Estudio aleatorizado en el que se compara blinatumomab alternado con quimioterapia de baja intensidad con el tratamiento estándar de quimioterapia en adultos mayores con leucemia linfoblástica aguda de precursores B con cromosoma Filadelfia negativo recién diagnosticada, con un período de preinclusión de seguridad (estudio Golden Gate)

Estado	**Tipo de Participantes**	**Rangos de Edad**
EC Finalizado	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase III	134
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Tiene resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Sin determinar	seguridad, eficacia, farmacocinética	NO

Información

Identificador
2023-503640-14-00 (CTIS)

Cod. Protocolo
20190360

Transicionado 2019-004304-36

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

Enfermedad investigada
Leucemia linfoblástica aguda (LLA) de precursores B con cromosoma Filadelfia (Ph) negativo recién diagnosticada

Título Científico

Estudio de fase 3 aleatorizado y controlado de blinatumomab
alternado con quimioterapia de baja intensidad frente al tratamiento estándar en adultos mayores con leucemia linfoblástica aguda de precursores B con cromosoma
Filadelfia negativo recién diagnosticada, con un período de preinclusión de seguridad
(estudio Golden Gate)

Justificación

No aportado

Objetivo Principal

Período de preinclusión de seguridad: Evaluar la seguridad y la tolerabilidad de blinatumomab alternado con quimioterapia de baja intensidad. Fase 3: Comparar la supervivencia libre de acontecimientos (SLA) de los sujetos que reciben blinatumomab alternado con quimioterapia de baja intensidad con la SLA de los sujetos que reciben el tratamiento estándar (SOC) de quimioterapia.
Fase 3: Comparar la supervivencia global (SG) de blinatumomab alternado con quimioterapia de baja intensidad con la del SOC de quimioterapia.

Variables de Evaluación Primaria

Período de preinclusión de seguridad: Acontecimientos adversos aparecidos durante el tratamiento, acontecimientos adversos relacionados con el tratamiento y acontecimientos adversos de interés.
Fase 3: SLA: tiempo desde la aleatorización hasta el fracaso del tratamiento, la recaída o la muerte por cualquier causa, lo que ocurra antes. Los sujetos sin ningún acontecimiento se censurarán en la última fecha de evaluación de la enfermedad
evaluable.
Fase 3: SG: el tiempo desde la aleatorización hasta la muerte por cualquier causa. Los sujetos que sigan con vida serán censurados en la última fecha en que se sabe que estaban vivos

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

Período de preinclusión de seguridad: Evaluar las variables de eficacia de blinatumomab alternado con quimioterapia de baja intensidad.
Período de preinclusión de seguridad: Caracterizar la farmacocinética (FC) de blinatumomab alternado con quimioterapia de baja intensidad.
Fase 3: Comparar las fatigas notificadas por los pacientes tratados con blinatumomab alternado con quimioterapia de baja intensidad con las del SOC de quimioterapia.
Fase 3: Comparar el dolor notificado por los pacientes con blinatumomab alternado con quimioterapia de baja intensidad con el de SOC de quimioterapia.
Fase 3: Comparar los resultados adicionales notificados por los pacientes (PRO) y el estado de salud global

mediante el cuestionario de calidad de vidadel cáncer de la organización Europea para la Investigación y el Tratamiento del Cáncer (EORTC QLQ-C30).
Fase 3: Comparar las otras variables de eficacia de blinatumomab alternado con quimioterapia de baja intensidad con el SOC de quimioterapia.
Fase 3: Comparar la seguridad de blinatumomab alternado con quimioterapia de baja intensidad con el SOC de quimioterapia.
Fase 3: Caracterizar las recaídas egún la expresión del clúster de diferenciación (CD)19, el cambio de linaje y la localización de la recaída en ambos grupos de tratamiento.
Fase 3: Evaluar la mortalidad sin recaída en ambos grupos de tratamiento.
Fase 3: Evaluar la proporción de TCPH alogénicos y autólogos en la primera RC continua después de recibir blinatumomab alternado con quimioterapia de baja intensidad en comparación con el SOC de quimioterapia.
Fase 3: valuar la mortalidad sin recaída después del TCPH autólogo y alogénico en ambos grupos de tratamiento.
Fase 3: Evaluar la tasa de recaída después del TCPH autólogo y alogénico en ambos grupos de tratamiento.
Fase 3: Comparar las fatigas notificadas por los pacientes tratados con blinatumomab alternado con quimioterapia de baja intensidad con las del SOC de quimioterapia.
Fase 3: Comparar las fatigas notificadas por los pacientes tratados con blinatumomab alternado con quimioterapia de baja intensidad con las del SOC de quimioterapia.
Fase 3: Comparar el dolor notificado por los pacientes con blinatumomab alternado con quimioterapia de baja intensidad con el de SOC de quimioterapia.
Fase 3: Comparar los PRO y el estado de salud global mediante el EORTC QLQ-C30.
Fase 3: Evaluar la farmacocinética (FC) de blinatumoma

Variables de Evaluación Secundaria

SRI: Complete remission (CR) by the end of the initial disease assessment period SRI: Minimal residual disease (MRD) response < 10-4 by the end of the initial disease assessment period SRI: Relapse-free survival (RFS): in subjects who achieve CR, the time from first achievement of this response until date of the first relapse including hematologic relapse, extramedullary relapse, or death due to any cause, whichever occurs first. Subjects without an event will be censored at their last evaluable disease assessment date. SRI: MRD RFS in subjects who achieve CR with MRD response, the time from first achievement of this response until date of the first relapse including molecular relapse, hematologic relapse, and/or extramedullary relapse, or death due to any cause, whichever occurs first. Molecular relapse will be defined 2 ways: MRD 10-3 and MRD 10-4. Subjects without an event will be censored at their last evaluable disease assessment date. SRI: PK parameters for blinatumomab including, but not limited to, steady state concentration (Css) and clearance (CL) Ph3: Change from baseline to end of the initial disease assessment period in fatigue score measured by Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue Short Form 7a Ph3: Change from baseline to end of the initial disease assessment period in pain score measured by Brief Pain Inventory Short Form (BPI-SF); Item 3: pain at its worst in the last 24 hours Ph3: Change from baseline to end of the initial disease assessment period in global health status measured by the QLQ-C30 global health status quality of life scale Ph3: Change from baseline to end of the initial disease assessment period in physical function measured by the QLQ-C30 functional scale Ph3: Change from baseline to end of the initial disease assessment period in nausea/vomiting measured by the QLQ-C30 symptom scale Ph3: CR by the end of the initial disease assessment period Ph3: MRD response < 10-4 by the end of the initial disease assessment period Ph3: RFS: in subjects who achieve CR, the time from first achievement of this response until date of the first relapse including hematologic relapse, extramedullary relapse, or death due to any cause, whichever occurs first. Subjects without an event will be censored at their last evaluable disease assessment date. Ph3: MRD RFS in subjects who achieve CR with MRD response, the time from first achievement of this response until date of the first relapse including molecular relapse, hematologic relapse, and/or extramedullary relapse, or death due to any cause, whichever occurs first. Molecular relapse will be defined 2 ways: MRD 10-3 and MRD 10-4. Subjects without an event will be censored at their last evaluable disease assessment date. Ph3: MRD level over time Ph3: treatment-emergent adverse events, treatment related adverse events, and adverse events of interest Ph3: CD19 positive relapse and CD19 negative relapse identified by flow cytometry or immunocytochemistry for bone marrow (mandatory) Ph3: CD19 positive relapse and CD19 negative relapse identified by flow cytometry or immunohistochemistry for cerebrospinal fluid (mandatory) Ph3: CD19 positive relapse and CD19 negative relapse for extramedullary sites other than cerebrospinal fluid (optional - if data is available) Ph3: Lineage switch to acute

myeloid leukemia (AML) Ph3: Localization of relapse by clinical assessment Ph3: Mortality in CR Ph3: Autologous and allogeneic HSCT in continuous first CR* Ph3: Mortality in CR after autologous and allogeneic HSCT* Ph3: Relapse after autologous and allogeneic HSCT Ph3: Time to deterioration and time to improvements for fatigue score measured by PROMIS Fatigue Short Form 7a Ph3: Time to deterioration and time to improvements for pain score measured by BPI-SF; Item 3: pain at its worst in the last 24 hours Ph3: Change from baseline in all other subscales of QLQ-C30 (role, cognitive, emotional, and social scales; pain and fatigue scales; single items: dyspnea, loss of appetite, insomnia, constipation, diarrhea, and perceived financial impact) Ph3: Time to deterioration and time to improvements for global health status, physical function, and nausea/vomiting scales. Ph3: Css and CL

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

El sujeto ha proporcionado su consentimiento informado antes de iniciar cualquier procedimiento/actividad específico del estudio. O Cuando la legislación local lo permita, el representante legal autorizado del sujeto ha proporcionado el consentimiento informado antes del inicio de cualquier procedimiento/actividad específico del estudio cuando el sujeto sufre cualquier tipo de enfermedad que, según la opinión del investigador, puede comprometer su capacidad para proporcionar el consentimiento informado por escrito. Edad ¿ 55 años en el momento del consentimiento informado. O Edad de 40 a < 55 años si presenta al menos 1 de las siguientes comorbilidades en el momento del consentimiento informado: - Antecedentes de pancreatitis de grado 3 y 4. - Diabetes mellitus con afectación de órganos específicos. - Enfermedad hepática grave, como cirrosis en estadio 2 con hipertensión portal o antecedentes de hemorragia por varices esofágicas y aspartato aminotransferasa (AST)/alanina aminotransferasa (ALT) > 10 x límite superior normal (LSN) (la cirrosis hepática debe confirmarse mediante biopsia). - Índice de masa corporal (IMC) ¿ 40 combinado con comorbilidades relevantes como el síndrome metabólico. - Cualquier otra combinación de comorbilidades graves documentadas que el investigador considere incompatible con la administración de un régimen de quimioterapia estándar intensivo de tipo pediátrico y adaptado a los adultos, pero que siga siendo compatible con el protocolo sugerido para los sujetos de mayor edad tanto en el grupo experimental como en el del SOC. El monitor médico necesitará revisar la historia clínica del sujeto durante la selección para determinar si su inclusión es aceptable en función de una lista estándar con los tipos de comorbilidades permitidos. Sujetos con leucemia linfoblástica aguda (LLA) de precursores B con cromosoma Filadelfia (Ph) negativo recién diagnosticada según criterios de la OMS. Estado funcional del Eastern Cooperative Oncology Group (ECOG) ¿ 2; se permite una puntuación ECOG más alta si está provocada por una leucemia subyacente. Todos los sujetos deben presentar una función orgánica adecuada, definida de la manera siguiente: - Función renal: tasa de filtración glomerular estimada basada en el cálculo de la Modificación de Dieta en Enfermedad Renal (MDRD) ¿ 50 ml/min/1,73 m2. - Función hepática: bilirrubina total ¿ 2 x el límite superior de la normalidad (LSN; a menos que se trate de la enfermedad de Gilbert o exista afectación hepática con leucemia); excepción para los sujetos de 40 a < 55 años si la comorbilidad corresponde al criterio de inclusión 102: enfermedad hepática grave, como cirrosis en estadio 2 con hipertensión portal o antecedentes de hemorragia por varices esofágicas y AST/ALT > 10 x LSN (la cirrosis hepática debe confirmarse mediante biopsia). - Función cardíaca: fracción de eyección del ventrículo izquierdo (FEVI) ¿ 50% y no se han presentado enfermedades cardiovasculares clínicamente significativas, no controladas o activas (p. ej infarto de miocardio o accidente cerebrovascular en los últimos 3 meses). Se consultará al monitor médico según sea necesario

Criterios de Exclusión

Leucemia activa del SNC (p.ej leucemia del SNC-3, confirmada por punción lumbar) no resuelta con quimioterapia IT durante la selección

Antecedentes de otras neoplasias malignas en los últimos 3 años, con las excepciones siguientes:
- Tumor maligno tratado con intención curativa y sin presencia de enfermedad activa confirmada durante ¿ 3 años antes de la inclusión y que el médico responsable del tratamiento considere de bajo riesgo de recurrencia.
Nota: Los antecedentes de otra neoplasia maligna (por ejemplo, mieloma múltiple) tratada con fármacos inmunomoduladores (por ejemplo, lenalidomida, talidomida) en los últimos 3 años constituyen un criterio de exclusión.
- Cáncer de piel no melanomatoso o lentigo maligno tratados adecuadamente sin evidencia de enfermedad.
- Carcinoma in situ de cuello uterino tratado adecuadamente sin evidencia de enfermedad.
- Carcinoma ductal in situ de mama tratado adecuadamente sin evidencia de enfermedad.
- Neoplasia intraepitelial prostática sin evidencia de cáncer de próstata.
- Carcinoma urotelial papilar no invasivo o carcinoma in situ tratados adecuadamente.
Antecedentes o presencia de patología o evento del sistema nervioso central clínicamente relevante, como epilepsia, convulsiones en la infancia o la edad adulta, paresia, afasia, accidente cerebrovascular, lesiones cerebrales graves, demencia, enfermedad de Parkinson, enfermedad cerebelosa, síndrome cerebral orgánico o trastornos psiquiátricos que contraindican el uso de dosis altas de corticosteroides. Se consultará al monitor médico según sea necesario.
Enfermedad autoinmune actual o antecedentes de enfermedad autoinmune con posible afectación del SNC.
Infección conocida por el virus de la inmunodeficiencia humana (VIH).
Infección conocida crónica o activa por el virus de la hepatitis B (p. ej., reactiva al antígeno de superficie de la hepatitis B [HBs] o carga viral cuantificable de virus de la hepatitis B [VHB]) o de la hepatitis C (VHC) (p. ej., detección de ARN del VHC [cualitativa]).
Hepatitis B y C activas según los siguientes resultados:
¿Positivo para el antígeno de superficie de la hepatitis B (HepBsAg) (indica hepatitis B crónica o hepatitis B aguda reciente).
¿Negativo para HepBsAg y positivo para anticuerpos del núcleo de la hepatitis B: es necesario un resultado negativo para el ADN del VHB mediante RCP para la inclusión.
¿Positivo para anticuerpos del virus de la hepatitis C (HepCAb): es necesario un resultado negativo para el ARN del virus de la hepatitis C mediante RCP para la inclusión.
Sujeto con síntomas y/o signos clínicos y/o radiográficos y/o ecográficos que indiquen una infección aguda o crónica no controlada.
Quimioterapia contra el cáncer para esta LLA de precursores B recién diagnosticada antes de iniciar el tratamiento requerido por el protocolo, con la excepción de la quimioterapia IT o la quimioterapia en la prefase. Se permite la irradiación de una lesión puntual como un cloroma o una lesión lítica ósea o vertebral para el dolor o la estabilización vertebral.
Estar recibiendo actualmente tratamiento en otro estudio de un fármaco o producto sanitario en investigación o que hayan transcurrido menos de 30 días desde el fin del tratamiento en otro estudio de un fármaco o producto sanitario en investigación. Queda excluido cualquier otro procedimiento de investigación mientras se participe en este estudio

Calendario

(Última actualización: 15/10/2026)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
13/11/2020	17/02/2022	29/05/2023	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
20/07/2022	No aportado	No aportado	24/01/2023	No aportado

Promotor

Amgen Inc. United States

1 Amgen Center Drive

Contact Person

Medical Information

+441895525000

euctlegalrep@amgen.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Hospital General Universitario Gregorio Marañón

C/ Doctor Esquerdo, 46 28007 Madrid

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915867007

Centros

Cerrado (11/01/2021)

HOSPITAL CLINIC DE BARCELONA

Barcelona

BARCELONA

Servicio de Hematología

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

Hospital General Universitario Reina Sofia

Cordoba

CÓRDOBA

Servicio de Hematologia

Cerrado (24/01/2023)

HOSPITAL UNIVERSITARI GERMANS TRIAS I PUJOL DE BADALONA

Badalona

BARCELONA

Servicio de Hematologia

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

Hospital Universitari Vall D Hebron

Barcelona

BARCELONA

Servicio de Hematologia

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

Hospital Universitario De Salamanca

Salamanca

SALAMANCA

Servicio de Hematologia

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

Hospital Universitario Marques De Valdecilla

Santander

CANTABRIA

Servicio de Hematologia

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

Hospital Universitario Y Politecnico La Fe

Valencia

VALENCIA

Servicio de Hematologia

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

Hospital Universitario 12 De Octubre

Madrid

MADRID

Servicio de Hematologia

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

Institut Catala D´oncologia

L'hospitalet De Llobregat

BARCELONA

Servicio de Hematologia Clinica

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

Institut Catala D´oncologia

Badalona

BARCELONA

Servicio de Hematologia Clinica

Medicamentos

CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

CYTARABINE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

RITUXIMAB
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

PREDNISONE
TABLET
ORAL USE

-

Principios Activos: N/A

Experimental

METHOTREXATE SODIUM
TABLET
ORAL USE

-

Principios Activos: N/A

Experimental

METHOTREXATE SODIUM
TABLET
ORAL USE

-

Principios Activos: N/A

Experimental

VINCRISTINE SULFATE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

CYTARABINE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

IDARUBICIN
POWDER FOR SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

METHOTREXATE SODIUM
SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

ASPARAGINASE
SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

BLINATUMOMAB
SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Huérfano

Experimental

METHOTREXATE SODIUM
SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

DOXORUBICIN
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

BLINATUMOMAB
SOLUTION FOR INFUSION
INTRAVENOUS USE

DEXAMETHASONE
TABLET
ORAL USE

-

Principios Activos: N/A

Huérfano **Experimental**

-

Principios Activos: N/A

Experimental

MERCAPTOPURINE

TABLETS

ORAL USE

-

Principios Activos: N/A

Experimental

PEGASPARGASE

SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

CYCLOPHOSPHAMIDE

POWDER FOR SOLUTION FOR INJECTION

INTRAVENOUS

-

Principios Activos: N/A

Experimental

DEXAMETHASONE

SOLUTION FOR INJECTION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

MERCAPTOPURINE

TABLETS

ORAL USE

-

Principios Activos: N/A

Experimental

CRISANTASPASE

POWDER FOR SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

RITUXIMAB

CONCENTRATE FOR SOLUTION FOR INFUSION

INTRAVENOUS USE

-

Principios Activos: N/A

Experimental

Tiene resultados

A Randomized Study Comparing Blinatumomab Alternating With Low-intensity Chemotherapy Versus Standard of Care Chemotherapy for Older Adults With Newly Diagnosed Philadelphia-negative B-cell Precursor Acute Lymphoblastic Leukemia with Safety Run-in (Golden Gate Study)

State	**Type of participants**	**Age Ranges**
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	134
Results	**Low level of intervention**	**Rare disease**
Has results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
Undetermined	safety, effectiveness, pharmacokinetics	NO

Information

Identifier
2023-503640-14-00 (CTIS)

Protocol Code
20190360

Transitioned 2019-004304-36

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

Investigated Disease
Newly diagnosed Philadelphia-negative B-cell precursor Acute Lymphoblastic Leukemia in older adults

Scientific Title
Phase 3 Randomized, Controlled Study of Blinatumomab Alternating With Low-intensity Chemotherapy Versus

Standard of Care for Older Adults With Newly Diagnosed Philadelphia-negative B-cell Precursor Acute Lymphoblastic Leukemia With Safety Run-in (Golden Gate Study)

Rationale

Not provided

Main Objective

Safety Run In (SRI): To evaluate the safety and tolerability of blinatumomab alternating with low-intensity chemotherapy Phase 3 (Ph3): To compare event-free survival (EFS) of subjects receiving blinatumomab alternating with low-intensity chemotherapy to EFS of subjects receiving standard of care (SOC) chemotherapy
Ph3: To compare overall survival (OS) of blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy

Primary Endpoints

SRI: Treatment-emergent adverse events, treatment-related adverse events, and adverse events of interest
Ph3: EFS: time from randomization until treatment failure, relapse, or death from any cause, whichever is earlier. Subjects without an event will be censored at their last evaluable disease assessment date.
Ph3: OS: time from randomization until death due to any cause. Subjects alive will be censored at the date last known to be alive.

Temporary moments of secondary assessment

Not provided

Secondary Objective

SRI: To evaluate efficacy endpoints of blinatumomab alternating with low-intensity chemotherapy
SRI: To characterize the pharmacokinetics (PK) of blinatumomab alternating with low-intensity chemotherapy
Ph3: To compare patient-reported fatigues with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
Ph3: To compare patient-reported pain with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
Ph3: To compare additional patient-reported outcomes (PROs) and global health status as measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQC30)
Ph3: To compare other efficacy endpoints of blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
Ph3: To compare the safety of blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
Ph3: To characterize relapses by cluster of differentiation (CD)19 expression, lineage switch and relapse localization in both treatment arms.
Ph3: To evaluate non-relapse mortality in both treatment arms
Ph3: To evaluate the proportion of allogeneic and autologous HSCT in continuous first CR after receiving blinatumomab alternating with low-intensity chemotherapy compared to SOC chemotherapy

Ph3: To evaluate non-relapse mortality following autologous and allogeneic HSCT in both treatment arms
Ph3: To evaluate relapse rate following autologous and allogeneic HSCT in both treatment arms
Ph3: To compare patient-reported fatigues with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
Ph3: To compare patient-reported pain with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
Ph3: To compare additional PROs and global health status as measured by the EORTC QLQ-C30
Ph3: To evaluate the PK of blinatumomab

Secondary Endpoints

SRI: Complete remission (CR) by the end of the initial disease assessment period SRI: Minimal residual disease (MRD) response < 10-4 by the end of the initial disease assessment period SRI: Relapse-free survival (RFS): in subjects who achieve CR, the time from first achievement of this response until date of the first relapse including hematologic relapse, extramedullary relapse, or death due to any cause, whichever occurs first. Subjects without an event will be censored at their last evaluable disease assessment date. SRI: MRD RFS in subjects who achieve CR with MRD response, the time from first achievement of this response until date of the first relapse including molecular relapse, hematologic relapse, and/or extramedullary relapse, or death due to any cause, whichever occurs first. Molecular relapse will be defined 2 ways: MRD 10-3 and MRD 10-4. Subjects without an event will be censored at their last evaluable disease assessment date. SRI: PK parameters for blinatumomab including, but not limited to, steady state concentration (Css) and clearance (CL) Ph3: Change from baseline to end of the initial disease assessment period in fatigue score measured by Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue Short Form 7a Ph3: Change from baseline to end of the initial disease assessment period in pain score measured by Brief Pain Inventory Short Form (BPI-SF); Item 3: pain at its worst in the last 24 hours Ph3: Change from baseline to end of the initial disease assessment period in global health status measured by the QLQ-C30 global health status quality of life scale Ph3: Change from baseline to end of the initial disease assessment period in physical function measured by the QLQ-C30 functional scale Ph3: Change from baseline to end of the initial disease assessment period in nausea/vomiting measured by the QLQ-C30 symptom scale Ph3: CR by the end of the initial disease assessment period Ph3: MRD response < 10-4 by the end of the initial disease assessment period Ph3: RFS: in subjects who achieve CR, the time from first achievement of this response until date of the first relapse including hematologic relapse, extramedullary relapse, or death due to any cause, whichever occurs first. Subjects without an event will be censored at their last evaluable disease assessment date. Ph3: MRD RFS in subjects who achieve CR with MRD response, the time from first achievement of this response until date of the first relapse including molecular relapse, hematologic relapse, and/or extramedullary relapse, or death due to any cause, whichever occurs first. Molecular relapse will be defined 2 ways: MRD 10-3 and MRD 10-4. Subjects without an event will be censored at their last evaluable disease assessment date. Ph3: MRD level over time Ph3: treatment-emergent adverse events, treatment related adverse events, and adverse events of interest Ph3: CD19 positive relapse and CD19 negative relapse identified by flow cytometry or immunocytochemistry for bone marrow (mandatory) Ph3: CD19 positive relapse and CD19 negative relapse identified by flow cytometry or immunohistochemistry for cerebrospinal fluid (mandatory) Ph3: CD19 positive relapse and CD19 negative relapse for extramedullary sites other than cerebrospinal fluid (optional - if data is available) Ph3: Lineage switch to acute myeloid leukemia (AML) Ph3: Localization of relapse by clinical assessment Ph3: Mortality in CR Ph3: Autologous and allogeneic HSCT in continuous first CR* Ph3: Mortality in CR after autologous and allogeneic HSCT* Ph3: Relapse after autologous and allogeneic HSCT Ph3: Time to deterioration and time to improvements for fatigue score measured by PROMIS Fatigue Short Form 7a Ph3: Time to deterioration and time to improvements for pain score measured by BPI-SF; Item 3: pain at its worst in the last 24 hours Ph3: Change from baseline in all other subscales of QLQ-C30 (role, cognitive, emotional, and social scales; pain and fatigue scales; single items: dyspnea, loss of appetite, insomnia, constipation, diarrhea, and perceived financial impact) Ph3: Time to deterioration and time to improvements for global health status, physical function, and nausea/vomiting scales. Ph3: Css and CL

Temporary moments of secondary assessment

Not provided

Inclusion criteria

Subject has provided informed consent prior to initiation of any study specific activities/procedures OR Where permitted by local law, subjects legally acceptable representative has provided informed consent prior to any study-specific activities/procedures being initiated when the subject has any kind of condition that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent. Age 55 years at the time of informed consent OR Age 40 to < 55 years of age if at least 1 of the following comorbidities at the time of informed consent: - history of grades 3 and 4 pancreatitis - diabetes mellitus with end-organ damage - severe liver disease such as cirrhosis stage 2 with portal hypertension or history of esophageal variceal bleeding and aspartate aminotransferase (AST)/alanine aminotransferase (ALT) > 10 x upper limit of normal (ULN) (liver cirrhosis must be confirmed by biopsy) - body mass index (BMI) 40 combined with relevant comorbidities such as metabolic syndrome - Any further combination of documented severe comorbidities that the investigator judges to be incompatible with administering an intensive pediatric-based, adult adapted standard chemotherapy regimen but still compatible with the suggested protocol for older subjects in both the experimental and the SOC arm. The subject history needs to be reviewed by the medical monitor during screening to determine enrollment acceptability based on a standard list with types of comorbidities allowed. Subjects with newly diagnosed Philadelphia (Ph)-negative B-cell precursor acute lymphoblastic leukemia (ALL) per WHO criteria Eastern Cooperative Oncology Group (ECOG) performance status 2, higher ECOG score allowed if due to underlying leukemia. All subjects must have adequate organ function as defined below: - renal: estimated glomerular filtration rate based on Modification of Diet in Renal Disease (MDRD) calculation 50 mL/min/1.73 m2 - liver function: total bilirubin 2x upper limit of normal (ULN; unless Gilberts Disease or if liver involvement with leukemia); exception for subjects 40 to < 55 years of age if comorbidity is per inclusion 102: severe liver disease such as cirrhosis stage 2 with portal hypertension or history of esophageal variceal bleeding and AST/ALT >10 x ULN (liver cirrhosis must be confirmed by biopsy) - cardiac: left ventricular ejection fraction (LVEF) 50% and no clinically significant, uncontrolled, or active cardiovascular disease (eg, myocardial infarction or stroke within 3 months). Consult with medical monitor as needed.

Exclusion criteria

Active CNS leukemia (i.e, CNS 3 leukemia, confirmed by lumbar puncture) not resolved with IT chemotherapy during screening
202 History of other malignancy within the past 3 years, with the following exceptions: - Malignancy treated with curative intent and with no known active disease present for 3 years before enrollment and felt to be at low risk for recurrence by the treating physician. Note: History of other malignancy (eg, multiple myeloma) treated with immunomodulatory drugs (eg, lenalidomide, thalidomide) in the past 3 years is an exclusion. - Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease. - Adequately treated cervical carcinoma in situ without evidence of disease. - Adequately treated breast ductal carcinoma in situ without evidence of disease. - Prostatic intraepithelial neoplasia without evidence of prostate cancer. - Adequately treated urothelial papillary noninvasive carcinoma or carcinoma in situ.
History or presence of clinically relevant CNS pathology or eventsuch as epilepsy, childhood or adult seizure, paresis, aphasia, stroke, severe brain injuries, dementia, Parkinson's diease, cerebellar disease, organic brain syndrome, or psychiatric conditions that preclude the use of high dose of corticosteroids. Consult with medical monitor as needed.
Current autoimmune disease or history of autoimmune disease with potential CNS involvement
Known infection with human immunodeficiency virus (HIV)
Known infection with chronic or active hepatitis B (eg, hepatitis b surface [HBs] antigen reactive or quantifiable hepatitis b virus [HBV] viral load) or hepatitis C virus (HCV) (eg, HCV RNA [qualitative] is detected). Active hepatitis B and C based on the following results: - Positive for hepatitis B surface antigen (HepBsAg) (indicative of chronic hepatitis B or recent acute hepatitis B) - Negative HepBsAg and positive for hepatitis B core antibody: negative HBV DNA by PCR result is necessary to enroll. - Positive Hepatitis C virus antibody (HepCAb): negative hepatitis C virus

RNA by PCR result is necessary to enroll.
Subject with symptoms and/or clinical signs and/or radiographic and/or sonographic signs that indicate an acute or uncontrolled chronic infection.
Cancer chemotherapy for this newly diagnosed B cell ALL before the start of protocol-required therapy with the exception of IT chemotherapy or pre-phase chemotherapy. Radiation to a spot lesion such as chloroma or lytic lesion of bone or vertebrae for pain or vertebral stabilization is allowed.
Currently receiving treatment in another investigational device or drug study, or less than 30 days since ending treatment on another investigational device or drug study(ies). Other investigational procedures while participating in this study are excluded.

Calendar

(Last Update: 15/10/2026)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
13/11/2020	17/02/2022	29/05/2023	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
20/07/2022	Not aported	Not aported	24/01/2023	Not aported

Sponsor

Amgen Inc. United States

1 Amgen Center Drive

Contact Person

Medical Information

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Monetary support: N/A

Sponsor type: Commercial

Ceim

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Sites

Closed (11/01/2021)

HOSPITAL CLINIC DE BARCELONA

Barcelona

BARCELONA

Servicio de Hematología

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

Hospital General Universitario Reina Sofia

Cordoba

CÓRDOBA

Servicio de Hematologia

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HOSPITAL UNIVERSITARI GERMANS TRIAS I PUJOL DE BADALONA

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Hospital Universitari Vall D Hebron

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Institut Catala D´oncologia

L'hospitalet De Llobregat

BARCELONA

Servicio de Hematologia Clinica

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Institut Catala D´oncologia

Badalona

BARCELONA

Servicio de Hematologia Clinica

Medication

CYCLOPHOSPHAMIDE
POWDER FOR SOLUTION FOR INJECTION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

CYTARABINE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

RITUXIMAB
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

PREDNISONE
TABLET
ORAL USE

-

Active Principles: N/A

Experimental

METHOTREXATE SODIUM
TABLET
ORAL USE

-

Active Principles: N/A

Experimental

METHOTREXATE SODIUM
TABLET
ORAL USE

-

Active Principles: N/A

Experimental

VINCRISTINE SULFATE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

CYTARABINE
SOLUTION FOR INJECTION/INFUSION
INTRAVENOUS USE

-

Active Principles: N/A

Experimental

IDARUBICIN
POWDER FOR SOLUTION FOR INJECTION
INTRAVENOUS USE

-
Active Principles: N/A
Experimental

METHOTREXATE SODIUM
SOLUTION FOR INJECTION
INTRAVENOUS USE

-
Active Principles: N/A
Experimental

ASPARAGINASE
SOLUTION FOR INFUSION
INTRAVENOUS USE

-
Active Principles: N/A
Experimental

BLINATUMOMAB
SOLUTION FOR INFUSION
INTRAVENOUS USE

-
Active Principles: N/A
Orphan
Experimental

METHOTREXATE SODIUM
SOLUTION FOR INJECTION
INTRAVENOUS USE

-
Active Principles: N/A
Experimental

DOXORUBICIN
CONCENTRATE FOR SOLUTION FOR INFUSION
INTRAVENOUS USE

-
Active Principles: N/A
Experimental

BLINATUMOMAB
SOLUTION FOR INFUSION
INTRAVENOUS USE

DEXAMETHASONE
TABLET
ORAL USE

-

Active Principles: N/A

Orphan

Experimental

-

Active Principles: N/A

Experimental

MERCAPTOPURINE

TABLETS

ORAL USE

-

Active Principles: N/A

Experimental

PEGASPARGASE

SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS USE

-

Active Principles: N/A

Experimental

CYCLOPHOSPHAMIDE

POWDER FOR SOLUTION FOR INJECTION

INTRAVENOUS

-

Active Principles: N/A

Experimental

DEXAMETHASONE

SOLUTION FOR INJECTION

INTRAVENOUS USE

-

Active Principles: N/A

Experimental

MERCAPTOPURINE

TABLETS

ORAL USE

-

Active Principles: N/A

Experimental

CRISANTASPASE

POWDER FOR SOLUTION FOR INJECTION/INFUSION

INTRAVENOUS USE

-

Active Principles: N/A

Experimental

RITUXIMAB

CONCENTRATE FOR SOLUTION FOR INFUSION

INTRAVENOUS USE

-

Active Principles: N/A

Experimental

Has results