Phase I/II clinical trial of autologous hematopoietic stem cell gene therapy in rag1-deficient severe combined immunodeficiency

Estado	**Tipo de Participantes**	**Rangos de Edad**
Interrumpido	Sujetos incapaces de otorgar consentimiento	Menores de 18 , Recién nacidos (0-27 días)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I	5
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Unicéntrico nacional	eficacia	Terapia génica

Información

Identificador
2023-510204-50-00 (CTIS)

Cod. Protocolo
RAG1

Transicionado 2019-002343-14

Área terapéutica
Enfermedades [C] - Patologías del sistema inmunitario [C20]|

Enfermedad investigada
Severe combined immunodeficiency based on genetic defect in the Recombinase Activating Gene 1 (RAG1)

Título Científico
Phase I/II clinical trial of autologous hematopoietic stem cell gene therapy in rag1-deficient severe combined immunodeficiency

Justificación

No aportado

Objetivo Principal

To evaluate the effect of RAG1 gene therapy on overall survival
To evaluate the efficacy of RAG1 gene therapy in achieving reconstitution of the T and B cell immune system in patients with RAG1-SCID at 6 months
To evaluate the safety and tolerability of the RAG1 gene therapy product, including identification of short- and long-term adverse events

Variables de Evaluación Primaria

Overall survival Evaluation of immune reconstitution at Month 6 defined as -Presence of naive CD4+ T cells -Total CD3+ T-cells > 300 cells/µL -Total CD4+ T-cells > 200 cells/µL

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To evaluate the effect of RAG1 gene therapy on event-free survival.
To evaluate the efficacy of RAG1 gene therapy in achieving independence of Immunoglobulin substitution and serologic response to vaccination.
To evaluate the long-term efficacy of RAG1 gene therapy in reconstituting the immune system in patients with RAG1-SCID.
To evaluate the pharmacodynamic effects of RAG1 gene therapy
To evaluate the effects of RAG1 gene therapy on quality of life.

Variables de Evaluación Secundaria

Event-free survival (survival without the need for rescue treatment defined as infusion of autologous unmanipulated backup stem cell product and/or allogeneic HSCT) Independence from immunoglobulin substitution at Month 24 Serologic response to vaccination Immune system reconstitution o T-cell repopulation: -Total CD3+ T-cells > 300 cells/µL (at Month 12, 18, 24, 30, 36, 42, 48, 54, 60) - Total CD4+ T-cells > 200 cells/µL (at Month 12, 18, 24, 30, 36, 42, 48, 54, 60) - Presence of naive CD4+ T cells (at Month 12, 18, 24, 30, 36, 42, 48, 54, 60) o B-cell repopulation: - Total B-cell counts (at Month 6, 12, 18, 24, 30, 36, 42, 48, 54, 60) - Memory B-cell count (at Month 6, 12, 18, 24, 30, 36, 42, 48, 54, 60) - Switched memory B-cell count (at Month 6, 12, 18, 24, 30, 36, 42, 48, 54, 60) o Immune function: - Level of IgG (at Month 6, 12, 18, 24, 36, 48, 60) - Level of IgA (at Month 6, 12, 18, 24, 36, 48, 60) - Level of IgM (at Month 6, 12, 18, 24, 36, 48, 60) - IG repertoire and T cell receptor (TCR) repertoire on PBMCs at Month 12 Pharmacodynamics o Vector copy number (VCN) in PBMCs and granulocytes o TRECs and KRECs Quality of Life: Change from baseline in PedsQL

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

RAG1-deficient SCID as confirmed by genetic analysis Peripheral blood T cells < 300/L and/or naïve T cells < 1/L Age < 2 years Age at least 8 weeks by the time of busulfan and fludarabine administration Lack of an available HLA-matched donor (HLA-identical sibling or 10/10 (A, B, C, DR, DQ) allele-matched (un)related donor) Signed informed consent (parental or guardian) Able to return to the local HSCT centre for follow-up (per protocol) during the 2-year study and the 15-year long-term off study review Absence of peripheral blood naïve CD4+ T cells

Criterios de Exclusión

Omenn syndrome Previous allogeneic HSCT Significant organ dysfunction/co-morbidity (including but not limited to): Mechanical ventilation, Shortening fraction on echocardiogram <25%, Renal failure defined as dialysis dependence, uncontrolled seizure disorder.) Any other condition that the investigator considers is a contraindication to collection and/or infusion of transduced cells for that individual or indicate patient's inability to follow the protocol, for example contraindication f to busulfan, major congenital abnormalities, ineligible to receive anaesthesia, or documented refusal or inability of the family to return for scheduled visits. Human immunodeficiency virus (HIV) infection or Human T-cell Leukemia Virus (HTLV) infection.

Calendario

(Última actualización: 04/08/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
03/02/2023	01/06/2023	01/06/2023	17/06/2026	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
17/06/2026	No aportado	No aportado	No aportado	No aportado

Promotor

Videja B.V. Netherlands

De Limes 7

Contact Person

W. Krebber

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Monetary support: N/A

Tipo de promotor: No comercial

Ceim

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Centros

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

Fundacio Hospital Universitari Vall DHebron Institut De Recerca

Barcelona

BARCELONA

Cap de secció. Unitat de Patologia Infecciosa i Immunodeficiències de Pediatria

Medicamentos

RAG1-LV-CD34+ cells

INFUSION

INTRAVENOUS

-

Principios Activos: N/A

Huérfano **Experimental**

Sin resultados

Phase I/II clinical trial of autologous hematopoietic stem cell gene therapy in rag1-deficient severe combined immunodeficiency

State	Type of participants	Age Ranges
Halted	Incapable subjects of giving consent	Less than 18 , Newborn infants (0-27 days)
Gender	**Phases**	**Expected Participants**
Both	Phase I	5
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
National One-center	effectiveness	Gene therapy

Information

Identifier
2023-510204-50-00 (CTIS)

Protocol Code
RAG1

Transitioned 2019-002343-14

Therapeutic area
Diseases [C] - Immune System Diseases [C20]|

Investigated Disease
Severe combined immunodeficiency based on genetic defect in the Recombinase Activating Gene 1 (RAG1)

Scientific Title
Phase I/II clinical trial of autologous hematopoietic stem cell gene therapy in rag1-deficient severe combined immunodeficiency

Rationale

Not provided

Main Objective

To evaluate the effect of RAG1 gene therapy on overall survival
To evaluate the efficacy of RAG1 gene therapy in achieving reconstitution of the T and B cell immune system in patients with RAG1-SCID at 6 months
To evaluate the safety and tolerability of the RAG1 gene therapy product, including identification of short- and long-term adverse events

Primary Endpoints

Overall survival Evaluation of immune reconstitution at Month 6 defined as -Presence of naive CD4+ T cells -Total CD3+ T-cells > 300 cells/µL -Total CD4+ T-cells > 200 cells/µL

Temporary moments of secondary assessment

Not provided

Secondary Objective

To evaluate the effect of RAG1 gene therapy on event-free survival.
To evaluate the efficacy of RAG1 gene therapy in achieving independence of Immunoglobulin substitution and serologic response to vaccination.
To evaluate the long-term efficacy of RAG1 gene therapy in reconstituting the immune system in patients with RAG1-SCID.
To evaluate the pharmacodynamic effects of RAG1 gene therapy
To evaluate the effects of RAG1 gene therapy on quality of life.

Secondary Endpoints

Event-free survival (survival without the need for rescue treatment defined as infusion of autologous unmanipulated backup stem cell product and/or allogeneic HSCT) Independence from immunoglobulin substitution at Month 24 Serologic response to vaccination Immune system reconstitution o T-cell repopulation: -Total CD3+ T-cells > 300 cells/µL (at Month 12, 18, 24, 30, 36, 42, 48, 54, 60) - Total CD4+ T-cells > 200 cells/µL (at Month 12, 18, 24, 30, 36, 42, 48, 54, 60) - Presence of naive CD4+ T cells (at Month 12, 18, 24, 30, 36, 42, 48, 54, 60) o B-cell repopulation: - Total B-cell counts (at Month 6, 12, 18, 24, 30, 36, 42, 48, 54, 60) - Memory B-cell count (at Month 6, 12, 18, 24, 30, 36, 42, 48, 54, 60) - Switched memory B-cell count (at Month 6, 12, 18, 24, 30, 36, 42, 48, 54, 60) o Immune function: - Level of IgG (at Month 6, 12, 18, 24, 36, 48, 60) - Level of IgA (at Month 6, 12, 18, 24, 36, 48, 60) - Level of IgM (at Month 6, 12, 18, 24, 36, 48, 60) - IG repertoire and T cell receptor (TCR) repertoire on PBMCs at Month 12 Pharmacodynamics o Vector copy number (VCN) in PBMCs and granulocytes o TRECs and KRECs Quality of Life: Change from baseline in PedsQL

Temporary moments of secondary assessment

Not provided

Inclusion criteria

RAG1-deficient SCID as confirmed by genetic analysis Peripheral blood T cells < 300/L and/or naïve T cells < 1/L Age < 2 years Age at least 8 weeks by the time of busulfan and fludarabine administration Lack of an available HLA-matched donor (HLA-identical sibling or 10/10 (A, B, C, DR, DQ) allele-matched (un)related donor) Signed informed consent (parental or guardian) Able to return to the local HSCT centre for follow-up (per protocol) during the 2-year study and the 15-year long-term off study review Absence of peripheral blood naïve CD4+ T cells

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Calendar

(Last Update: 04/08/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
03/02/2023	01/06/2023	01/06/2023	17/06/2026	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
17/06/2026	Not aported	Not aported	Not aported	Not aported

Sponsor

Videja B.V. Netherlands

De Limes 7

Contact Person

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Monetary support: N/A

Sponsor type: No commercial

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Sites

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

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Medication

RAG1-LV-CD34+ cells

INFUSION

INTRAVENOUS

-

Active Principles: N/A

Orphan **Experimental**

No results