A first-in-human clinical trial in adult patients with metastatic or recurrent melanoma of a personalised therapy targeting specific mutations that occur in all cancer cells within a single patient

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	40
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico nacional	tratamiento, seguridad, eficacia, dosis	Terapia celular

Información

Identificador
2024-513062-19-00 (CTIS)

Cod. Protocolo
ATX-ME-001

Transicionado 2018-003446-16

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

Enfermedad investigada
Metastatic or recurrent melanoma

Título Científico
An open-label, multi-centre, phase I/IIa study evaluating the safety and clinical activity of neoantigen reactive T cells in patients with metastatic or recurrent melanoma

Justificación

No aportado

Objetivo Principal

To assess the safety and tolerability of ATL001 as a monotherapy and in combination with nivolumab

Variables de Evaluación Primaria

Frequency and severity of adverse events (AEs) and serious adverse events (SAEs) following tissue procurement and administration of lymphodepletion agents, ATL001 (monotherapy or in combination with nivolumab) and IL-2

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To evaluate the clinical activity of ATL001 treatment as a monotherapy and in combination with nivolumab

Variables de Evaluación Secundaria

Percentage change from baseline in tumour size at 6 weeks, 12 weeks and best change from baseline
Overall Response Rate (ORR) (based on RECIST v1.1 and imRECIST)
Time to response (based on RECIST v1.1 and imRECIST)
Duration of response (based on RECIST v1.1 and imRECIST)
Disease Control Rate (CR + PR + durable SD) (based on RECIST v1.1)
Progression free survival (PFS) (based on RECIST v1.1 and imRECIST)
Overall survival (OS)

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Patient must be at least 18 years old at the screening visit Female patients who are of childbearing potential must agree to use a highly effective method of contraception during the study and for at least 12 months after the ATL001 infusion. Non-sterilised male participants who intend to be sexually active with a female partner of childbearing

potential must use an acceptable method of contraception from the time of screening, throughout the duration of the study and for at least 6 months after the ATL001 infusion To be eligible to enter this study for procurement, the patient must fall into one of the following groups: a. Patients with metastatic or recurrent disease who have had no prior systemic therapy for advanced disease and who have accessible sites of disease suitable for collection of adequate tissue for ATL001 manufacture. b. Patients with metastatic or recurrent disease who are on or have completed first line systemic therapy and have accessible sites of disease suitable for collection of adequate tissue for ATL001 manufacture. c. Other patients with advanced stage disease for whom no other alternative approved treatments are available, may be considered on a case-by-case basis and should be discussed with the Sponsor prior to enrolment Anticipated life expectancy 6 months at the time of tissue procurement Patients must have metastatic melanoma and: a. Whose disease has progressed or recurred following standard of care. This includes patients who have received a component of standard of care therapy as part of a previous clinical trial in first line treatment; or b. Who are ineligible for, or who cannot tolerate, standard of care therapies. Patients who stop treatment due to immunotherapy toxicities do not need to progress in order to receive treatment with ATL001. Patients must have measurable disease according to RECIST v1.1 criteria prior to lymphodepletion Patient is considered, in the opinion of the Investigator, well enough (i.e. ECOG Performance Status 0-1) to receive ATL001 treatment (this will be checked prior to lymphodepletion and again prior to receiving ATL001) Prior to treatment with ATL001, the treatment regimen must have included a PD-1/PD-L1 inhibitor and patients should have experienced: a. Radiological disease progression; or b. Stable disease following at least 4 doses of a PD-1/PD-L1 inhibitor In addition to the need for highly effective contraception as outlined in Inclusion Criterion 10 above, female patients in Cohort B of childbearing potential must agree to use effective contraception during treatment with nivolumab and for at least 5 months after the last dose of nivolumab. Patients must also agree to provide a serum or urine pregnancy test before each nivolumab administration during the treatment period in Cohort B Patient must have given written informed consent to participate in the study Patients must have histologically confirmed diagnosis of melanoma Patients must have received a PD-1/PD-L1 inhibitor prior to treatment with ATL001 (unless contraindicated) Patients whose tumour is known to have a BRAF V600 mutation must have received BRAF targeted therapy (as well as a PD-1/PD-L1 inhibitor unless contraindicated) prior to treatment with ATL001 Patient is considered medically fit enough to undergo all study procedures and interventions: procedures to procure blood and tumour tissue, including a general anaesthetic if required, and to receive fludarabine, cyclophosphamide and IL-2 at protocol doses and schedules Patient is considered, in the opinion of the Investigator, capable of adhering to the protocol Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1 Adequate organ function indicated by the following laboratory parameters: a. Haemoglobin 10.0 g/dL. b. White Blood Cell Count (WBC) 3.0 x10/L. c. Absolute Neutrophil Count (ANC) 1.5 x10/L. d. Platelets 100 x10/L. e. INR/PT and APTR/APTT < 1.5x ULN, unless receiving therapeutic anticoagulation. Investigator discretion is required to ensure surgery is safe or that anticoagulants can be safely stopped. f. AST or ALT 2.5x ULN. g. Bilirubin < 1.5x ULN (or < 3x ULN if Gilberts Syndrome) h. Creatinine clearance/estimated glomerular filtration rate (GFR) 50 mL/min.

Criterios de Exclusión

Patients with known leptomeningeal disease or central nervous system (CNS) metastases that are untreated or symptomatic or progressing. Lesions should be clinically and radiologically stable for 2 months after treatment, as determined by MRI or CT evaluation, in line with accepted standard of care procedures, and should not require steroids Patients who have undergone major surgery in the previous 3 weeks Patients with an active concurrent cancer or a history of cancer within the past 3 years (except for in situ carcinomas, early prostate cancer with normal Prostate-Specific Antigen (PSA) or non-melanomatous skin cancers) Patients with a history of organ transplantation Patients who have previously received any investigational cell or gene therapies Patients with contraindications for cyclophosphamide, fludarabine and IL-2 at per protocol doses Patients with a confirmed history of allergic reactions to amphotericin b, penicillin and/or streptomycin Patients who have received any cytotoxic chemotherapy within the 3 weeks prior to tissue and blood procurement Patients with a history of (non-infectious) pneumonitis that required systemic steroids, or current pneumonitis/interstitial lung disease Patients with a history of severe hypersensitivity to a monoclonal antibody, allergy or hypersensitivity to nivolumab itself and/or its components Patients who have received a live vaccination within the 28 days prior to the first dose of nivolumab Patients with ocular, acral or mucosal melanoma Patients with any contraindications for nivolumab Patients with a Left Ventricular Ejection Fraction (LVEF) < 45% Patients with a forced expiratory volume in one second (FEV1) of less than or equal to 60% of their predicted normal Patients who have received a live vaccination within the 28 days prior to lymphodepletion

Patients with an active infection requiring antibiotics Patients who have received any cytotoxic chemotherapy within the 3 weeks prior to lymphodepletion Patients with hepatitis B or C, human immunodeficiency virus infection (HIV1/2), syphilis or HTLVI/II infection Patients with active, known, or suspected, autoimmune disease requiring immunosuppressive treatments Patients requiring regular treatment with steroids at a dose higher than prednisolone 10 mg/day (or equivalent) Patients with a current or recent history, as determined by the Investigator, of clinically significant, progressive, and/or uncontrolled renal, hepatic, haematological, endocrine, pulmonary, cardiac, gastroenterological or neurological disease Patients with a history of immune mediated central nervous system toxicity that was caused by, or suspected to be caused by, immunotherapy Patients with a history of Grade 2 diarrhoea/colitis caused by previous immunotherapy within 6 months of screening. Patients that have been asymptomatic for at least 6 months or have had a normal colonoscopy post-immunotherapy (with uninflamed mucosa by visual assessment following discontinuation of immune suppression other than permitted modified release steroids) are not excluded Patients who are pregnant or breastfeeding

Calendario

(Última actualización: 29/05/2024)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
27/07/2022	22/12/2022	28/03/2023	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

Achilles Therapeutics UK Limited United Kingdom

245 Hammersmith Road

Contact Person

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+442081544600

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Monetary support: N/A

Tipo de promotor: Comercial

Ceim

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Centros

Activo (22/12/2022)

HOSPITAL UNIVERSITARIO FUNDACION JIMENEZ DIAZ

Madrid

MADRID

Oncologia

Activo (14/02/2023)

HOSPITAL UNIVERSITARIO HM SANCHINARRO

Madrid

MADRID

Oncología - START MADRID

Medicamentos

OPDIVO 10 mg/mL concentrate for solution for infusion.
SOLUTION FOR INFUSION
INTRAVENOUS USE

Código ATC: L01FF01 - NIVOLUMAB
Principios Activos: N/A

Experimental

ATL001
DISPERSION FOR INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

Sin resultados

A first-in-human clinical trial in adult patients with metastatic or recurrent melanoma of a personalised therapy targeting specific mutations that occur in all cancer cells within a single patient

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	40
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
National multicenter	treatment, safety, effectiveness, dose	Cellular therapy

Information

Identifier
2024-513062-19-00 (CTIS)

Protocol Code
ATX-ME-001

Transitioned 2018-003446-16

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

Investigated Disease
Metastatic or recurrent melanoma

Scientific Title
An open-label, multi-centre, phase I/IIa study evaluating the safety and clinical activity of neoantigen reactive T cells in patients with metastatic or recurrent melanoma

Rationale

Not provided

Main Objective

To assess the safety and tolerability of ATL001 as a monotherapy and in combination with nivolumab

Primary Endpoints

Frequency and severity of adverse events (AEs) and serious adverse events (SAEs) following tissue procurement and administration of lymphodepletion agents, ATL001 (monotherapy or in combination with nivolumab) and IL-2

Temporary moments of secondary assessment

Not provided

Secondary Objective

To evaluate the clinical activity of ATL001 treatment as a monotherapy and in combination with nivolumab

Secondary Endpoints

Percentage change from baseline in tumour size at 6 weeks, 12 weeks and best change from baseline
Overall Response Rate (ORR) (based on RECIST v1.1 and imRECIST)
Time to response (based on RECIST v1.1 and imRECIST)
Duration of response (based on RECIST v1.1 and imRECIST)
Disease Control Rate (CR + PR + durable SD) (based on RECIST v1.1)
Progression free survival (PFS) (based on RECIST v1.1 and imRECIST)
Overall survival (OS)

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Patient must be at least 18 years old at the screening visit Female patients who are of childbearing potential must agree to use a highly effective method of contraception during the study and for at least 12 months after the ATL001 infusion. Non-sterilised male participants who intend to be sexually active with a female partner of childbearing

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Exclusion criteria

Patients with known leptomeningeal disease or central nervous system (CNS) metastases that are untreated or symptomatic or progressing. Lesions should be clinically and radiologically stable for 2 months after treatment, as determined by MRI or CT evaluation, in line with accepted standard of care procedures, and should not require steroids Patients who have undergone major surgery in the previous 3 weeks Patients with an active concurrent cancer or a history of cancer within the past 3 years (except for in situ carcinomas, early prostate cancer with normal Prostate-Specific Antigen (PSA) or non-melanomatous skin cancers) Patients with a history of organ transplantation Patients who have previously received any investigational cell or gene therapies Patients with contraindications for cyclophosphamide, fludarabine and IL-2 at per protocol doses Patients with a confirmed history of allergic reactions to amphotericin b, penicillin and/or streptomycin Patients who have received any cytotoxic chemotherapy within the 3 weeks prior to tissue and blood procurement Patients with a history of (non-infectious) pneumonitis that required systemic steroids, or current pneumonitis/interstitial lung disease Patients with a history of severe hypersensitivity to a monoclonal antibody, allergy or hypersensitivity to nivolumab itself and/or its components Patients who have received a live vaccination within the 28 days prior to the first dose of nivolumab Patients with ocular, acral or mucosal melanoma Patients with any contraindications for nivolumab Patients with a Left Ventricular Ejection Fraction (LVEF) < 45% Patients with a forced expiratory volume in one second (FEV1) of less than or equal to 60% of their predicted normal Patients who have received a live vaccination within the 28 days prior to lymphodepletion

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Calendar

(Last Update: 29/05/2024)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
27/07/2022	22/12/2022	28/03/2023	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

Achilles Therapeutics UK Limited United Kingdom

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Monetary support: N/A

Sponsor type: Commercial

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Sites

Active (22/12/2022)

HOSPITAL UNIVERSITARIO FUNDACION JIMENEZ DIAZ

Madrid

MADRID

Oncologia

Active (14/02/2023)

HOSPITAL UNIVERSITARIO HM SANCHINARRO

Madrid

MADRID

Oncología - START MADRID

Medication

OPDIVO 10 mg/mL concentrate for solution for infusion.

SOLUTION FOR INFUSION

INTRAVENOUS USE

ATC code: L01FF01 - NIVOLUMAB

Active Principles: N/A

Experimental

ATL001

DISPERSION FOR INFUSION

INTRAVENOUS USE

-

Active Principles: N/A

Experimental

No results