Transplant BRaVE NHL: Phase I-II study combining Brentuximab Vedotin with second line salvage chemotherapy (R-DHAP) in CD30 positive diffuse large B-cell lymphoma patients refractory to first line chemotherapy or in first relapse who are eligible for high dose treatment followed by autologous stem cell transplantation. Transplant BRaVE NHL

Estado	**Tipo de Participantes**	**Rangos de Edad**
Fin Reclutamiento	No aportado	Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase II	36
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	tratamiento, seguridad, eficacia	NO

Información

Identificador
2023-510556-22-00 (CTIS)

Cod. Protocolo
HO136

Transicionado 2016-001211-21

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

Enfermedad investigada
non-Hodgkin lymphoma (NHL)
Diffuse large B-cell lymphoma (DLBCL)

Título Científico

HOVON 136 NHL: Phase I-II study combining Brentuximab Vedotin with second line salvage chemotherapy (RDHAP) in CD30 positive diffuse large B-cell lymphoma patients refractory to first line chemotherapy or in first relapse who are eligible for high dose treatment followed by autologous stem cell transplantation.

Justificación

No aportado

Objetivo Principal

Phase 1 part:
- To identify the feasibility and RDL (recommended dose level) of brentuximab vedotin in combination with R-DHAP
Phase 2 part:
- To evaluate the efficacy of the combination of brentuximab -vedotin and R-DHAP as salvage treatment in relapse/refractory DLBCL patients in terms of metabolic CR rate after the third cycle
- To establish the rate of CTCAE grade 3/4 non-hematological toxicity, including neurotoxicity after each cycle of brentuximab vedotin-R-DHAP

Variables de Evaluación Primaria

Phase 1 part: The rate of patients with serious toxicity during cycle 1-2 of the combination BV-R-DHAP. Phase 2 part: 1) Primary efficacy endpoint: Metaftabolic CR rate (PET-diagnostic CT) er the third cycle of BV-R-DHAP salvage therapy. 2) Primary feasibility/toxicity endpoints: Rate of grade 3/4 non-hematological toxicity, including neurotoxicity after each cycle of BV-R-DHAP

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Phase 1 part: To assess the toxicity of brentuximab vedotin in combination with R-DHAP
Phase 1 part: To assess the success rate of autologous peripheral blood stem cell harvest after brentuximab vedotin-R-DHAP
Phase 2 part: To asses the overall response rate (ORR) after 3 cycles and after ASCT
Phase 2 part: To assess the toxicity profile of brentuximab vedotin in combination with R-DHAP
Phase 2 part: To assess hematological recovery after each cycle of brentuximab vedotin-R-DHAP
Phase 2 part: To assess the success rate of harvesting an autologous peripheral blood stem cell graft
Phase 2 part: To assess the fraction of patients (CR/PR) eligible for ASCT who actually undergo ASCT
Phase 2 part: To assess peripheral blood neutrophil and platelet recovery after ASCT
Phase 2 part: To evaluate the progression free survival (PFS), event free survival (EFS), and overall survival (OS)
Phase 2 part: To identify predictive factors for response, PFS, EFS and OS (exploratory analysis)

Variables de Evaluación Secundaria

Phase 1 part: (Serious) Adverse Events during combination treatment
Phase 1 part: Time to hematological recovery after each cycle of BV-R-DHAP
Phase 1 part: Time to recovery from non-hematological toxicity after each cycle of BV-R-DHAP
Phase 1 part: Administration of treatment: dose reductions, interval between cycles, discontinuation rate
Phase 1 part: Rate of successful PBSC collection (2x106 CD34+ cells/kg) after the third cycle of BV-R-DHAP
Phase 2 part: Overall response rate (PR + CR) after the third cycle of BV-R-DHAP salvage therapy (based on the results of the FDG-PET/CT scan)
Phase 2 part: Overall response rate (PR + CR) after ASCT (based on the results of the FDG-PET/CT scan)
Phase 2 part: Metabolic CR rate (PET-CT) after ASCT
Phase 2 part: Fraction of patients (CR/PR) eligible for ASCT who actually undergo ASCT
Phase 2 part: Progression free survival (PFS), Event free survival (EFS), Overall survival (OS)
Phase 2 part: (Serious) Adverse Events during the combination treatment
Phase 2 part: Time to hematological recovery after each cycle of BV + R-DHAP
Phase 2 part: Administration of treatment: dose reductions, interval between courses, discontinuation rate
Phase 2 part: Rate of successful PBSC collection (2 x106 CD34+ cells/kg) after the second or third cycle of BV-R-DHAP
Phase 2 part: Time to hematological recovery after ASCT
Phase 2 part: (Serious) Adverse Events after ASCT

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

CD30 positive DLBCL, i.e. more than 1% of DLBCL cells CD30 positive according to the WHO classification 2008: CD30 positive DLBCL, including EBV positive DLBCL. CD30 positive primary mediastinal B-cell lymphoma Eligible for high-dose chemotherapy and ASCT Resolution of relevant toxicities from first-line therapy Life expectancy of > 3 months with treatment Negative pregnancy test at study entry, if applicable Female patient is either post-menopausal for at least 1 year before screening visit or surgically sterile or if of childbearing potential, agrees to practice 2 effective methods of contraception, at the same time, or agrees to completely abstain from heterosexual intercourse, from the time of signing the informed consent through 12 months after the last dose of study drug Male patients, even if surgically sterilized, (i.e. status post vasectomy) agree to practice effective barrier contraception, or agrees to completely abstain from heterosexual intercourse, during the entire study period and through 12 months after the last dose of study drug Written informed consent Patient is capable of giving informed consent Primary refractory to or in first relapse after first line therapy with R-CHOP or R-CHOP-like therapy Age 18 years (upper age limit for ASCT at the discretion of the participating center) Measurable disease: on CT scan at least 1 lesion/node with a long axis of > 1.5 cm and at least one positive lesion on 18F-FDG PET scan WHO performance status 0-2 Adequate hepatic function Adequate renal function Adequate bone marrow function Hemoglobin must be 8 g/dL (5.0 mmol/L), transfusion is allowed

Criterios de Exclusión

Peripheral sensory or motor neuropathy grade 2
History of another malignancy less than 3 years before study inclusion, or previously diagnosed with another malignancy and have evidence of residual disease, with the exception of non-melanoma skin cancer, completely resected melanoma TNMpT1 and carcinoma in situ of the uterine cervix

Known hypersensitivity to recombinant proteins, murine proteins, or to any excipient contained in the drug formulation of brentuximab vedotin
Active hepatitis B or C infection
HIV positivity
Radiation therapy within 8 weeks prior to start of protocol treatment. Emergency radiation therapy is allowed, as long as measurable disease (at non-irradiated sites) persists
Patients with a serious psychiatric disorder that could, in the investigator's opinion, potentially interfere with the completion of treatment according to protocol
Major organ dysfunction, unless NHL-related
Patients who have any severe and/or uncontrolled medical condition or other conditions that could affect their participation in the study
Thyroid abnormalities when thyroid function cannot be maintained in the normal range by medication
Current participation in another clinical trial interfering with this trial
Known cerebral or meningeal disease (NHL or any other etiology), including signs and symptoms of progressive multifocal leukoencephalopathy (PML)
Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule
Claustrophobia to the extent that PET-CT is impossible
Symptomatic neurological disease compromising normal activities of daily living or requiring medications
Transformed lymphoma
DLBCL after organ transplantation
Immunodeficiency-associated B-cell lymphoproliferative disease
Use of other investigational agents within at least 5 half-lives of the most recent agent used prior to study entry
Treatment with myelosuppressive chemotherapy or biological therapy 4 weeks before study entry
Female patients who are breast feeding

Calendario

(Última actualización: 13/11/2024)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
29/04/2020	14/07/2020	15/05/2020	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
18/07/2023	No aportado	No aportado	No aportado	No aportado

Promotor

Hemato-Oncologie voor Volwassenen Nederland (Hovon) Stichting Netherlands

Dr. Molewaterplein 40

Contact Person

HOVON

+31107041560

hovon@erasmusmc.nl

Monetary support: N/A

Tipo de promotor: No comercial

Ceim

CEIm Hospital Universitari de Bellvitge

Feixa Llarga, s/n - Antiguo Módulo Banco de Santander 08907 Hospitalet de Llobregat

mcruz@idibell.cat

Centros

Activo (28/05/2020)

COMPLEJO ASISTENCIAL UNIVERSITARIO DE SALAMANCA

Salamanca

SALAMANCA

Hematología

Activo (30/06/2020)

COMPLEJO HOSPITALARIO GREGORIO MARAÑÓN

Madrid

MADRID

Hematología

Activo (23/09/2020)

HOSPITAL CLÍNIC DE BARCELONA

Barcelona

BARCELONA

Hematología

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

Hospital General Universitario Gregorio Maranon

Madrid

MADRID

Hematology

Activo (16/06/2020)

HOSPITAL UNIVERSITARIO Y POLITÉCNICO LA FE

Valencia

VALENCIA

Hematología

Activo (30/06/2020)

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

Madrid

MADRID

Hematología

Activo (15/05/2020)

Institut Catala D'oncologia

Hospitalet de Llobregat, L'

BARCELONA

Hematology Department and Hematopoietic Stem Cell Transplant Programme

Medicamentos

ADCETRIS 50 mg powder for concentrate for solution for infusion

SOLUTION FOR INFUSION

INTRAVENOUS USE

Código ATC: L01XC12 - BRENTUXIMAB VEDOTINA

Principios Activos: N/A

Experimental

Sin resultados

Transplant BRaVE NHL: Phase I-II study combining Brentuximab Vedotin with second line salvage chemotherapy (R-DHAP) in CD30 positive diffuse large B-cell lymphoma patients refractory to first line chemotherapy or in first relapse who are eligible for high dose treatment followed by autologous stem cell transplantation. Transplant BRaVE NHL

State	Type of participants	Age Ranges
End of recruitment	Not provided	Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase II	36
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	treatment, safety, effectiveness	NO

Information

Identifier
2023-510556-22-00 (CTIS)

Protocol Code
HO136

Transitioned 2016-001211-21

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

Investigated Disease
non-Hodgkin lymphoma (NHL)
Diffuse large B-cell lymphoma (DLBCL)

Scientific Title

HOVON 136 NHL: Phase I-II study combining Brentuximab Vedotin with second line salvage chemotherapy (RDHAP) in CD30 positive diffuse large B-cell lymphoma patients refractory to first line chemotherapy or in first relapse who are eligible for high dose treatment followed by autologous stem cell transplantation.

Rationale

Not provided

Main Objective

Phase 1 part:
- To identify the feasibility and RDL (recommended dose level) of brentuximab vedotin in combination with R-DHAP
Phase 2 part:
- To evaluate the efficacy of the combination of brentuximab -vedotin and R-DHAP as salvage treatment in relapse/refractory DLBCL patients in terms of metabolic CR rate after the third cycle
- To establish the rate of CTCAE grade 3/4 non-hematological toxicity, including neurotoxicity after each cycle of brentuximab vedotin-R-DHAP

Primary Endpoints

Phase 1 part: The rate of patients with serious toxicity during cycle 1-2 of the combination BV-R-DHAP. Phase 2 part: 1) Primary efficacy endpoint: Metaftabolic CR rate (PET-diagnostic CT) er the third cycle of BV-R-DHAP salvage therapy. 2) Primary feasibility/toxicity endpoints: Rate of grade 3/4 non-hematological toxicity, including neurotoxicity after each cycle of BV-R-DHAP

Temporary moments of secondary assessment

Not provided

Secondary Objective

Phase 1 part: To assess the toxicity of brentuximab vedotin in combination with R-DHAP
Phase 1 part: To assess the success rate of autologous peripheral blood stem cell harvest after brentuximab vedotin-R-DHAP
Phase 2 part: To asses the overall response rate (ORR) after 3 cycles and after ASCT
Phase 2 part: To assess the toxicity profile of brentuximab vedotin in combination with R-DHAP
Phase 2 part: To assess hematological recovery after each cycle of brentuximab vedotin-R-DHAP
Phase 2 part: To assess the success rate of harvesting an autologous peripheral blood stem cell graft
Phase 2 part: To assess the fraction of patients (CR/PR) eligible for ASCT who actually undergo ASCT
Phase 2 part: To assess peripheral blood neutrophil and platelet recovery after ASCT
Phase 2 part: To evaluate the progression free survival (PFS), event free survival (EFS), and overall survival (OS)
Phase 2 part: To identify predictive factors for response, PFS, EFS and OS (exploratory analysis)

Secondary Endpoints

Phase 1 part: (Serious) Adverse Events during combination treatment
Phase 1 part: Time to hematological recovery after each cycle of BV-R-DHAP
Phase 1 part: Time to recovery from non-hematological toxicity after each cycle of BV-R-DHAP
Phase 1 part: Administration of treatment: dose reductions, interval between cycles, discontinuation rate
Phase 1 part: Rate of successful PBSC collection (2x106 CD34+ cells/kg) after the third cycle of BV-R-DHAP
Phase 2 part: Overall response rate (PR + CR) after the third cycle of BV-R-DHAP salvage therapy (based on the results of the FDG-PET/CT scan)
Phase 2 part: Overall response rate (PR + CR) after ASCT (based on the results of the FDG-PET/CT scan)
Phase 2 part: Metabolic CR rate (PET-CT) after ASCT
Phase 2 part: Fraction of patients (CR/PR) eligible for ASCT who actually undergo ASCT
Phase 2 part: Progression free survival (PFS), Event free survival (EFS), Overall survival (OS)
Phase 2 part: (Serious) Adverse Events during the combination treatment
Phase 2 part: Time to hematological recovery after each cycle of BV + R-DHAP
Phase 2 part: Administration of treatment: dose reductions, interval between courses, discontinuation rate
Phase 2 part: Rate of successful PBSC collection (2 x106 CD34+ cells/kg) after the second or third cycle of BV-R-DHAP
Phase 2 part: Time to hematological recovery after ASCT
Phase 2 part: (Serious) Adverse Events after ASCT

Temporary moments of secondary assessment

Not provided

Inclusion criteria

CD30 positive DLBCL, i.e. more than 1% of DLBCL cells CD30 positive according to the WHO classification 2008: CD30 positive DLBCL, including EBV positive DLBCL. CD30 positive primary mediastinal B-cell lymphoma Eligible for high-dose chemotherapy and ASCT Resolution of relevant toxicities from first-line therapy Life expectancy of > 3 months with treatment Negative pregnancy test at study entry, if applicable Female patient is either post-menopausal for at least 1 year before screening visit or surgically sterile or if of childbearing potential, agrees to practice 2 effective methods of contraception, at the same time, or agrees to completely abstain from heterosexual intercourse, from the time of signing the informed consent through 12 months after the last dose of study drug Male patients, even if surgically sterilized, (i.e. status post vasectomy) agree to practice effective barrier contraception, or agrees to completely abstain from heterosexual intercourse, during the entire study period and through 12 months after the last dose of study drug Written informed consent Patient is capable of giving informed consent Primary refractory to or in first relapse after first line therapy with R-CHOP or R-CHOP-like therapy Age 18 years (upper age limit for ASCT at the discretion of the participating center) Measurable disease: on CT scan at least 1 lesion/node with a long axis of > 1.5 cm and at least one positive lesion on 18F-FDG PET scan WHO performance status 0-2 Adequate hepatic function Adequate renal function Adequate bone marrow function Hemoglobin must be 8 g/dL (5.0 mmol/L), transfusion is allowed

Exclusion criteria

Peripheral sensory or motor neuropathy grade 2
History of another malignancy less than 3 years before study inclusion, or previously diagnosed with another malignancy and have evidence of residual disease, with the exception of non-melanoma skin cancer, completely resected melanoma TNMpT1 and carcinoma in situ of the uterine cervix

Known hypersensitivity to recombinant proteins, murine proteins, or to any excipient contained in the drug formulation of brentuximab vedotin
Active hepatitis B or C infection
HIV positivity
Radiation therapy within 8 weeks prior to start of protocol treatment. Emergency radiation therapy is allowed, as long as measurable disease (at non-irradiated sites) persists
Patients with a serious psychiatric disorder that could, in the investigator's opinion, potentially interfere with the completion of treatment according to protocol
Major organ dysfunction, unless NHL-related
Patients who have any severe and/or uncontrolled medical condition or other conditions that could affect their participation in the study
Thyroid abnormalities when thyroid function cannot be maintained in the normal range by medication
Current participation in another clinical trial interfering with this trial
Known cerebral or meningeal disease (NHL or any other etiology), including signs and symptoms of progressive multifocal leukoencephalopathy (PML)
Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule
Claustrophobia to the extent that PET-CT is impossible
Symptomatic neurological disease compromising normal activities of daily living or requiring medications
Transformed lymphoma
DLBCL after organ transplantation
Immunodeficiency-associated B-cell lymphoproliferative disease
Use of other investigational agents within at least 5 half-lives of the most recent agent used prior to study entry
Treatment with myelosuppressive chemotherapy or biological therapy 4 weeks before study entry
Female patients who are breast feeding

Calendar

(Last Update: 13/11/2024)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
29/04/2020	14/07/2020	15/05/2020	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
18/07/2023	Not aported	Not aported	Not aported	Not aported

Sponsor

Hemato-Oncologie voor Volwassenen Nederland (Hovon) Stichting Netherlands

Dr. Molewaterplein 40

Contact Person

HOVON

+31107041560

hovon@erasmusmc.nl

Monetary support: N/A

Sponsor type: No commercial

Ceim

CEIm Hospital Universitari de Bellvitge

Feixa Llarga, s/n - Antiguo Módulo Banco de Santander 08907 Hospitalet de Llobregat

mcruz@idibell.cat

Sites

Active (28/05/2020)

COMPLEJO ASISTENCIAL UNIVERSITARIO DE SALAMANCA

Salamanca

SALAMANCA

Hematología

Active (30/06/2020)

COMPLEJO HOSPITALARIO GREGORIO MARAÑÓN

Madrid

MADRID

Hematología

Active (23/09/2020)

HOSPITAL CLÍNIC DE BARCELONA

Barcelona

BARCELONA

Hematología

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

Hospital General Universitario Gregorio Maranon

Madrid

MADRID

Hematology

Active (16/06/2020)

HOSPITAL UNIVERSITARIO Y POLITÉCNICO LA FE

Valencia

VALENCIA

Hematología

Active (30/06/2020)

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

Madrid

MADRID

Hematología

Active (15/05/2020)

Institut Catala D'oncologia

Hospitalet de Llobregat, L'

BARCELONA

Hematology Department and Hematopoietic Stem Cell Transplant Programme

Medication

ADCETRIS 50 mg powder for concentrate for solution for infusion

SOLUTION FOR INFUSION

INTRAVENOUS USE

ATC code: L01XC12 - BRENTUXIMAB VEDOTINA

Active Principles: N/A

Experimental

No results