eXalt3: Study Comparing X-396 (Ensartinib) to Crizotinib in ALK Positive Non-Small Cell Lung Cancer (NSCLC) Patients

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	288
Resultados	**Bajo nivel intervención**	**Enfermedad rara**
Sin resultados	No	No
Cobertura geográfica	**Ámbitos del ensayo**	**Terapia avanzada**
Multicéntrico internacional	seguridad, eficacia	NO

Información

Identificador
2024-513454-29-00 (CTIS)

Cod. Protocolo
X396-CLI-301

Transicionado 2015-004147-40

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

Enfermedad investigada
Non-Small Cell Lung Cancer (NSCLC)

Título Científico
eXALT3: Phase 3 Randomized Study Comparing Ensartinib to Crizotinib in Anaplastic Lymphoma Kinase (ALK) Positive Non-Small Cell Lung Cancer (NSCLC) Patients

Justificación

No aportado

Objetivo Principal

To evaluate the efficacy and safety of ensartinib vs. crizotinib in patients with ALK-positive NSCLC that have received up to 1 prior chemotherapy regimen and no prior ALK tyrosine kinase inhibitor (TKI)

Variables de Evaluación Primaria

Progression-free survival (PFS) as assessed by independent radiology review (IRR) based on RECIST v. 1.1 criteria.

Momentos temporales de evaluación primaria

No aportado

Objetivo Secundario

To obtain additional pharmacokinetic (PK) data on ensartinib from sparse PK sampling from patients at selected sites.
To compare the quality of life (QoL) in patients receiving ensartinib vs. crizotinib
To evaluate the status of exploratory biomarkers and correlate with clinical outcome
To obtain germline DNA samples for possible pharmacogenetic analysis in the event that outliers with respect to efficacy, tolerability/safety, or exposure are identified

Variables de Evaluación Secundaria

Key Secondary Efficacy Endpoints: Overall survival, CNS response rate (based on IRR), time to CNS progression (based on IRR), objective response rate (based on IRR)
PFS (based on investigator assessment)
ORR (based on investigator assessment)
Time to response (based on investigator assessment and IRR)
Duration of response (based on investigator assessment and IRR)
CNS response rate (based on investigator assessment)
Time to CNS progression (based on investigator assessment)
Patient reported time to deterioration (TTD) as measured by the EORTC C30/LC13 QoL questionnaire and Lung Cancer Symptom Scale (LCSS)
Patient reported health-related quality of life (HRQoL) as measured by the EORTC C30/LC13 QoL questionnaire and LCSS.
Pharmacodynamic (PD) and possible pharmacogenetic (PG) assessments and biomarkers in blood or/and tissue sample. Biomarkers in the blood or tissue related to efficacy.

Momentos temporales de evaluación secundaria

No aportado

Criterios de Inclusión

Histologically or cytologically confirmed diagnosis of advanced or recurrent (Stage IIIB not amenable for multimodality treatment) or metastatic (Stage IV) NSCLC that is ALK-positive by an FDA-approved assay, performed centrally. Patients must be ALK positive by local test prior to submitting tissue to the central lab. Randomization will occur after ALK positive confirmation is received from the central lab. Patients may have received up to 1 prior chemotherapy regimen for metastatic disease, which may also include maintenance therapy. Note that patients that have received adjuvant or neoadjuvant chemotherapy and developed metastatic disease within 6 months from the end of that therapy would be considered to have received 1 prior regimen for metastatic disease Patients must have measurable disease per RECIST v. 1.1. Willingness and ability to comply with the trial and follow-up procedures. Ability to understand the nature of this trial and give written informed consent. Note the following pertains to patients enrolled in France Specific to France: Subjects will be eligible for inclusion in this study only affiliated to the French Social Security system, and currently benefit from the corresponding rights and cover. Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) score of 0 to 2. (see Appendix A) Life expectancy of at least 12 weeks. Ability to swallow and retain oral medication. Adequate organ system function, defined as follows: a. Absolute neutrophil count (ANC) 1.5 x 109/L b. Platelets 100 x 109/L c. Hemoglobin 9 g/dL (90 g/L). Note that transfusions are allowed to meet the required hemoglobin level d. Total bilirubin 1.5 times the upper limit of normal (ULN) e. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) 2.5 x ULN if no liver involvement or 5 x ULN with liver involvement. f. Creatinine 1.5 x ULN. If >1.5 x ULN, patient may still be eligible if calculated creatinine clearance ³50 mL/min (0.83 mL/s) as calculated by the Cockcroft-Gault method. Brain metastases allowed if asymptomatic at study baseline. Patients with untreated brain metastases must not be on corticosteroids. If patients have neurological symptoms or signs due to CNS metastases, patients need to complete whole brain radiation or focal treatment at least 14 days before start of study treatment and be asymptomatic on stable or decreasing doses of corticosteroids at baseline. Men with partners of childbearing potential willing to use adequate contraceptive measures during the study and for 90 days after the last dose of study medication. Women who are not of child-bearing potential, and women of child-bearing potential who agree to use adequate contraceptive measures during the study and for 90 days after the last dose of study medication, and who have a negative serum or urine pregnancy test within 1 week prior to initial trial treatment. Patients must be 18 years of age.

Criterios de Exclusión

Patients that have previously received an ALK TKI or PD-1/PD-L1 therapy, and patients currently receiving cancer therapy (i.e., other targeted therapies, chemotherapy, radiation therapy, immunotherapy, biologic therapy, hormonal therapy, surgery and/or tumor embolization). Patients at risk for GI perforation. Clinically significant cardiovascular disease including: QTcF interval >450 ms for men and >470 ms for women, symptomatic bradycardia <45 beats per minute or other significant ECG abnormalities in the investigators opinion. Clinically uncontrolled hypertension in the investigators opinion (e.g., blood pressure >160/100 mmHg; note that isolated elevated readings considered to not be indicative of uncontrolled hypertension are allowed). The following within 6 months prior to Cycle 1 Day 1: Congestive heart failure (New York Heart Class III or IV (see Appendix D). Arrhythmia or conduction abnormality requiring medication. Note: patients with atrial fibrillation/flutter controlled by medication and arrhythmias controlled by pacemakers are eligible. Severe/unstable angina, coronary artery/peripheral bypass graft, or myocardial infarction. Cerebrovascular accident or transient ischemia. Patients who are immunosuppressed (including known HIV infection), have a serious active infection at the time of treatment, have interstitial lung disease/pneumonitis, or have any serious underlying medical condition that would impair the ability of the patient to receive protocol treatment. Patients with controlled hepatitis C, in the investigators opinion, are allowed. Patients with known hepatitis B must be HBeAg and HB viral DNA negative for enrollment. Note that, because of the high prevalence, all patients in the Asia-Pacific region (except Australia, New Zealand, and Japan) must be tested and, if HBsAg positive, must be

HBeAg and HB viral DNA negative for enrollment. Known hypersensitivity to tartrazine, a dye used in the ensartinib 100 mg capsule. Psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol. Concurrent condition that in the investigators opinion would jeopardize compliance with the protocol or would impart excessive risk associated with study participation that would make it inappropriate for the patient to be enrolled. Inability or unwillingness to comply with study and/or follow-up procedures outlined in the protocol. Note the following pertains to patients enrolled in France. Specific to France: Subjects will not be eligible when under legal protection. Use of an investigational drug within 21 days prior to the first dose of study drug. Note that to be eligible, any drug-related toxicity should have recovered to Grade 1 or less, with the exception of alopecia. Any chemotherapy within 4 weeks, or major surgery or radiotherapy within the last 14 days. Patients with primary CNS tumors and leptomeningeal disease are ineligible. Patients with a previous malignancy within the past 3 years (other than curatively treated basal cell carcinoma of the skin, in situ carcinoma of the cervix, or any cancer that is considered to be cured and have no impact on PFS and OS for the current NSCLC). Concomitant systemic use of anticancer herbal medications. These should be stopped prior to study entry. Patients receiving: a. Strong CYP3A inhibitors (including, but not limited to, atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin, voriconazole, grapefruit, grapefruit juice) b. Strong CYP3A inducers (including, but not limited to, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, St. John's Wort) c. CYP3A substrates with narrow therapeutic window (including, but not limited to, alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus). Women who are pregnant or breastfeeding. Presence of active gastrointestinal (GI) disease or other condition that will interfere significantly with the absorption, distribution, metabolism, or excretion of study medications.

Calendario

(Última actualización: 30/05/2025)

Autorización	Inicio de Ensayo	Inclusión Primer Paciente	Interrumpido	Reiniciado
29/07/2016	28/11/2016	15/03/2017	No aportado	No aportado

Fin de reclutamiento	Fin prematuro (España)	Fin prematuro (Global)	Fin del ensayo en España	Fin del ensayo global
01/11/2018	No aportado	No aportado	08/07/2024	No aportado

Promotor

Xcovery Holding Co. LLC United States

11780 Us Highway 1 Suite 202

Contact Person

Esteban Sanchez

0015618359356

esteban@xcovery.com

Monetary support: N/A

Tipo de promotor: Comercial

Ceim

CEIm Parc de Salut Mar

Doctor Aiguader, 88 Edificio PRBB 08003 Barcelona

ceic-psmar@imim.es

933160679

Centros

No iniciado (01/08/2016)

Hospital de Sabadell

Sabadell

BARCELONA

Oncolog?a m?dica

Activo (29/03/2017)

Hospital del Mar

Barcelona

BARCELONA

Oncologia m?dica

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

Hospital Son Llatzer

Palma

BALEARES

Oncology

Cerrado (25/02/2019)

Hospital Universitari Quir?n Dexeus

Barcelona

BARCELONA

Oncolog?a M?dica

Medicamentos

XALKORI 200 mg hard capsules
CAPSULE, HARD
ORAL USE

Código ATC: L01ED01 - CRIZOTINIB
Principios Activos: N/A

Experimental

XALKORI 250 mg hard capsules
CAPSULE, HARD
ORAL USE

Código ATC: L01ED01 - CRIZOTINIB
Principios Activos: N/A

Experimental

X-396 Capsules
CAPSULES
ORAL USE

-
Principios Activos: N/A

Experimental

Sin resultados

eXalt3: Study Comparing X-396 (Ensartinib) to Crizotinib in ALK Positive Non-Small Cell Lung Cancer (NSCLC) Patients

State	**Type of participants**	**Age Ranges**
Finished CT	Not provided	Older than 64 , Adults (18-64 years)
Gender	**Phases**	**Expected Participants**
Both	Phase III	288
Results	**Low level of intervention**	**Rare disease**
No results	No	No
Geographic coverage	**Areas of the study**	**Advanced therapy**
International multicenter	safety, effectiveness	NO

Information

Identifier
2024-513454-29-00 (CTIS)

Protocol Code
X396-CLI-301

Transitioned 2015-004147-40

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

Investigated Disease
Non-Small Cell Lung Cancer (NSCLC)

Scientific Title
eXALT3: Phase 3 Randomized Study Comparing Ensartinib to Crizotinib in Anaplastic Lymphoma Kinase (ALK) Positive Non-Small Cell Lung Cancer (NSCLC) Patients

Rationale

Not provided

Main Objective

To evaluate the efficacy and safety of ensartinib vs. crizotinib in patients with ALK-positive NSCLC that have received up to 1 prior chemotherapy regimen and no prior ALK tyrosine kinase inhibitor (TKI)

Primary Endpoints

Progression-free survival (PFS) as assessed by independent radiology review (IRR) based on RECIST v. 1.1 criteria.

Temporary moments of secondary assessment

Not provided

Secondary Objective

To obtain additional pharmacokinetic (PK) data on ensartinib from sparse PK sampling from patients at selected sites.
To compare the quality of life (QoL) in patients receiving ensartinib vs. crizotinib
To evaluate the status of exploratory biomarkers and correlate with clinical outcome
To obtain germline DNA samples for possible pharmacogenetic analysis in the event that outliers with respect to efficacy, tolerability/safety, or exposure are identified

Secondary Endpoints

Key Secondary Efficacy Endpoints: Overall survival, CNS response rate (based on IRR), time to CNS progression (based on IRR), objective response rate (based on IRR)
PFS (based on investigator assessment)
ORR (based on investigator assessment)
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Inclusion criteria

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Calendar

(Last Update: 30/05/2025)

Authorization	Start of Trial	First patient inclusion	Halted	Restarted
29/07/2016	28/11/2016	15/03/2017	Not aported	Not aported

End of recruitment	Premature end (Spain)	Premature End (Global)	Trial end (Spain)	Trial end (Global)
01/11/2018	Not aported	Not aported	08/07/2024	Not aported

Sponsor

Xcovery Holding Co. LLC United States

11780 Us Highway 1 Suite 202

Contact Person

Esteban Sanchez

0015618359356

esteban@xcovery.com

Monetary support: N/A

Sponsor type: Commercial

Ceim

CEIm Parc de Salut Mar

Doctor Aiguader, 88 Edificio PRBB 08003 Barcelona

ceic-psmar@imim.es

933160679

Sites

not initialized (01/08/2016)

Hospital de Sabadell

Sabadell

BARCELONA

Oncolog?a m?dica

Active (29/03/2017)

Hospital del Mar

Barcelona

BARCELONA

Oncologia m?dica

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

Hospital Son Llatzer

Palma

BALEARES

Oncology

Closed (25/02/2019)

Hospital Universitari Quir?n Dexeus

Barcelona

BARCELONA

Oncolog?a M?dica

Medication

XALKORI 200 mg hard capsules
CAPSULE, HARD
ORAL USE

ATC code: L01ED01 - CRIZOTINIB
Active Principles: N/A

Experimental

XALKORI 250 mg hard capsules
CAPSULE, HARD
ORAL USE

ATC code: L01ED01 - CRIZOTINIB
Active Principles: N/A

Experimental

X-396 Capsules
CAPSULES
ORAL USE

-

Active Principles: N/A

Experimental

No results