A Phase I/II Study of NMS-03592088, a FLT3, KIT and CSF1R Inhibitor, in Patients with Relapsed or Refractory AML or CMML

Estado	**Tipo de Participantes**	**Rangos de Edad**
EC Finalizado	No aportado	Mayores de 64 , Adultos (18-64 años)
Género	**Fases**	**Participantes esperados**
Ambos	Fase I , Fase II	168
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	seguridad, eficacia, farmacocinética	NO

Información

Identificador
2023-508655-39-00 (CTIS)

Cod. Protocolo
MKIA-088-001

Transicionado 2018-002793-47

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

Enfermedad investigada
Acute Myeloid Leukemia (AML) or Chronic Myelomonocytic Leukemia(CMML) relapsed or refractory

Título Científico
A Phase I/II Study of NMS-03592088, a FLT3, KIT and CSF1R Inhibitor, in Patients with Relapsed or Refractory AML or CMML

Justificación

No aportado

Objetivo Principal

Phase I To determine the maximum tolerated dose (MTD) or maximum administered dose (MAD) and the recommended Phase II dose (RP2D) of NMS-03592088 administered orally once daily for 21 consecutive days followed by 7 days of rest in a 28 day cycle (Schedule A) or once daily for 28 consecutive days (Schedule B) in adult patients with selected hematologic malignancies who have exhausted standard treatment options or for whom standard therapy is considered unsuitable. Phase II To explore the antitumor activity of NMS-03592088 in FLT3-ITD mut AML.

Variables de Evaluación Primaria

Phase I Drug related first-cycle dose limiting toxicities (DLTs) Phase II FLT3-ITD mut AML: Composite Complete Remission (CRc) Rate, i.e. Complete Remission (CR) + Complete Remission with Incomplete Hematologic Recovery (CRi), as defined by the Investigators based on the 2022 European LeukemiaNet (ELN) recommendations

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

No aportado

Variables de Evaluación Secundaria

No aportado

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Patients with relapsed/refractory disease who have failed standard therapy or are unsuitable for standard treatment, with the following confirmed diagnosis: AML as defined by the ELN recommendations Patients must use highly effective contraception. Female patients must be surgically sterile or be postmenopausal or must agree to the use of

highly effective contraception during the period of therapy and in the following 90 (IT and ES) and 208 (FR) days after discontinuation of study treatment. Since NMS-03592088 has potential induction of CYP3A4, WOCBP must be advised that hormonal contraceptives might lose efficacy and must use alternate form of highly effective contraception. Male patients must be surgically sterile or must agree to use highly effective contraception during the period of therapy and in the following 90 (IT and ES) and 118 (FR) days after discontinuation of study treatment. Capability to swallow capsules intact (without chewing, crushing, or opening) Willingness and ability to comply with scheduled visits, treatment plan, laboratory tests and other study indications or procedures Signed and dated IEC or IRB-approved informed consent form indicating that the patient is aware of the neoplastic nature of his/her disease and has been informed of the procedures to be followed, the investigational nature of the therapy, potential benefits, side effects, discomforts, risks and alternative treatments. Patients with confirmed diagnosis of AML as defined by the 2022 ELN recommendations positive for FLT3-ITD mutation in the BM or PB as determined by central laboratory test performed at study entry. Patients with very rapidly proliferative disease who, in the opinion of the Investigator, cannot wait for the central laboratory results can be enrolled based on a local test performed at study entry. Patients with an allelic ratio 0.05 will be considered to have FLT3ITD-mutated disease. Patients positive for FLT3- D835 or I836 mutations will not be eligible. Patients must have failed standard of care including venetoclax and gilteritinib based therapies (cohort 1) or standard of care (cohort 2) Adult (age >= 18 years) patients ECOG performance status <= 2 The interval from prior antitumor treatment to time of NMS-03592088 administration should be at least 2 weeks for any agents other than hydroxyurea. All acute toxic effects (excluding alopecia) of any prior therapy must have resolved to NCI CTCAE version 5.0 Grade 1 Adequate hepatic function, as defined by serum transaminases (i.e., AST/ALT) <= 2.5 x ULN, ALP <= 2.5 x ULN and total bilirubin <= 1.5 x ULN unless abnormality considered due to Gilberts syndrome (FR: in which case the limit is 2 mg/dL). Adequate renal function, as defined by serum creatinine 1.5 x ULN and an estimated glomerular filtration rate (eGFR) 45 mL/min as calculated by the BSA-unadjusted Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, * (eGFR (mL/min)= eGFR (mL/min/1.73 m2) x [BSA (m2)/1.73] where eGFR (mL/min/1.73 m2) = 141 x min(Scr/,1) x max(Scr/, 1)-1.209 x 0.993Age x 1.018 [if female] x 1.159 [if African American

Criterios de Exclusión

Current enrollment in another interventional clinical study
Known hypersensitivity to any of the components of the NMS-03592088 drug product
Any of the following in the previous 6 months: myocardial infarction, unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident or transient ischemic attack, pulmonary embolism, deep vein thrombosis
Known active, life threatening or clinically significant uncontrolled systemic infection.
Known human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS)-related illness.
Active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) C infection.
Known active gastrointestinal disease (e.g., Crohns disease, ulcerative colitis, or short gut syndrome) or other malabsorption syndromes that would impact on drug absorption.
Known active gastrointestinal ulcer
Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration or may interfere with the interpretation of study results and, in the judgment of the Investigator, would make the patient inappropriate for entry into this study or could compromise protocol objectives in the opinion of the Investigator and/or the Sponsor.
Known diagnosis of myasthenia gravis
France specific: Concomitant anticoagulant use that is not already stabilized therapeutically
Diagnosis of acute promyelocytic leukemia or BCR-ABL-positive leukaemia
France specific: Subjects under legal protection or unable to express their consent; subjects deprived of liberty; subjects who are not members or not beneficiaries of a social security scheme.
Currently active second malignancy, except for adequately treated basal or squamous cell skin cancer and/or cone biopsied in situ carcinoma of the cervix uteri and/or superficial bladder cancer.
Patients with known leukemia involvement of CNS.
Hematopoietic stem cell transplantation (HSCT) within 3 months of treatment start and/or persistent nonhematologic toxicities of Grade 2 related to the transplant
Active acute or chronic graft versus host disease (GVHD) requiring immunosuppressive treatment

Patients with QTcF interval 480 milliseconds or with risk factors for torsade de pointes (e.g., uncontrolled heart failure, uncontrolled hypokalemia, history of prolonged QTc interval or family history of long QT syndrome). For patients receiving treatment with concomitant medications known to prolong the QTc interval, replacement with another treatment needs to be considered. If replacement or discontinuation is not clinically feasible, a careful risk/benefit evaluation should be performed prior to enrollment.
Pregnancy. All female patients with reproductive potential must have a negative pregnancy test (serum or urine) within the screening period prior to start of study drug.
Breast-feeding or planning to breast feed during the study or within 3 months after study treatment.

Calendario

(Última actualización: 19/12/2024)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
28/09/2021	09/12/2021	13/01/2022	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
03/05/2024	No aportado	No aportado	29/08/2024	No aportado

Promotor

Nerviano Medical Sciences S.r.l. Italy

Via Louis Pasteur 10

Contact Person

Global Clinical Development

00390331581566

Regulatory@nervianoms.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

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Centros

Cerrado (05/07/2024)

HOSPITAL SAN PEDRO DE ALCANTARA

Cáceres

CÁCERES

Hematology

Cerrado (05/07/2024)

HOSPITAL UNIVERSITARI GERMANS TRIAS I PUJOL DE BADALONA

Badalona

BARCELONA

Cerrado (19/12/2024)

HOSPITAL UNIVERSITARIO Y POLITECNICO LA FE

València

VALENCIA

Hematology Service

Medicamentos

PRD7122996
CAPSULE, HARD
ORAL USE

-

Principios Activos: N/A

Experimental

Sin resultados

A Phase I/II Study of NMS-03592088, a FLT3, KIT and CSF1R Inhibitor, in Patients with Relapsed or Refractory AML or CMML

State	**Type of participants**	**Age Ranges**
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase I , Phase II	168
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	safety, effectiveness, pharmacokinetics	NO

Information

Identifier
2023-508655-39-00 (CTIS)

Protocol Code
MKIA-088-001

Transitioned 2018-002793-47

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

Investigated Disease
Acute Myeloid Leukemia (AML) or Chronic Myelomonocytic Leukemia(CMML) relapsed or refractory

Scientific Title
A Phase I/II Study of NMS-03592088, a FLT3, KIT and CSF1R Inhibitor, in Patients with Relapsed or Refractory AML or CMML

Rationale

Not provided

Main Objective

Phase I To determine the maximum tolerated dose (MTD) or maximum administered dose (MAD) and the recommended Phase II dose (RP2D) of NMS-03592088 administered orally once daily for 21 consecutive days followed by 7 days of rest in a 28 day cycle (Schedule A) or once daily for 28 consecutive days (Schedule B) in adult patients with selected hematologic malignancies who have exhausted standard treatment options or for whom standard therapy is considered unsuitable. Phase II To explore the antitumor activity of NMS-03592088 in FLT3-ITD mut AML.

Primary Endpoints

Phase I Drug related first-cycle dose limiting toxicities (DLTs) Phase II FLT3-ITD mut AML: Composite Complete Remission (CRc) Rate, i.e. Complete Remission (CR) + Complete Remission with Incomplete Hematologic Recovery (CRi), as defined by the Investigators based on the 2022 European LeukemiaNet (ELN) recommendations

Temporary moments of secondary assessment

Not provided

Secondary Objective

Not provided

Secondary Endpoints

Not provided

Temporary moments of secondary assessment

Not provided

Inclusion criteria

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Calendar

(Last Update: 19/12/2024)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
28/09/2021	09/12/2021	13/01/2022	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
03/05/2024	Not aported	Not aported	29/08/2024	Not aported

Sponsor

Nerviano Medical Sciences S.r.l. Italy

Via Louis Pasteur 10

Contact Person

Global Clinical Development

00390331581566

Regulatory@nervianoms.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

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Sites

Closed (05/07/2024)

HOSPITAL SAN PEDRO DE ALCANTARA

Cáceres

CÁCERES

Hematology

Closed (05/07/2024)

HOSPITAL UNIVERSITARI GERMANS TRIAS I PUJOL DE BADALONA

Badalona

BARCELONA

Closed (19/12/2024)

HOSPITAL UNIVERSITARIO Y POLITECNICO LA FE

València

VALENCIA

Hematology Service

Medication

PRD7122996
CAPSULE, HARD
ORAL USE

-

Active Principles: N/A

Experimental

No results