Preparation for bone marrow transplantation through the combined use of chemo and radiotherapy (Reduced intensity: with lower doses or different combinations).

Estado	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	46
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Unicéntrico nacional	tratamiento, seguridad, eficacia, dosis	NO

Información

Identificador
2024-514483-11-00 (CTIS)

Cod. Protocolo
TMLI-RI

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 REDUCED-INTENSITY REGIMEN BASED ON FLUDARABINE AND MELPHALAN AS 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 TMLI administered, in combination with fludarabine and melphalan for (AHSCT) in patients with risk MDS or AML who are not candidates for myeloablative conditions, as assessed by 2-year progression-free survival.

Variables de Evaluación Primaria

The primary endpoint for the primary patient safety segment of this study is toxicity. Toxicity will be graded on both the Bearman Scale (Appendix I) and the NCI CTCAE Scale and v5.0 (Appendix II).
The primary endpoint is 2 year progression-free survival (PFS). PFS will be defined as time from the start of treatment to the date of death, disease relapse/progression, or date of last follow-up, and estimated using the Kaplan-Meier method. Patients are considered a failure for this endpoint if they die or if they relapse/progress. The time to this event is the time from the start of protocol therapy to death, relapse/progression, or the last follow-up, whichever comes first.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To estimate overall survival, cumulative incidence (CI) of recurrence/progression, and non-relapse mortality (NRM) at 100 days, 1 year, and 2 years post-transplantation.
To determine the complete remission (CR) rate at day +30.
Minimal residual disease (MRD) monitoring at 30, 90, 180, 270, 360, 575 and 720 days post-transplant.
To assess early and late toxicities/complications by organ/severity (including graft-versus-host disease (GVHD) in its acute and chronic variants), as well as to characterize toxicities by dose/dose-volume across organs.

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. Time to event is measured from the day of infusion to the time of CR.
Non-relapse mortality (NRM): Patients are considered a failure for this endpoint if they die from causes other than

relapse or progression. 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: Acute graft-versus-host disease is classified according to the consensus classification. The first day of onset of acute GVHD to a certain degree will be used to calculate the cumulative incidence curves for that grade of GVHD. 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. (For adults, only participants with mild cognitive abilities may use a legally authorized representative).
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.
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. If a woman becomes pregnant or suspects she is pregnant while participating in the trial, she should inform her treating physician immediately.
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 MUGA or echocardiogram.
Documented (signed) informed consent. The patient, family member, and doctor of the transplant staff (doctor, nurse, and social worker) meet at least once before the transplant procedure begins. During this meeting, all relevant information regarding the risks and benefits to the donor and recipient will be presented. Alternative treatment modalities will be discussed. The risks are explained in detail in the attached consent forms.
Age: 50 years or HCT-CI pre-transplant score 3 or any other condition that precludes the use of a fully myeloablative conditioning regimen.
Karnofsky's performance status 70%
Patients with myelodysplastic syndrome/acute myeloid leukemia (per ICC 2022 criteria) or acute myeloid leukemia with relapsed/refractory active disease (i.e. 5% bone marrow blasts), or in complete remission (CR) or morphologic leukemia-free state (MLFS) 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 8/8 HLA-identical (A, B, C, DR) or an unrelated donor with at least 8/8 HLA matching. A single allele mismatch in A, B, C, DR or DQ and a KIR mismatch in C shall be allowed. All combinations of donor/recipient ABO blood types are acceptable; as even major ABO compatibilities can be treated using a variety of techniques (red blood cell exchange or plasma exchange).
The time elapsed since the end of the last induction or re-induction cycle must be greater than or equal to 14 days.
Total bilirubin 1.5 mg/dL x Upper Limit of Normality (ULN) OR 3 x ULN for Gilbert's disease.

Serum glutamic-oxaloacetic transaminase (SGOT) & serum glutamic-pyruvic transaminase (SGPT) 5 x ULN.

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 fludarabine or melphalan.
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
13/11/2024	10/02/2025	21/05/2025	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

955013428

claram.rosso.sspa@juntadeandalucia.es

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

TACROLIMUS
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS

-
Principios Activos: N/A
Experimental

FLUDARABINE PHOSPHATE
CONCENTRATE FOR SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS

-
Principios Activos: N/A
Experimental

MYCOPHENOLATE MOFETIL
FILM-COATED TABLET
ORAL

-
Principios Activos: N/A
Experimental

MELPHALAN
POWDER AND SOLVENT FOR SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS

-
Principios Activos: N/A
Experimental

CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS

-
Principios Activos: N/A
Experimental

MYCOPHENOLATE MOFETIL
POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS

-
Principios Activos: N/A
Experimental

Sin resultados

Preparation for bone marrow transplantation through the combined use of chemo and radiotherapy (Reduced intensity: with lower doses or different combinations).

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	46
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, dose	NO

Information

Identifier
2024-514483-11-00 (CTIS)

Protocol Code
TMLI-RI

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 REDUCED-INTENSITY REGIMEN BASED ON FLUDARABINE AND MELPHALAN AS 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 TMLI administered, in combination with fludarabine and melphalan for (AHSCT) in patients with risk MDS or AML who are not candidates for myeloablative conditions, as assessed by 2-year progression-free survival.

Primary Endpoints

The primary endpoint for the primary patient safety segment of this study is toxicity. Toxicity will be graded on both the Bearman Scale (Appendix I) and the NCI CTCAE Scale and v5.0 (Appendix II).
The primary endpoint is 2 year progression-free survival (PFS). PFS will be defined as time from the start of treatment to the date of death, disease relapse/progression, or date of last follow-up, and estimated using the Kaplan-Meier method. Patients are considered a failure for this endpoint if they die or if they relapse/progress. The time to this event is the time from the start of protocol therapy to death, relapse/progression, or the last follow-up, whichever comes first.

Temporary moments of secondary assessment

Not provided

Secondary Objective

To estimate overall survival, cumulative incidence (CI) of recurrence/progression, and non-relapse mortality (NRM) at 100 days, 1 year, and 2 years post-transplantation.
To determine the complete remission (CR) rate at day +30.
Minimal residual disease (MRD) monitoring at 30, 90, 180, 270, 360, 575 and 720 days post-transplant.
To assess early and late toxicities/complications by organ/severity (including graft-versus-host disease (GVHD) in its acute and chronic variants), as well as to characterize toxicities by dose/dose-volume across organs.

Secondary Endpoints

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Not provided

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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
13/11/2024	10/02/2025	21/05/2025	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

Clara María Rosso Fernández

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claram.rosso.sspa@juntadeandalucia.es

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

TACROLIMUS
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS

-
Active Principles: N/A
Experimental

FLUDARABINE PHOSPHATE
CONCENTRATE FOR SOLUTION FOR INJECTION/INFUSION
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-
Active Principles: N/A
Experimental

MYCOPHENOLATE MOFETIL
FILM-COATED TABLET
ORAL

-
Active Principles: N/A
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MELPHALAN
POWDER AND SOLVENT FOR SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS

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CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS

-
Active Principles: N/A
Experimental

MYCOPHENOLATE MOFETIL
POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS

-
Active Principles: N/A
Experimental

No results