ALERT-lung

ALEctinib for the Treatment of Pretreated RET-rearranged Advanced Non-small Cell Lung Cancer

NCT-Nummer:
NCT03445000

Studienbeginn:
November 2018

Letztes Update:
14.04.2021

Wirkstoff:
Alectinib
Indikation (Clinical Trials):
Lung Neoplasms, Carcinoma, Non-Small-Cell Lung

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
Phase 2

Sponsor:
European Thoracic Oncology Platform

Collaborator:
Hoffmann-La Roche

Studien-Informationen

Detailed Description:

The trial is investigating the efficacy of alectinib in patients with advanced stage

RET-rearranged NSCLC, treated with at least one platinum based systemic chemotherapy regimen.

Preclinical studies have shown that alectinib, a highly selective next generation ALK inhibitor, has potent anti-tumour activity in RET-rearranged NSCLC. Therapeutically, several multiple kinases inhibitors, are potentially able to inhibit RET kinase function, which has been tested in several unselected NCSLC trials. However, those result were negative and none of the tested drugs was approved for lung cancer treatment.

The ALERT-lung trial is a single arm, phase II trial with the primary objective to assess the efficacy of alectinib in terms of best overall response (OR) assessed by RECIST v1.1 in selected NSCLC patients with RET rearrangement. The secondary objectives are to evaluate secondary measures of clinical efficacy including disease control, progression-free survival (PFS), and overall survival (OS) as well as to assess safety and tolerability of the treatment and to describe the association of primary and secondary outcomes with tumour characteristics.

Alectinib is administered orally, 600 mg, twice per day, until progression, refusal or unacceptable toxicity. Trial treatment may also continue beyond progression, with physician and patient agreement, for as long as the patient may still derive clinical benefit. A total sample size of 44 patients is required.

Ein-/Ausschlusskriterien

Inclusion Criteria:

1. Histologically or cytologically documented non-small cell lung carcinoma

2. Advanced disease defined as recurrent stage IV (according to 8th TNM classification) or recurrent or progressive disease following multimodal therapy (radiation therapy, surgical resection, or definitive chemo-radiation therapy for locally advanced disease)

3. At least one prior platinum-based systemic regimen: Adjuvant or neoadjuvant or definitive platinum-based chemo-radiotherapy treatments are considered as a line of

treatment only if completed less than 6 months before enrolment. Maintenance therapy following platinum doublet-based chemotherapy is not considered a separate regimen of therapy.

4. RET rearrangement detected by FISH, Nanostring or by parallel-sequencing on FFPE tumour tissue assessed locally.

5. Availability of FFPE tumour material for central confirmation of RETrearrangement

6. Measurable or non-measurable, but radiologically evaluable (except for skin lesions) disease according to RECIST v1.1 criteria

7. Age ≥18 years

8. Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2

9. Life expectancy >3 months

10. Adequate haematological function:

- Haemoglobin ≥9 g/dL

- Neutrophil count ≥1.5 ×109/L

- Platelet count ≥100 × 109/L

- WBC ≥2 ×109/L

11. Adequate renal function: Calculated creatinine clearance ≥45 mL/min (according to Cockcroft-Gault formula)

12. Adequate liver function:

- Total bilirubin ≤2x ULN (except patients with Gilbert Syndrome, who can have total bilirubin ≤3.0 mg/dL)

- ALT and AST ≤3x ULN (≤5x ULN for patients with concurrent liver ¨ metastasis)

13. Patient capable of proper therapeutic compliance, and accessible to correct followup.

14. Women of childbearing potential, including women who had their last menstrual period in the last 2 years, must have a negative serum or urine beta HCG pregnancy test within 7 days before enrolment into the trial and within 3 days before alectinib treatment start.

15. Sexually active men and women of childbearing potential must use an effective contraceptive method (intrauterine devices without hormones, bilateral tubal occlusion, vasectomized partner or total abstinence) during the trial treatment and for a period of at least 3 months following the last dose of alectinib.

16. Recovered from any previous therapy related toxicity to Grade ≤1 at date of enrolment (except for recovery to Grade ≤2 of alopecia, fatigue, creatinine increased, lack of appetite or peripheral neuropathy)

17. Written Informed Consent (IC) for trial treatment must be signed and dated by the patient and the investigator prior to any trial-related intervention.

Exclusion Criteria:

1. Untreated, active CNS metastases

2. Carcinomatous meningitis

3. Any previous (in the past 3 years) or concomitant malignancy EXCEPT adequately treated basal or squamous cell carcinoma of the skin, in situ carcinoma of the cervix or bladder, in situ ductal carcinoma of the breast

4. Any serious diseases or clinical conditions, including but not limited to uncontrolled active infection and any other serious underlying medical processes, that could affect the patient's capacity to participate in the trial

5. Liver disease characterized by:

- ALT or AST >3 × ULN (>5 × ULN for patients with concurrent liver metastasis) confirmed on two consecutive measurements or
- Impaired excretory function (e.g., hyperbilirubinaemia) or synthetic function or other conditions of decompensated liver disease such as coagulopathy, hepatic encephalopathy, hypoalbuminaemia, ascites, and bleeding from oesophageal varices or
- Acute viral or active autoimmune, alcoholic, or other types of acute hepatitis

6. Patients with baseline symptomatic bradycardia

7. Previous treatment with any RET TKI or RET targeted therapy.

8. Known EGFR, ALK, ROS, and BRAF mutation (in addition to RET rearrangement)

9. Any concurrent systemic anticancer therapy.

10. Any GI disorder that may affect absorption of oral medications, such as malabsorption

syndrome or status post major bowel resection.

11. History of hypersensitivity to any of the additives in the alectinib drug formulation.

12. Known HIV positivity or AIDS-related illness.

13. Women who are pregnant or in the period of lactation.

Studien-Rationale

Primary outcome:

1. Best overall response (Time Frame - From the start of trial treatment across all time points until the end of trial treatment, asssed up to 44 months.):
Best overall response (OR = CR or PR), per investigator assessment according to RECIST 1.1.

Secondary outcome:

1. Best overall response per independent review (Time Frame - From the start of trial treatment across all time points until the end of trial treatment, asssed up to 44 months.):
Best overall response (OR = CR or PR), per independent review assessment according to RECIST 1.1.

2. Disease control at 24-weeks (Time Frame - 24 weeks after treatment start):
Best overall response of CR or PR, or SD (or non-CR/non-PD in the case of non-measurable disease only)

3. Progression-free survival (PFS) (Time Frame - From date of enrolment until date of documented progression or death, if progression is not documented, assessed up to 44 months.):
PFS will be assessed according to RECIST 1.1 criteria.

4. Overall survival (OS) (Time Frame - From date of enrolment until date of death from any cause, assessed up to 44 months.):
Defined as the time from date of enrollment until death from any cause.

5. Safety and tolerability of alectinib treatment (Time Frame - Assessed from date of signature of informed consent until 30 days after treatment is ceased for any reason.):
The safety and tolerability of alectinib treatment will be assessed through analysis of the worst grade of toxicity/adverse events according to CTCAE v4.0 criteria observed over the whole treatment period.

Geprüfte Regime

- Alectinib (Alecensa):
  Alectinib is administered orally 600mg (4x150mg capsules), twice per day (8 capsules, total 1200mg daily). The appropriate number of alectinib capsules will be provided to patients to be self-administered at home. Alectinib capsules must be taken at the same time each day with food. If a planned dose of alectinib is missed, patients can take the missed dose up until 6 hours before the next dose.

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Quelle: ClinicalTrials.gov