ALINA

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Main Information

Primary registry identifying number
LBCTR2020104622

Protocol number
BO40336

MOH registration number

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
12/10/2020

Primary sponsor
F. Hoffmann-La Roche Ltd

Primary sponsor: Country of origin
Germany

Date of registration in primary registry
06/06/2022

Date of registration in national regulatory agency
12/10/2020

Public title
ALINA

Acronym
ALINA

Scientific title
A PHASE III, OPEN-LABEL, RANDOMIZED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ADJUVANT ALECTINIB VERSUS ADJUVANT PLATINUM-BASED CHEMOTHERAPY IN PATIENTS WITH COMPLETELY RESECTED STAGE IB (TUMORS 4 CM) TO STAGE IIIA ANAPLASTIC LYMPHOMA KINASEPOSITIVE NONSMALL CELL LUNG CANCER

Acronym
ALINA

Brief summary of the study: English

This study will evaluate the efficacy and safety of alectinib compared with platinum-based chemotherapy in patients with completely resected Stage IB (tumors 4 cm) to Stage IIIA, anaplastic lymphoma kinasepositive nonsmall cell lung cancer (NSCLC). Specific objectives and corresponding endpoints for the study are outlined below.The primary and secondary efficacy objectives will be analyzed in the intent-to-treat (ITT) population of randomized patients with resected Stage IB (tumors 4 cm) to Stage IIIA NSCLC and in thesubpopulation of patients with resected Stage IIIIIA
 NSCLC. Disease-free survival (DFS) as an endpoint does not distinguish between the location of the first documented recurrence of disease
or new primary NSCLC. Descriptive statistics (i.e., frequencies and percentages) will be used to explore the first site of recurrence of disease or new primary NSCLC.

Brief summary of the study: Arabic

ستقوم هذه الدراسة بتقييم فعالية وسلامة alectinib مقارنة مع العلاج الكيميائي القائم على البلاتين في المرضى الذين يعانون من المرحلة IB سم) إلى المرحلة4المستأصلة بالكامل (أورام IIIA ، سرطان الغدد الليمفاوية الكشمي غير الصغرى الخلايا (NSCLC). سيتم تحليل أهداف الفعالية الأولية والثانوية في مجموعة العلاج (ITT) للمرضى من المرحلة IB سم) إلى المرحلة4(الأورام IIIA NSCLC الذين خضعوا للاستئصال وفي تعداد المرضى المصابين بالمرحلة المستأصلة IIIIIA .
البقاء بدون مرض (DFS) كنقطة نهاية لا يميز بين موقع أول موقع موثق لتكرار للمرض أو NSCLC الأولي الجديد. سيتم استخدام الإحصاء الأولي الجديد.
NSCLC الوصفي (أي التكرارات والنسب المئوية) لاستكشاف الموقع الأول لتكرار مرض أو

Health conditions/problem studied: Specify

The study population will consist of patients who have undergone complete resection with negative margins (R0) of histologically confirmed Stage IB (tumors equal to or larger than 4 cm) to Stage IIIA NSCLC as per UICC/AJCC, 7th edition. Patients will be randomized to receive either alectinib or platinum-based chemotherapy.

Interventions: Specify

This study has three parts: 1) Screening 2) Treatment 3) Follow-up
The patient will be randomly placed in one of the following groups:
•One group will receive alectinib, (given as 4 capsules by mouth twice a day for up to 24 months)
•The other group will receive treatment with chemotherapy, given by intravenous (IV) infusion (in the vein), for 4 cycles, with each cycle lasting 21 days. Chemotherapy is the current standard of care for lung cancer. Patients in this group will receive one out of the following treatment options at the discretion of the investigator: Cisplatin plus vinorelbine OR cisplatin plus gemcitabine OR cisplatin plus pemetrexed. Carboplatin may be administered instead of cisplatin in one of the previous combinations if at any time, following the first dose, the patient cannot tolerate cisplatin.
During this study, the patient could have up to 18 visits for treatment administration, safety monitoring, and monitoring of the disease for the first 2 years. Afterward, the patient will be monitored for their disease every 24 weeks during Years 3 to 5, and every year thereafter. If the cancer comes back, the study doctor will follow up with the patient about every 6 months until the study is closed down.
This study will comprise approximately 200 centers in around 30 countries worldwide. Approximately 255 patients will be enrolled into the study

Key inclusion and exclusion criteria: Inclusion criteria

•Signed Informed Consent Form
•Age equal to and larger than 18 at time of signing Informed Consent Form
•Complete resection of histologically confirmed Stage IB (tumor equal to and larger than 4 cm) to Stage IIIA (T2-3 N0, T1-3 N1, T1-3 N2, T4 N0 -1) NSCLC as per UICC/AJCC, 7th edition, with negative margins, at 4-12 weeks before enrollment
Accepted types of resection include any of the following: lobectomy, sleeve lobectomy, bilobectomy, or pneumonectomy.
Resection by segmentectomy or wedge resection is not allowed.
N3 disease is not allowed.
•If mediastinoscopy was not performed preoperatively, it is expected that, at a minimum, mediastinal lymph node systematic sampling will have occurred.
Systematic sampling is defined as removal of at least one representative lymph node at specified levels.
Complete mediastinal lymph node dissection (MLND) is preferred. MLND entails resection of all lymph nodes at those same levels.
For patients who have undergone a right thoracotomy, sampling or MLND is required at Levels 4 and 7; for those who have undergone a left thoracotomy, sampling or MLND is required at Levels 5 and/or 6 and 7.
Exceptions will be granted for the following situations:
If patients have documented N2 disease in one level (per the UICC/AJCC staging system, 7th edition), not all levels need to be sampled.
If the preoperative staging imaging results (contrast computed tomography [CT] and positron emission tomography scans) do not suggest evidence of disease in the mediastinum, the patient may be considered eligible even if N2 nodal sampling was not performed per surgeon's decision.
•Documented ALK-positive disease according to an FDA-approved and CE-marked test
•Eligible to receive a platinum-based chemotherapy regimen according to the local labels or guidelines
•Eastern Cooperative Oncology Group (ECOG) Performance Status of Grade 0 or 1
•Adequate hematologic function, defined by the following laboratory test results, obtained within 3 days prior to initiation of study treatment:
Platelet count 100 109/L
ANC 1500/L
Hemoglobin 9 g/dL
•Adequate renal function, defined by the following laboratory test results, obtained within 3 days prior to initiation of study treatment:
Serum creatinine 1.5 upper limit of normal (ULN) and
Creatinine clearance (CrCl) 60 mL/min
•For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods with a failure rate of 1% per year during the treatment period and for at least 90 days after the last dose of alectinib or according to local labels or guidelines for chemotherapy
A woman is considered to be of childbearing potential if she is postmenarcheal, has not reached a postmenopausal state (12 continuous months of amenorrhea with no identified cause other than menopause), and is not permanently infertile due to surgery (i.e., removal of ovaries, fallopian tubes, and/or uterus) or another cause as determined by the investigator (e.g., Müllerian agenesis).
Examples of contraceptive methods with a failure rate of 1% per year include bilateral tubal ligation, male sterilization
contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices. Hormonal contraceptive methods must be supplemented by a barrier method.
The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods of contraception
Women of childbearing potential must have a negative serum pregnancy test results prior to randomization (maximum of 3 days) and within 10 days of the first dose of study drug. First dose of study drug (alectinib or chemotherapy) must be administered within 7 days from randomization.
•For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm, as defined below:
With female partners of childbearing potential, men must remain abstinent or use a condom plus an additional contraceptive method that

together result in a failure rate of 1% per year during the treatment period and for at least 90 days after the last dose of alectinib or according to local labels or guidelines for chemotherapy. Men must refrain from donating sperm during this same period.
With pregnant female partners, men must remain abstinent or use a condom during the treatment period and for at least 90 days after the last dose of alectinib or according to local labels or guidelines for chemotherapy to avoid exposing the embryo.
The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or post ovulation methods) and withdrawal are not acceptable methods of contraception.
•Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

100

Key inclusion and exclusion criteria: Exclusion criteria

•Pregnant or breastfeeding, or intending to become pregnant during the study or within 90 days after the last dose of alectinib or according to local labels or guidelines for chemotherapy
•Prior adjuvant radiotherapy for NSCLC
Radiotherapy in the neo-adjuvant setting is allowed and must be completed at least 4 weeks prior to initiation of study treatment.
•Prior exposure to systemic chemotherapy
Chemotherapy for early-stage of malignancy with curative intent, provided that the last dose received was more than 5 years prior to enrollment, may be allowed upon approval by the Medical Monitor.
•Prior exposure to ALK inhibitors
•Stage IIIA N2 patients that, in the investigator's opinion, should receive PORT are excluded from the study
PORT is not allowed in the study.
•Known sensitivity to any component of study drug (alectinib or planned chemotherapy) to which the patient may be randomized
This includes, but is not limited to, patients with galactose intolerance, a congenital lactase deficiency, or glucose-galactose malabsorption.
•Malignancies other than NSCLC within 5 years prior to enrollment, except for curatively treated basal cell carcinoma of the skin, early gastrointestinal (GI) cancer by endoscopic resection, in situ carcinoma of the cervix, ductal carcinoma in situ, papillary thyroid cancer, or any cured cancer that is considered to have no impact on DFS or OS for the current NSCLC
•Any GI disorder that may affect absorption of oral medications, such as malabsorption syndrome or status postmajor bowel resection
•Liver disease characterized by any of the following:
ALT and AST 3 ULN
or
Impaired excretory function or synthetic function or other conditions of decompensated liver disease such as coagulopathy, hepatic encephalopathy, hypoalbuminemia, ascites, or bleeding from esophageal varices
or
Active viral or active autoimmune, alcoholic, or other types of acute hepatitis.
Active viral hepatitis B is defined as having positive hepatitis B surface antigen (HBsAg).
Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (hepatitis B core antibody [HBcAb] – HbcAb positive, but negative HBsAg) are eligible only if the HBV DNA test is negative.
Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction (PCR) is negative for HCV RNA.
•Any exclusion criteria based on local labels or guidelines for chemotherapy
•Patients with symptomatic bradycardia
•History of organ transplant
•Known HIV positivity or AIDS-related illness
•Any clinically significant concomitant disease or condition that could interfere with or for which the treatment might interfere with the conduct of the study or the absorption of oral medications or that would pose an unacceptable risk to the patients in this study, in the opinion of the Principal Investigator
•Any psychological, familial, sociological, or geographical condition potentially hampering compliance with the study protocol requirements and/or follow-up procedures; those conditions should be discussed with the patient before tria

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Other

Trial scope: Specify scope

Study design: Allocation

Randomized controlled trial

Study design: Masking

Open (masking not used)

Study design: Control

Study phase

Active

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

Yes, Worldwide

IMP has market authorization: Specify

In November 2017 the FDA approved alectinib for the first-line treatment of patients with ALK-positive metastatic non-small cell lung cancer

Name of IMP	Year of authorization	Month of authorization
Alectinib	2017	11

Type of IMP

Others

Pharmaceutical class

Alectinib is a potent and selective inhibitor of the enzyme activity of ALK (50% of maximum inhibitory concentration [IC50] = 1.9 nM).

Therapeutic indication

Alectinib has been approved in Japan for patients with ALK-positive lung cancer that is advanced, has come back, and/or the tumor cannot be removed by surgery. Alectinib has also been approved in the United States and other countries for patients with ALK-positive lung cancer that has spread to other parts of the body.

Therapeutic benefit

Alectinib inhibits mutant forms of the ALK enzyme, including mutations responsible for resistance to crizotinib. Alectinib suppressed ALK auto-phosphorylation in cells and showed selective antitumor activity against cell lines with gene alterations of ALK, such as NSCLC and anaplastic large-cell lymphoma (ALCL) cell lines harboring ALK fusions, and a neuroblastoma cell line harboring amplified ALK. In mouse models of subcutaneously grafted human cancer cell lines with gene alterations of ALK, alectinib also exhibited tumor growth inhibition (TGI) and tumor regression when administered orally once daily. In an NCI-H2228 xenograft model of echinoderm microtubule-associated protein-like 4 (EML4) -ALK-positive NSCLC cells induced tumor regression. The rate of TGI at 20 mg/kg/day was 168%, and the effective dose causing 50% TGI (ED50) was calculated to be 0.46 mg/kg/day. At doses of 6 mg/kg/day and above tumor regression occurred. After administration of alectinib for 11 days, the potent antitumor effect was maintained and tumor re-growth did not occur. Additionally, alectinib showed an enhancement of anti-tumor efficacy with good tolerability in combination with other standard chemotherapeutic agents for NSCLC (cisplatin, paclitaxel, gemcitabine and bevacizumab). Alectinib is efficacious in tumor models expressing an ALK fusion bearing mutations, which are associated with resistance to crizotinib, such as L1196M, G1269A and S1206Y. Alectinib is also effective in mouse NCI-H2228 NSCLC xenografts that are already maximally suppressed by crizotinib. Moreover, compared to crizotinib, alectinib reduced tumor growth and prolonged survival in models of brain metastases

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

The following samples will be sent to one or several central laboratories or to theSponsor or a designee for analysis:
-Samples for PK analysis
-Pretreatment tumor tissue sample obtained at screening for determination of ALK status for patient eligibility
-Tumor tissue sample obtained at the time of recurrence, if deemed clinically feasible, for exploratory research on biomarkers
- Plasma samples for exploratory research on biomarkers
-Biomarker plasma and tissue sampling will be in accordance with the IRB/EC-approved

Target sample size

225

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

29/10/2020

Date of study closure: Type

Anticipated

Date of study closure: Date

01/11/2026

Recruitment status

Other

Recruitment status: Specify

No recruitment occurred and the sites will be closed

Date of completion

01/11/2026

IPD sharing statement plan

Yes

IPD sharing statement description

The Sponsor maintains confidentiality standards by coding each patient enrolled in the study through assignment of a unique patient identification number. This means that patient names are not included in data sets that are transmitted to any Sponsor location.
Patient medical information obtained by this study is confidential and may be disclosed to third parties only as permitted by the Informed Consent Form (or separate authorization for use and disclosure of personal health information) signed by the patient, unless permitted or required by law.
Medical information may be given to a patient's personal physician or other appropriate medical personnel responsible for the patient's welfare, for treatment purposes.
Given the complexity and exploratory nature of exploratory biomarker analyses, data derived from these analyses will generally not be provided to study investigators or patients unless required by law. The aggregate results of any conducted research will be available in accordance with the effective Roche policy on study data publication.

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

No Numbers

Sources of Monetary or Material Support

No Sources

Secondary Sponsors

No Sponsors

Contact for Public/Scientific Queries

No Contacts

Centers/Hospitals Involved in the Study

No Centers/Hospitals

Ethics Review

No Reviews

Countries of Recruitment

No Countries

Health Conditions or Problems Studied

No Problems Studied

Interventions

No Interventions

Primary Outcomes

No Outcomes

Key Secondary Outcomes

No Outcomes

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files