Brigatinib in pediatric and young adult patients with ALK+ ALCL, IMT or other solid tumors (Briga-PED)

Estado	**Tipo de Participantes**	**Rangos de Edad**
Reclutando	Sujetos incapaces de otorgar consentimiento	Menores de 18 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	11
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	Si
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	tratamiento, seguridad, eficacia, farmacocinética, farmacodinamica	NO

Información

Identificador

2024-513412-10-00 (CTIS)

Cod. Protocolo

BrigaPED ITCC-098

Transicionado 2021-002713-34

Área terapéutica

Enfermedades [C] - Cáncer [C04]|

Enfermedad investigada

Inflammatory Myofibroblastic Tumors (IMT)
Anaplastic Large Cell Lymphoma (ALCL)
Other solid tumors

Título Científico

A Phase I/II study of Brigatinib in pediatric and young adult patients with ALK+ Anaplastic Large Cell Lymphoma,

Inflammatory Myofibroblastic Tumors or other solid tumors

Justificación

No aportado

Objetivo Principal

To determine the MTD/RP2D regimen of brigatinib monotherapy when administered in pediatric and AYA patients with ALK+ ALCL or ALK+ solid tumors, including ALK+ IMT.
To characterize the PK of brigatinib administered as monotherapy in pediatric and AYA patients with ALK+ ALCL or ALK+ solid tumors, including ALK+ IMT.
To establish the anti-tumor activity of single agent brigatinib when administered to children with ALK+ IMT.
To establish the efficacy of single agent brigatinib when administered to children with ALK+ ALCL for a duration of 2 years, without planned HSCT in consolidation.

Variables de Evaluación Primaria

Phase 1: dose-limiting toxicities (DLTs) during the first course of therapy. Phase 1: Brigatinib plasma PK parameters to be determined: o maximum observed concentration (Cmax), o time of first occurrence of maximum observed concentration (Tmax), o area under the concentration-time curve from time 0 to the time of the last quantifiable concentration (AUClast). Phase 1: The RP2D will be selected by the DSMB and will be based on the dose that results in equivalent (approximately ±20% of the adult values) PK exposure to the adult comparator and with <2 out of 6 patients at this dose level present with a DLT and taking into account responses observed in phase 1. Cohort B1: Overall response rate (ORR), defined as the percentage of patients with CR or PR according to RECIST 1.1 after 1 course and best ORR during brigatinib treatment. Cohort B2: EFS (using the IPNHL response criteria), defined as the time between start of study treatment and first event being progressive disease, relapse, death of any cause and second malignancies, whatever happens first. Patients consolidated with HSCT will be censored. Cohort B1R: Overall response rate (ORR), defined as the percentage of patients with CR or PR according to RECIST 1.1 after 1 course and best ORR during brigatinib re-treatment. Cohort B2R: EFS (using the IPNHL response criteria), defined as the time between restart of study treatment and first event being progressive disease, relapse, death of any cause and second malignancies, whatever happens first. Patients consolidated with HSCT will be censored.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To assess the safety and tolerability of brigatinib administered as monotherapy in pediatric and AYA patients during course 1, as well as the cumulative toxicities in patients receiving multiple courses of brigatinib.
To assess the acceptability and palatability of brigatinib.
To describe long term toxicity (toxicity during the off-therapy period up to 5 years after study inclusion), with special attention to ocular, pulmonary, endocrine adverse events and height, weight or growth abnormalities
Cohort B1: To estimate the activity of brigatinib in terms of: o time to best response, o duration of response (DOR), o

the number of patients that undergo a complete (microscopic radical R0) resection after treatment with brigatinib, o cumulative incidence of non-response or relapse on treatment and during follow-up, o event-free survival (EFS), o overall survival (OS), o on treatment survival.
Cohort B2: To estimate the activity of brigatinib in terms of: o ORR after one course and best ORR during brigatinib treatment, o time to best response, o duration of response (DOR), o the cumulative incidence of non-response or relapse on treatment and after two years of brigatinib treatment, o overall survival (OS), o on treatment survival, o To describe outcome for ALCL patients with and without HSCT, after a remission induced with brigatinib. o To describe anti-tumor activity for ALCL patients that are re-challenged with brigatinib for a relapse occurring after brigatinib discontinuation.
Cohort B2R: To estimate the activity of brigatinib re-treatment in terms of: o ORR after one course and best ORR during brigatinib re-treatment, o time to best response, o duration of response (DOR), o the cumulative incidence of non-response or relapse on treatment and after 24 cycles of brigatinib re-treatment, o overall survival (OS), o on treatment survival,
Cohort B1R: To estimate the activity of brigatinib re-treatment in terms of: o time to best response, o duration of response (DOR), o the number of patients that undergo a complete (microscopic radical R0) resection after treatment with brigatinib, o cumulative incidence of non-response or relapse on treatment and during follow-up, o event-free survival (EFS), o overall survival (OS), o on treatment survival.

Variables de Evaluación Secundaria

No aportado

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Patients must be 1 and < 26 years of age at the time of enrollment, and able to swallow brigatinib tablets at the time of enrollment, with a minimum weight of 10 kg. Patients must have a histologically confirmed diagnosis of cancer at baseline. In patients where a repeat biopsy at relapse (or moment of refractory disease) is considered not feasible by the treating physician, archived material from diagnosis needs to be available for central review. Patients are required to provide prior results showing an activating ALK aberration in the tumor per local laboratory results, and material needs to be available for central laboratory confirmation of ALK status. For ALK+ ALCL, detection of ALK with immunohistochemistry (IHC) is sufficient for inclusion, all others require molecular evidence of a ALK fusion gene or mutation by FISH, PCR or NGS. ALK detection will be confirmed centrally with FISH. Phase 1: Patients with ALCL must be relapsed/refractory or intolerant to standard therapies. Refractory disease for ALCL is defined as: o no response to at least one course of ALCL99/other standard of care chemotherapy (SD or PD of measurable lesions), and/or o MRD-positivity by qualitative PCR for NPM-ALK after at least one course of ALCL99/other standard of care chemotherapy (before the second course of chemotherapy). Patients with relapsed/refractory (R/R) IMT must not be suitable for curative surgical resection without causing mutilation. Newly diagnosed patients with locally advanced IMT, for whom surgery may not be feasible for close proximity to vital structures, without prior tumor-shrinkage, may also be included, as well as metastatic disease. Patients with other solid tumors (excluding IMT) must have relapsed or refractory disease. Phase 2: Patients with ALCL must be relapsed/refractory. Refractory disease for ALCL is defined as: o no response to at least one course of ALCL99/other standard of care chemotherapy (SD or PD of measurable lesions), and/or o MRD-positivity by qualitative PCR for NPM-ALK after at least one course of ALCL99/other standard of care chemotherapy (before the second course of chemotherapy). Patients with R/R IMT Relapsed/refractory IMT, or newly diagnosed, including locally advanced and metastatic IMT which cannot be surgically resected without causing mutilation. Performance Status: Karnofsky performance status 40% for patients

>16 years of age or Lansky Play Scale 40% for patients 16 years of age for ALCL patients in phase 2. Karnofsky performance status 50% for patients >16 years of age or Lansky Play Scale 50% for patients 16 years of age, for IMT and other solid tumors and for ALCL patients in phase 1. Patients must not be receiving other investigational medications (defined as medicinal products not yet approved for any indications, including alternative/herbal therapies) within 30 days of first dose of study drug or while on study. Cohort B1R and B2R: Patients who were previously treated in the phase 1 or phase 2 part of this study, who completed brigatinib treatment as defined in this protocol, who responded to prior brigatinib treatment on protocol, and who developed a relapse or progression within 12 months after completion of brigatinib treatment (defined as per the EOT visit date).

Criterios de Exclusión

Patients receiving systemic treatment with strong or moderate CYP3A inhibitors or inducers within 14 days or five half-lives, whichever the less, prior to the first dose of study drug (refer to Section 5.2 for a list of example medications).
Diagnosis of another concurrent primary malignancy.

Calendario

(Última actualización: 09/12/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
26/05/2022	30/08/2022	02/05/2024	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

Prinses Maxima Centrum voor Kinderoncologie B.V. Netherlands

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Contact Person

Secretary TDC

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Monetary support: N/A

Tipo de promotor: No comercial

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Centros

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

Hospital Infantil Universitario Nino Jesus

Madrid

MADRID

Department of Onco-Haematology and Haematopoietic Transplant.

No iniciado (26/05/2022)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

Translational Research in Child and Adolescent Cancer

No iniciado (26/05/2022)

HOSPITAL UNIVERSITARIO Y POLITECNICO LA FE

València

VALENCIA

Clinical and Translational Cancer Research Group

Medicamentos

Alunbrig 30 mg film-coated tablets
FILM-COATED TABLET
ORAL

Código ATC: L01XE43 - BRIGATINIB
Principios Activos: N/A

Experimental

Alunbrig 180 mg film-coated tablets
FILM-COATED TABLET
ORAL

Código ATC: L01XE43 - BRIGATINIB
Principios Activos: N/A

Experimental

Alunbrig 90 mg film-coated tablets
FILM-COATED TABLET
ORAL

Código ATC: L01XE43 - BRIGATINIB
Principios Activos: N/A

Experimental

BRIGATINIB
ORAL SOLUTION
ORAL USE

-

Principios Activos: N/A

Experimental

Sin resultados

Brigatinib in pediatric and young adult patients with ALK+ ALCL, IMT or other solid tumors (Briga-PED)

State	Type of participants	Age Ranges
Recruiting	Incapable subjects of giving consent	Less than 18 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	11
Results	**Low level of intervention**	**Rare disease**
No results	No	Yes
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	treatment, safety, effectiveness, pharmacokinetics, pharmacodynamics	NO

Information

Identifier
2024-513412-10-00 (CTIS)

Protocol Code
BrigaPED ITCC-098

Transitioned 2021-002713-34

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

Investigated Disease
Inflammatory Myofibroblastic Tumors (IMT)
Anaplastic Large Cell Lymphoma (ALCL)
Other solid tumors

Scientific Title
A Phase I/II study of Brigatinib in pediatric and young adult patients with ALK+ Anaplastic Large Cell Lymphoma,

Inflammatory Myofibroblastic Tumors or other solid tumors

Rationale

Not provided

Main Objective

To determine the MTD/RP2D regimen of brigatinib monotherapy when administered in pediatric and AYA patients with ALK+ ALCL or ALK+ solid tumors, including ALK+ IMT.
To characterize the PK of brigatinib administered as monotherapy in pediatric and AYA patients with ALK+ ALCL or ALK+ solid tumors, including ALK+ IMT.
To establish the anti-tumor activity of single agent brigatinib when administered to children with ALK+ IMT.
To establish the efficacy of single agent brigatinib when administered to children with ALK+ ALCL for a duration of 2 years, without planned HSCT in consolidation.

Primary Endpoints

Phase 1: dose-limiting toxicities (DLTs) during the first course of therapy. Phase 1: Brigatinib plasma PK parameters to be determined: o maximum observed concentration (Cmax), o time of first occurrence of maximum observed concentration (Tmax), o area under the concentration-time curve from time 0 to the time of the last quantifiable concentration (AUClast). Phase 1: The RP2D will be selected by the DSMB and will be based on the dose that results in equivalent (approximately ±20% of the adult values) PK exposure to the adult comparator and with <2 out of 6 patients at this dose level present with a DLT and taking into account responses observed in phase 1. Cohort B1: Overall response rate (ORR), defined as the percentage of patients with CR or PR according to RECIST 1.1 after 1 course and best ORR during brigatinib treatment. Cohort B2: EFS (using the IPNHL response criteria), defined as the time between start of study treatment and first event being progressive disease, relapse, death of any cause and second malignancies, whatever happens first. Patients consolidated with HSCT will be censored. Cohort B1R: Overall response rate (ORR), defined as the percentage of patients with CR or PR according to RECIST 1.1 after 1 course and best ORR during brigatinib re-treatment. Cohort B2R: EFS (using the IPNHL response criteria), defined as the time between restart of study treatment and first event being progressive disease, relapse, death of any cause and second malignancies, whatever happens first. Patients consolidated with HSCT will be censored.

Temporary moments of secondary assessment

Not provided

Secondary Objective

To assess the safety and tolerability of brigatinib administered as monotherapy in pediatric and AYA patients during course 1, as well as the cumulative toxicities in patients receiving multiple courses of brigatinib.
To assess the acceptability and palatability of brigatinib.
To describe long term toxicity (toxicity during the off-therapy period up to 5 years after study inclusion), with special attention to ocular, pulmonary, endocrine adverse events and height, weight or growth abnormalities
Cohort B1: To estimate the activity of brigatinib in terms of: o time to best response, o duration of response (DOR), o

the number of patients that undergo a complete (microscopic radical R0) resection after treatment with brigatinib, o cumulative incidence of non-response or relapse on treatment and during follow-up, o event-free survival (EFS), o overall survival (OS), o on treatment survival.
Cohort B2: To estimate the activity of brigatinib in terms of: o ORR after one course and best ORR during brigatinib treatment, o time to best response, o duration of response (DOR), o the cumulative incidence of non-response or relapse on treatment and after two years of brigatinib treatment, o overall survival (OS), o on treatment survival, o To describe outcome for ALCL patients with and without HSCT, after a remission induced with brigatinib. o To describe anti-tumor activity for ALCL patients that are re-challenged with brigatinib for a relapse occurring after brigatinib discontinuation.
Cohort B2R: To estimate the activity of brigatinib re-treatment in terms of: o ORR after one course and best ORR during brigatinib re-treatment, o time to best response, o duration of response (DOR), o the cumulative incidence of non-response or relapse on treatment and after 24 cycles of brigatinib re-treatment, o overall survival (OS), o on treatment survival,
Cohort B1R: To estimate the activity of brigatinib re-treatment in terms of: o time to best response, o duration of response (DOR), o the number of patients that undergo a complete (microscopic radical R0) resection after treatment with brigatinib, o cumulative incidence of non-response or relapse on treatment and during follow-up, o event-free survival (EFS), o overall survival (OS), o on treatment survival.

Secondary Endpoints

Not provided

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Patients must be 1 and < 26 years of age at the time of enrollment, and able to swallow brigatinib tablets at the time of enrollment, with a minimum weight of 10 kg. Patients must have a histologically confirmed diagnosis of cancer at baseline. In patients where a repeat biopsy at relapse (or moment of refractory disease) is considered not feasible by the treating physician, archived material from diagnosis needs to be available for central review. Patients are required to provide prior results showing an activating ALK aberration in the tumor per local laboratory results, and material needs to be available for central laboratory confirmation of ALK status. For ALK+ ALCL, detection of ALK with immunohistochemistry (IHC) is sufficient for inclusion, all others require molecular evidence of a ALK fusion gene or mutation by FISH, PCR or NGS. ALK detection will be confirmed centrally with FISH. Phase 1: Patients with ALCL must be relapsed/refractory or intolerant to standard therapies. Refractory disease for ALCL is defined as: o no response to at least one course of ALCL99/other standard of care chemotherapy (SD or PD of measurable lesions), and/or o MRD-positivity by qualitative PCR for NPM-ALK after at least one course of ALCL99/other standard of care chemotherapy (before the second course of chemotherapy). Patients with relapsed/refractory (R/R) IMT must not be suitable for curative surgical resection without causing mutilation. Newly diagnosed patients with locally advanced IMT, for whom surgery may not be feasible for close proximity to vital structures, without prior tumor-shrinkage, may also be included, as well as metastatic disease. Patients with other solid tumors (excluding IMT) must have relapsed or refractory disease. Phase 2: Patients with ALCL must be relapsed/refractory. Refractory disease for ALCL is defined as: o no response to at least one course of ALCL99/other standard of care chemotherapy (SD or PD of measurable lesions), and/or o MRD-positivity by qualitative PCR for NPM-ALK after at least one course of ALCL99/other standard of care chemotherapy (before the second course of chemotherapy). Patients with R/R IMT Relapsed/refractory IMT, or newly diagnosed, including locally advanced and metastatic IMT which cannot be surgically resected without causing mutilation. Performance Status: Karnofsky performance status 40% for patients

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Exclusion criteria

Patients receiving systemic treatment with strong or moderate CYP3A inhibitors or inducers within 14 days or five half-lives, whichever the less, prior to the first dose of study drug (refer to Section 5.2 for a list of example medications).
Diagnosis of another concurrent primary malignancy.

Calendar

(Last Update: 09/12/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
26/05/2022	30/08/2022	02/05/2024	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

Prinses Maxima Centrum voor Kinderoncologie B.V. Netherlands

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Contact Person

Secretary TDC

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Monetary support: N/A

Sponsor type: No commercial

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Sites

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

Hospital Infantil Universitario Nino Jesus

Madrid

MADRID

Department of Onco-Haematology and Haematopoietic Transplant.

not initialized (26/05/2022)

HOSPITAL UNIVERSITARI VALL D'HEBRON

Barcelona

BARCELONA

Translational Research in Child and Adolescent Cancer

not initialized (26/05/2022)

HOSPITAL UNIVERSITARIO Y POLITECNICO LA FE

València

VALENCIA

Clinical and Translational Cancer Research Group

Medication

Alunbrig 30 mg film-coated tablets
FILM-COATED TABLET
ORAL

ATC code: L01XE43 - BRIGATINIB
Active Principles: N/A

Experimental

Alunbrig 180 mg film-coated tablets
FILM-COATED TABLET
ORAL

ATC code: L01XE43 - BRIGATINIB
Active Principles: N/A

Experimental

Alunbrig 90 mg film-coated tablets
FILM-COATED TABLET
ORAL

ATC code: L01XE43 - BRIGATINIB
Active Principles: N/A

Experimental

BRIGATINIB
ORAL SOLUTION
ORAL USE

-

Active Principles: N/A

Experimental

No results