0 (hematologic) will be employed. Dose/dose-volume toxicity characterization across organs will be assessed
Acute graft-versus-host disease (GVHD) grades 2-4 and 3-4:. The endpoint will be assessed from day 0 to 100 days post-transplant
Chronic graft-versus-host disease (GVHD): Chronic graft-versus-host disease is graded according to the NIH consensus staging. The first day of onset of chronic GVHD will be used to calculate cumulative incidence curves

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

The participant has the ability and willingness to sign the informed consent document
3.Pulmonary function tests: forced expiratory volume in one second (FEV1) and Carbon Monoxide Diffusion Capacity (DLCO) (adjusted for Hb) 50% from expected normal value
Patients should undergo cardiac evaluation with an electrocardiogram showing no ischemic changes or clinically relevant arrhythmia, and a 50% ejection fraction established by Multi-Gated Acquisiton Scan (MUGA) or echocardiogram
ECG showing no ischemic changes or clinically significant arrhythmia
Men and women of childbearing potential agree to use appropriate contraceptives (hormonal or barrier contraception or abstinence) prior to study entry and for six months following the duration of study participation
The time elapsed since the end of the last induction or reinduction cycle must be greater than or equal to 14 days
Age 18 to 50 years
Karnofskys performance status should be 70%
Patients with myelodysplastic syndrome/acute myeloid leukemia or acute myeloid leukemia with relapsed/refractory active disease, or in complete remission or morphologic leukemia-free state with evidence of measurable residual disease as assessed by multiparameter flow cytometry (0,1%) or next-generation sequencing (in the case of FLT3-ITD-mutated AML)
All candidates for this study must have an HLA (A, B, C, DR) identical siblings who are willing to donate bone marrow or peripheral blood hematopoietic progenitors or an 8/8 matched unrelated donor. A single allele mismatch in A, B, C or DRB1 shall be allowed
Total bilirubin 1.5 x ULN OR 3 x ULN for Gilbert's disease
SGOT & SGPT 5 x LSN
Serum creatinine 1.3 mg/dL or creatinine clearance measured 80 mL/min for 24 hours of urine collection
Women of childbearing age only: Negative urine or serum pregnancy test

Criterios de Exclusión

Patients who have received a previous autologous (within the last year) or allogeneic transplant (at any time) are excluded
Subjects who, in the opinion of the investigator, may not be able to meet the safety control requirements of the study
Previous radiation therapy, which would preclude the use of TMLI
Plans during the trial to receive any other investigational (non-trial-related) agents
Uncontrolled disease, including ongoing or active infection
History of allergic reactions attributed to compounds of chemical or biological composition similar to cyclophosphamide or etoposide
Patients with other active malignancies are not eligible for this study, other than the malignancies discussed

Patients with a psychological or medical condition that the patient's physician deems unacceptable to proceed with allogeneic hematopoietic stem cell transplantation
Women who plan to become pregnant or breastfeed during the trial
Patients who do not agree to practice effective forms of contraception

Calendario

(Última actualización: 01/04/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
19/11/2024	10/02/2025	16/12/2025	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

Fundacion Publica Andaluza Para La Gestion De La Investigacion En Salud De Sevilla Spain

Avenida De Manuel Siurot Sn

Contact Person

Clara María Rosso Fernández

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Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Provincial de Sevilla

Avenida Doctor Fedriani 3 41009 Sevilla

administracion.eecc.hvm.sspa@juntadeandalucia.es

955043127

Centros

No iniciado (--/--/----)

University Hospital Virgen Del Rocio S.L.

Sevilla

SEVILLA

Hematology

Medicamentos

MYCOPHENOLATE MOFETIL
POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENIOUS INFUSION

-

Principios Activos: N/A

Experimental

TACROLIMUS
SOLUTION FOR INFUSION
INTRAVENIOUS INFUSION

-

Principios Activos: N/A

Experimental

MYCOPHENOLATE MOFETIL
TABLET
ORAL

-

Principios Activos: N/A

Experimental

SIROLIMUS
ORAL SOLUTION
ORAL

-

Principios Activos: N/A

Experimental

TACROLIMUS
TABLET
ORAL

-

Principios Activos: N/A

Experimental

CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION/INFUSION
INFUSION

-

Principios Activos: N/A

Experimental

ETOPOSIDE
SOLUTION FOR INFUSION
INFUSION

-

Principios Activos: N/A

Experimental

Sin resultados

Preparation for bone marrow transplant through the combined use of chemo and radiotherapy (intensive or myeloablative: eliminates stem cells)

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	49
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
National One-center	treatment, safety, effectiveness	NO

Information

Identifier
2024-514484-25-00 (CTIS)

Protocol Code
TMLI-MA

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

Investigated Disease
High-Risk Myelodisplastic Syndrome or Acute Myeloid Leukemia

Scientific Title
PHASE II STUDY OF TOTAL MARROW AND LYMPHOID IRRADIATION (TMLI) ADMINISTERED IN COMBINATION WITH A MYELOABLATIVE REGIMEN BASED ON CYCLOPHOSPHAMIDE AND ETOPOSIDE AS A CONDITIONING FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (AHSCT) IN PATIENTS WITH HIGH-RISK MYELODYSPLASTIC SYNDROME OR ACUTE MYELOID LEUKEMIA

Rationale

Not provided

Main Objective

The antitumor activity of the conditioning regimen with TMLI, cyclophosphamide and etoposide followed by AHSCT will be evaluated by means of the progression-free survival (PFS) at 2 years after a safety-lead phase.

Primary Endpoints

Toxicity, which will be graded on both the Bearman Scale and the NCI CTCAE Scale v5.0
The evaluation of 2-year PFS. PFS will be defined as time from the start of treatment to the ate of death, disease relapse/progression, or date of last follow-up, and estimated using the Kaplan-Meier method

Temporary moments of secondary assessment

Not provided

Secondary Objective

To determine the complete remission (CR) rate at day 30 post-transplant
To estimate overall survival (OS), cumulative incidence (CI) of recurrence/progression, and non-relapse mortality (NRM) at 100 days, 1 year, and 2 years
MRD monitoring at 30, 90, 180, 270, 360, 575 days and 720 days post-transplant
To assess early and late toxicities/complications by organ and severity, as well as dose/dose-volume toxicity characterization across organs, including acute/chronic GVHD, infection, and long-term complications

Secondary Endpoints

Overall survival (OS): patients are considered a failure for this endpoint if they die, regardless of the cause. The time to this event is the time from the start of protocol therapy to death, or the last follow-up, whichever comes first
Cumulative incidence (CI) of recurrence/progression: The event is relapse/progression either extramedullary (EM) or at bone marrow (BM) (date and place). The time to this event is measured from the start of therapy. Death without relapse/progression is considered a competing risk. Surviving patients with no history of relapse/progression are censored at the time of last follow-up
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Chronic graft-versus-host disease (GVHD): Chronic graft-versus-host disease is graded according to the NIH consensus staging. The first day of onset of chronic GVHD will be used to calculate cumulative incidence curves

Temporary moments of secondary assessment

Not provided

Inclusion criteria

The participant has the ability and willingness to sign the informed consent document
3.Pulmonary function tests: forced expiratory volume in one second (FEV1) and Carbon Monoxide Diffusion Capacity (DLCO) (adjusted for Hb) 50% from expected normal value
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Women who plan to become pregnant or breastfeed during the trial
Patients who do not agree to practice effective forms of contraception

Calendar

(Last Update: 01/04/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
19/11/2024	10/02/2025	16/12/2025	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

Fundacion Publica Andaluza Para La Gestion De La Investigacion En Salud De Sevilla Spain

Avenida De Manuel Siurot Sn

Contact Person

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Monetary support: N/A

Sponsor type: Commercial

Ceim

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955043127

Sites

not initialized (--/--/----)

University Hospital Virgen Del Rocio S.L.

Sevilla

SEVILLA

Hematology

Medication

MYCOPHENOLATE MOFETIL
POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENIOUS INFUSION

-
Active Principles: N/A
Experimental

TACROLIMUS
SOLUTION FOR INFUSION
INTRAVENIOUS INFUSION

-
Active Principles: N/A
Experimental

MYCOPHENOLATE MOFETIL
TABLET
ORAL

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Active Principles: N/A
Experimental

SIROLIMUS
ORAL SOLUTION
ORAL

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Active Principles: N/A
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CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION/INFUSION
INFUSION

-
Active Principles: N/A
Experimental

ETOPOSIDE
SOLUTION FOR INFUSION
INFUSION

-
Active Principles: N/A
Experimental

No results