A Study of DR-01 in Adult Subjects With Large Granular Lymphocytic Leukemia or Cytotoxic Lymphomas

Estado	Tipo de Participantes	Rangos de Edad
Reclutando	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	65
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia, farmacocinética, dosis	NO

Información

Identificador
2023-503550-13-00 (CTIS)

Cod. Protocolo
DR-01-ONC-001

Área terapéutica
Enfermedades [C] - Hematología [C15]|

Enfermedad investigada
Large Granular Lymphocytic Leukemia or Cytotoxic Lymphomas

Título Científico
A multicenter, open-label, first-in human, multiple expansion cohort, Phase 1/2 study to evaluate the safety and efficacy of DR-01 in adult subjects with large granular lymphocytic leukemia or cytotoxic lymphomas

Justificación

First in Humans<br/

Objetivo Principal

- To evaluate the safety and tolerability of escalating doses of DR-01 in adult subjects with relapsed/refractory LGLL or cytotoxic lymphomas
- To determine potential pharmacologically optimized dose/regimen(s) for DR-01 for the LGLL and cytotoxic lymphoma populations
- To estimate the ORR, CR rate, and PR rate based on disease-specific response criteria

Variables de Evaluación Primaria

Incidence, severity, and relationship of treatment-emergent adverse events (AEs) (including AEs of special interest [AESIs] and dose-limiting toxicities [DLTs]) and other safety findings
Potential pharmacologically optimized dose/regimen(s) of DR-01 in LGLL and cytotoxic lymphoma populations as determined using an integrated assessment of efficacy, safety, PK/ PD, and exposure-response relationships
ORR, defined as CR or PR based on disease-specific response criteria

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To estimate the overall response rate (ORR), complete response (CR) rate, and partial response (PR) rate based on disease-specific response criteria
To estimate the durability of response as measured by duration of response (DOR), best overall response (BOR), median progression- free survival (mPFS), overall survival (OS), median OS (mOS), and time to response
To characterize the PK profile of DR-01
To evaluate the immunogenicity of DR-01
To evaluate the safety and tolerability of the potential pharmacologically optimized dose/regimen(s) of DR-01 in adult subjects with relapsed/refractory LGLL or cytotoxic lymphomas

Variables de Evaluación Secundaria

ORR, defined as CR or PR based on disease-specific response criteria
Assessment of DOR, BOR, mPFS, OS, mOS, and time to response
PK parameters including Cmax, Ctrough, AUC, and T1/2 and dose proportionality
Incidence of anti-drug antibodies (ADAs) to DR 01
Incidence, severity, and relationship of treatment-emergent AEs (including AESIs) and other safety findings

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

18 years of age Histologically confirmed diagnosis of lymphoma by a hematopathologist (according to the WHO 2016 classification [Swerdlow 2016]). For Part A only, evaluable disease is acceptable. Able to understand and comply with protocol-required study procedures and voluntarily sign a written informed consent document For Part B2 only, evaluable by one of the following response criteria as documented during Screening: a.Subjects must have radiographically measurable disease by computed tomography (CT) or CT/positron emission tomography (CT/PET) scan defined as at least one node measuring >1.5 cm or measurable extranodal lesion of at least 1.0 cm in longest diameter to be evaluated by Lugano criteria (Cheson 2014). b.Subjects with primary cutaneous variants must have at least 1 measurable lesion that is evaluable using the Olsen criteria (Olsen 2021) or leukemic involvement that can be evaluated using a modified TPLL response criteria (Staber 2019). c.Subjects with hepatosplenic disease or other variants that do not have measurable disease by Lugano criteria (Cheson 2014) may be eligible upon discussion with the Medical Monitor if they have identifiable leukemic involvement in BM or peripheral blood (meeting the CD8+ cytotoxic phenotype definition) that can be evaluated for response using a modified TPLL response criteria (Staber 2019), or skin involvement that can be evaluated using Olsen criteria (Olsen 2021). Prothrombin time or international normalized ratio (INR) 1.5 × ULN Activated partial thromboplastin time 1.5 × ULN Creatinine clearance (CrCl) 50 mL/min (using Cockcroft-Gault) Total bilirubin 1.5 × ULN (3 × ULN if known Gilberts disease) Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) 2.5 × ULN (5 × ULN if malignant involvement of the liver and approval by the medical monitor) Amylase <1.5 × ULN Male subjects must agree to use acceptable effective method(s) of contraception (as specified in Appendix D or as permitted by regional regulatory authorities) from enrollment through at least 12 months after last dose of DR-01. Female subjects of childbearing potential (postmenarcheal, has an intact uterus and at least one ovary, and is <1 year postmenopausal) must agree to use a highly effective method of contraception (as specified in Appendix D or as permitted by regional regulatory authorities) from enrollment through at least 12 months after last dose of DR-01. Baseline clinical characteristics must be evaluable for disease assessment by the ECOG E5998 (Loughran 2015) response criteria Eastern Cooperative Oncology Group (ECOG) performance status 0 2 (Oken 1982). Must have discontinued at least one prior line of systemic therapy either due to lack or loss of response after at least 4 months of exposure or due to intolerability at any time and still require therapy. Subjects with T-cell subtype: Pathologically diagnosed LGLL as defined in ECOG E5998 (Loughran 2015) requiring peripheral blood showing CD3+CD57+ population >400/mm3 or CD3+CD8+ population >650/mm3, and evidence for clonal expansion (e.g., TCR PCR, TCR Vbeta by flow cytometry within 12 months prior to C1D1). Subjects with chronic lymphoproliferative disorder of NK cells (CLPD-NK) or NK cell subtype: Pathologically diagnosed LGLL requiring peripheral blood showing CD3-CD16+/CD56+ cells. ECOG performance status 0 1 (Oken 1982). Subjects must have failed at least one prior systemic regimen and still require therapy. If concurrent radio-chemotherapy was applied, the chemotherapy part will be considered one line of systemic therapy. Availability of post-progression tissue sample or willingness to consent to a baseline biopsy.

Criterios de Exclusión

A reactive LGL lymphocytosis to a viral infection or LGL or associated with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). Hepatitis B infection (hepatitis B virus surface antigen [HBsAg] positive), or hepatitis C (hepatitis C virus [HCV] antibody positive, confirmed by HCV ribonucleic acid). Subjects with HCV with undetectable virus after treatment are eligible. History of clinically significant cardiac disease or congestive heart failure greater than New York Heart Association (NYHA) Class II. Major cardiac abnormalities and clotting abnormalities (e.g., uncontrolled angina, unstable arrhythmias, pulmonary embolism, deep venous thrombosis, cerebrovascular accident, myocardial infarction, pericardial effusion, restrictive cardiomyopathy, severe untreated valvular stenosis) within 6 months prior to C1D1, except for adequately treated catheter-related venous thrombosis occurring more than 1 month before C1D1. Hemophagocytic lymphohistiocytosis (HLH); subjects with signs and

symptoms of HLH must have HLH ruled out by a BM biopsy. Electrocardiogram (ECG) QT interval corrected for heart rate (QTc) >475 msec, measured by Fridericias formula (QTcF = QT/[RR^0.33]). Use of biotin (i.e., vitamin B7) or supplements containing biotin higher than the daily adequate intake of 30 g (NIH 2022). Note: subjects who switch from a high dose to a dose of 30 g/day are eligible. Use of systemic corticosteroids at prohibited dose levels within 15 days prior to C1D1 (except for prophylaxis for radiodiagnostic contrast reactions and study-defined premedication) or use of other non-biological immunosuppressive drugs within 15 days or 5 half-lives (whichever is less), prior to C1D1. Any condition requiring hormonal therapy (except for contraception, hormone replacement therapy and hormonal prophylaxis for a prior malignancy). Any other medical or psychiatric condition, or laboratory abnormality that would increase the risk associated with study participation, in the opinion of the Investigator or Medical Monitor. Non-biologics anticancer therapy (e.g., chemotherapy, irradiation) within 14 days or 5 half-lives (whichever is less) of C1D1. Use of biological therapies within 30 days of C1D1. <250/mm3 neutrophils (LGLL & ANKL) Toxicities from previous anticancer therapies must have resolved to baseline levels or to Grade 1 (except for alopecia, peripheral neuropathy, or hematologic parameters meeting inclusion criteria). Autologous hematopoietic stem cell transplantation (HSCT) within 40 days of C1D1, allogeneic HSCT within 90 days Any immunosuppressive therapy for graft versus host disease (GVHD) for subjects who are post allogeneic HSCT. Major surgery within 28 days of C1D1 (requires more than local anesthesia or plexus blockade). <750/mm3 neutrophils (Cytotoxic lymphoma) <50,000/mm3 thrombocytes (for HSTCL and ANKL where leukemia manifestation is common, a lower platelet count may be allowed with Medical Monitor approval) Active systemic infection or severe localized infection requiring systemic antibiotics, antivirals or antifungals. Active or suspected malignant central nervous system involvement. Life-threatening, severe complications of malignancy (e.g., uncontrolled bleeding, pneumonia with hypoxia or shock, and/or disseminated intravascular coagulation). Active known second malignancy with the exception of any of the following: a.Adequately treated basal cell carcinoma, squamous cell carcinoma of the skin, or in situ cervical cancer b.Adequately treated Stage I cancer from which the subject is currently in remission and has been in remission for at least 2 years without therapeutic intervention (anti-hormonal therapy is acceptable) c.Low-risk prostate cancer with Gleason score <7 and prostate-specific antigen (PSA) <10 ng/mL Infection with human immunodeficiency virus (HIV) type 1 or 2 (HIV-1 or HIV-2).

Calendario

(Última actualización: 20/02/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
03/07/2023	13/09/2024	13/09/2024	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

Dren Bio 01 Inc. United States

835 Industrial Road Fl 4

Contact Person

Shalini Gidwani

+14086210819

sgidwani@drenbio.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIM Área de Salud de Salamanca

Pº San Vicente nº 55-182 37007 Salamanca

comite.etico.husa@saludcastillayleon.es

923291100

Centros

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

Hospital Universitari Vall D Hebron

Barcelona

BARCELONA

Hematology Department

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

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Ensayos clínicos (Hematología)

Medicamentos

DR-01
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Principios Activos: N/A

Experimental

Sin resultados

A Study of DR-01 in Adult Subjects With Large Granular Lymphocytic Leukemia or Cytotoxic Lymphomas

State	Type of participants	Age Ranges
Recruiting	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	65
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness, pharmacokinetics, dose	NO

Information

Identifier
2023-503550-13-00 (CTIS)

Protocol Code
DR-01-ONC-001

Therapeutic area
Diseases [C] - Hemic and Lymphatic Diseases [C15]|

Investigated Disease
Large Granular Lymphocytic Leukemia or Cytotoxic Lymphomas

Scientific Title
A multicenter, open-label, first-in human, multiple expansion cohort, Phase 1/2 study to evaluate the safety and efficacy of DR-01 in adult subjects with large granular lymphocytic leukemia or cytotoxic lymphomas

Rationale

First in Humans<br/

Main Objective

- To evaluate the safety and tolerability of escalating doses of DR-01 in adult subjects with relapsed/refractory LGLL or cytotoxic lymphomas
- To determine potential pharmacologically optimized dose/regimen(s) for DR-01 for the LGLL and cytotoxic lymphoma populations
- To estimate the ORR, CR rate, and PR rate based on disease-specific response criteria

Primary Endpoints

Incidence, severity, and relationship of treatment-emergent adverse events (AEs) (including AEs of special interest [AESIs] and dose-limiting toxicities [DLTs]) and other safety findings
Potential pharmacologically optimized dose/regimen(s) of DR-01 in LGLL and cytotoxic lymphoma populations as determined using an integrated assessment of efficacy, safety, PK/ PD, and exposure-response relationships
ORR, defined as CR or PR based on disease-specific response criteria

Temporary moments of secondary assessment

Not provided

Secondary Objective

To estimate the overall response rate (ORR), complete response (CR) rate, and partial response (PR) rate based on disease-specific response criteria
To estimate the durability of response as measured by duration of response (DOR), best overall response (BOR), median progression- free survival (mPFS), overall survival (OS), median OS (mOS), and time to response
To characterize the PK profile of DR-01
To evaluate the immunogenicity of DR-01
To evaluate the safety and tolerability of the potential pharmacologically optimized dose/regimen(s) of DR-01 in adult subjects with relapsed/refractory LGLL or cytotoxic lymphomas

Secondary Endpoints

ORR, defined as CR or PR based on disease-specific response criteria
Assessment of DOR, BOR, mPFS, OS, mOS, and time to response
PK parameters including Cmax, Ctrough, AUC, and T1/2 and dose proportionality
Incidence of anti-drug antibodies (ADAs) to DR 01
Incidence, severity, and relationship of treatment-emergent AEs (including AESIs) and other safety findings

Temporary moments of secondary assessment

Not provided

Inclusion criteria

18 years of age Histologically confirmed diagnosis of lymphoma by a hematopathologist (according to the WHO 2016 classification [Swerdlow 2016]). For Part A only, evaluable disease is acceptable. Able to understand and comply with protocol-required study procedures and voluntarily sign a written informed consent document For Part B2 only, evaluable by one of the following response criteria as documented during Screening: a.Subjects must have radiographically measurable disease by computed tomography (CT) or CT/positron emission tomography (CT/PET) scan defined as at least one node measuring >1.5 cm or measurable extranodal lesion of at least 1.0 cm in longest diameter to be evaluated by Lugano criteria (Cheson 2014). b.Subjects with primary cutaneous variants must have at least 1 measurable lesion that is evaluable using the Olsen criteria (Olsen 2021) or leukemic involvement that can be evaluated using a modified TPLL response criteria (Staber 2019). c.Subjects with hepatosplenic disease or other variants that do not have measurable disease by Lugano criteria (Cheson 2014) may be eligible upon discussion with the Medical Monitor if they have identifiable leukemic involvement in BM or peripheral blood (meeting the CD8+ cytotoxic phenotype definition) that can be evaluated for response using a modified TPLL response criteria (Staber 2019), or skin involvement that can be evaluated using Olsen criteria (Olsen 2021). Prothrombin time or international normalized ratio (INR) 1.5 × ULN Activated partial thromboplastin time 1.5 × ULN Creatinine clearance (CrCl) 50 mL/min (using Cockcroft-Gault) Total bilirubin 1.5 × ULN (3 × ULN if known Gilberts disease) Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) 2.5 × ULN (5 × ULN if malignant involvement of the liver and approval by the medical monitor) Amylase <1.5 × ULN Male subjects must agree to use acceptable effective method(s) of contraception (as specified in Appendix D or as permitted by regional regulatory authorities) from enrollment through at least 12 months after last dose of DR-01. Female subjects of childbearing potential (postmenarcheal, has an intact uterus and at least one ovary, and is <1 year postmenopausal) must agree to use a highly effective method of contraception (as specified in Appendix D or as permitted by regional regulatory authorities) from enrollment through at least 12 months after last dose of DR-01. Baseline clinical characteristics must be evaluable for disease assessment by the ECOG E5998 (Loughran 2015) response criteria Eastern Cooperative Oncology Group (ECOG) performance status 0 2 (Oken 1982). Must have discontinued at least one prior line of systemic therapy either due to lack or loss of response after at least 4 months of exposure or due to intolerability at any time and still require therapy. Subjects with T-cell subtype: Pathologically diagnosed LGLL as defined in ECOG E5998 (Loughran 2015) requiring peripheral blood showing CD3+CD57+ population >400/mm3 or CD3+CD8+ population >650/mm3, and evidence for clonal expansion (e.g., TCR PCR, TCR Vbeta by flow cytometry within 12 months prior to C1D1). Subjects with chronic lymphoproliferative disorder of NK cells (CLPD-NK) or NK cell subtype: Pathologically diagnosed LGLL requiring peripheral blood showing CD3-CD16+/CD56+ cells. ECOG performance status 0 1 (Oken 1982). Subjects must have failed at least one prior systemic regimen and still require therapy. If concurrent radio-chemotherapy was applied, the chemotherapy part will be considered one line of systemic therapy. Availability of post-progression tissue sample or willingness to consent to a baseline biopsy.

Exclusion criteria

A reactive LGL lymphocytosis to a viral infection or LGL or associated with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). Hepatitis B infection (hepatitis B virus surface antigen [HBsAg] positive), or hepatitis C (hepatitis C virus [HCV] antibody positive, confirmed by HCV ribonucleic acid). Subjects with HCV with undetectable virus after treatment are eligible. History of clinically significant cardiac disease or congestive heart failure greater than New York Heart Association (NYHA) Class II. Major cardiac abnormalities and clotting abnormalities (e.g., uncontrolled angina, unstable arrhythmias, pulmonary embolism, deep venous thrombosis, cerebrovascular accident, myocardial infarction, pericardial effusion, restrictive cardiomyopathy, severe untreated valvular stenosis) within 6 months prior to C1D1, except for adequately treated catheter-related venous thrombosis occurring more than 1 month before C1D1. Hemophagocytic lymphohistiocytosis (HLH); subjects with signs and

symptoms of HLH must have HLH ruled out by a BM biopsy. Electrocardiogram (ECG) QT interval corrected for heart rate (QTc) >475 msec, measured by Fridericias formula (QTcF = QT/[RR^0.33]). Use of biotin (i.e., vitamin B7) or supplements containing biotin higher than the daily adequate intake of 30 g (NIH 2022). Note: subjects who switch from a high dose to a dose of 30 g/day are eligible. Use of systemic corticosteroids at prohibited dose levels within 15 days prior to C1D1 (except for prophylaxis for radiodiagnostic contrast reactions and study-defined premedication) or use of other non-biological immunosuppressive drugs within 15 days or 5 half-lives (whichever is less), prior to C1D1. Any condition requiring hormonal therapy (except for contraception, hormone replacement therapy and hormonal prophylaxis for a prior malignancy). Any other medical or psychiatric condition, or laboratory abnormality that would increase the risk associated with study participation, in the opinion of the Investigator or Medical Monitor. Non-biologics anticancer therapy (e.g., chemotherapy, irradiation) within 14 days or 5 half-lives (whichever is less) of C1D1. Use of biological therapies within 30 days of C1D1. <250/mm3 neutrophils (LGLL & ANKL) Toxicities from previous anticancer therapies must have resolved to baseline levels or to Grade 1 (except for alopecia, peripheral neuropathy, or hematologic parameters meeting inclusion criteria). Autologous hematopoietic stem cell transplantation (HSCT) within 40 days of C1D1, allogeneic HSCT within 90 days Any immunosuppressive therapy for graft versus host disease (GVHD) for subjects who are post allogeneic HSCT. Major surgery within 28 days of C1D1 (requires more than local anesthesia or plexus blockade). <750/mm3 neutrophils (Cytotoxic lymphoma) <50,000/mm3 thrombocytes (for HSTCL and ANKL where leukemia manifestation is common, a lower platelet count may be allowed with Medical Monitor approval) Active systemic infection or severe localized infection requiring systemic antibiotics, antivirals or antifungals. Active or suspected malignant central nervous system involvement. Life-threatening, severe complications of malignancy (e.g., uncontrolled bleeding, pneumonia with hypoxia or shock, and/or disseminated intravascular coagulation). Active known second malignancy with the exception of any of the following: a.Adequately treated basal cell carcinoma, squamous cell carcinoma of the skin, or in situ cervical cancer b.Adequately treated Stage I cancer from which the subject is currently in remission and has been in remission for at least 2 years without therapeutic intervention (anti-hormonal therapy is acceptable) c.Low-risk prostate cancer with Gleason score <7 and prostate-specific antigen (PSA) <10 ng/mL Infection with human immunodeficiency virus (HIV) type 1 or 2 (HIV-1 or HIV-2).

Calendar

(Last Update: 20/02/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
03/07/2023	13/09/2024	13/09/2024	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

Dren Bio 01 Inc. United States

835 Industrial Road Fl 4

Contact Person

Shalini Gidwani

+14086210819

sgidwani@drenbio.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIM Área de Salud de Salamanca

Pº San Vicente nº 55-182 37007 Salamanca

comite.etico.husa@saludcastillayleon.es

923291100

Sites

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

Hospital Universitari Vall D Hebron

Barcelona

BARCELONA

Hematology Department

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

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Ensayos clínicos (Hematología)

Medication

DR-01
SOLUTION FOR INFUSION
INTRAVENOUS INFUSION

-

Active Principles: N/A

Experimental

No results