KURZPROTOKOLL
PACE-LUNG

Öffentlicher Titel	Phase II Studie zu zusätzlicher Chemotherapie bei EGFR-positivem nicht-kleinzelligem Lungenkrebs
Wissenschaftl. Titel	Additional chemotherapy for EGFRm patients with the continued presence of plasma ctDNA EGFRm at week 3 after start of osimertinib 1st-line treatment
Kurztitel	PACE-LUNG
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - Erstlinie
Einschlusskriterien	- Pre-Screening Phase: - 1. Provision of written informed consent for the pre-screening phase - 2. Age >= 18 years - 3. Histologically confirmed stage IIIB or IV NSCLC - 4. Tumor positive for Ex19del or L858R EGFR mutation assessed according to local standard - 5. Planned treatment with osimertinib 80mg/d 1st-line as SoC or ongoing treatment for a maximum of 28 days - 6. Available radiographic chest and abdominal CT or MRI scans performed up to 42 days before initial osimertinib treatment - 7. Previously untreated with systemic treatment given as primary therapy for advanced or metastatic disease, except for osimertinib for a maximum of 28 days (see above) - 8. At least one measurable site of disease as defined by RECISTv1.1 criteria - 9. Female subjects of childbearing potential (WOCBP) should be using highly effective contraceptive measures and must have a negative urine or serum pregnancy test within 7 days prior to start of study treatment and must not be breast-feeding prior to start of trial - 10. Non-child-bearing potential must be evidenced by fulfilling one of the following criteria at screening: - a) Post-menopausal defined as aged more than 50 years and amenorrheic for at least 12 months following cessation of all exogenous hormonal treatments - b) Women under 50 years old would be considered postmenopausal if they have been amenorrheic for 12 months or more following cessation of exogenous hormonal treatments and with LH and FSH levels in the post-menopausal range for the institution - c) Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation - Treatment Phase: - 1. Provision of informed consent for the screening and treatment phase prior to any study specific procedures, including screening evaluations that are not SoC - 2. Persistent mEGFR ctDNA signal 21 to 28 days after osimertinib initiation for advanced of metastatic ex19del or L858R EGFR mutation positive NSCLC as assessed by a liquid biopsy during the pre-screening phase of the trial in the central laboratory - 3. ECOG performance status 0-2 - 4. The patient is willing and able to comply with the protocol for the duration of the study, including hospital visits for treatment and scheduled follow-up visits and examinations

- 5. Osimertinib no longer than 10 weeks before start of chemotherapy in the treatment phase

Ausschlusskriterien

- Pre-Screening Phase:
- 1. History of another primary malignancy. Exceptions are:
- a) Malignancy treated with curative intent and with no known active disease 6 months before the first dose of IMP, and of low potential risk for recurrence
- b) Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
- c) Adequately treated carcinoma in situ without evidence of disease
- 2. History of leptomeningeal carcinomatosis
- 3. Concurrent enrolment in another clinical study, unless it is an observational (non-interventional) clinical study, or during the follow-up period of an interventional study
- 4. Previous enrolment in the present study
- Treatment Phase:
- 1. Symptomatic CNS metastases. [Patients with asymptomatic brain metastases may be included.]
- 2. Currently receiving (or unable to stop use prior to receiving the first dose of study treatment) medications or herbal supplements known to be strong inducers of CYP3A4 (at least 3 weeks prior)). All patients must try to avoid concomitant use of any medications, herbal supplements and/or ingestion of foods with known inducer effects on CYP3A4
- 3. Osimertinib had to be withheld or administered at reduced dosage for toxicity management for more than 7 days or persistent unresolved toxicities which preclude study treatment
- 4. Any unresolved toxicities other than osimertinib from prior therapy greater than CTCAE grade 1 at the time of starting study treatment, with the exception of alopecia and grade 2 prior platinum-therapy–related neuropathy
- 5. History of hypersensitivity to active or inactive excipients of osimertinib or drugs with a similar chemical structure or class to osimertinib. History of hypersensitivity to any of the chemotherapy drugs used
- 6. Any evidence of severe or uncontrolled systemic diseases, including uncontrolled hypertension and active bleeding diatheses, which in the investigator’s opinion makes it undesirable for the patient to participate in the trial or which would jeopardize compliance with the protocol, or active infection including hepatitis B, hepatitis C and human immunodeficiency virus (HIV). Screening for chronic conditions is not required
- 7. Refractory nausea and vomiting, chronic gastrointestinal diseases, inability to swallow the formulated product or previous significant bowel resection that would preclude adequate absorption of osimertinib
- 8. Any of the following cardiac criteria:
- a. Mean resting corrected QT interval (QTc) > 470 msec obtained from 3 electrocardiograms (ECGs), using the screening clinic ECG machine derived QTc value
- b. Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG e.g. complete left bundle branch block, third degree heart block and second degree heart block

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- c. Patient with any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, electrolyte abnormalities (including: Serum/plasma potassium < LLN; Serum/plasma magnesium < LLN; Serum/plasma calcium < LLN), congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age in first degree relatives or any concomitant medication known to prolong the QT interval and cause Torsades de Pointes. [Note: Electrolyte abnormalities (hypokalaemia, hypomagnesaemia, hypocalcaemia) can be corrected to be within normal ranges prior to first dose. No more than two re-tests may be performed in order to meet this criterion.]
- 9. Past medical history of interstitial lung disease, drug-induced interstitial lung disease, radiation pneumonitis which required steroid treatment, or any evidence of clinically active interstitial lung disease
- 10. Inadequate bone marrow reserve or organ function as demonstrated by any of the following laboratory values:
- a. Absolute neutrophil count below lower limit of normal (<LLN) *
- b. Platelet count below lower limit of normal (<LLN) *
- c. Hemoglobin <90 g/L *
- * The use of granulocyte colony stimulating factor support, platelet transfusion and blood transfusions to meet these criteria is not permitted
- d. Alanine aminotransferase >2.5 times ULN if no demonstrable liver metastases or >5 times ULN in the presence of liver metastases
- e. Aspartate aminotransferase >2.5 times ULN if no demonstrable liver metastases or >5 times ULN in the presence of liver metastases
- f. Total bilirubin >1.5 times ULN if no liver metastases or >3 times ULN in the presence of documented Gilbert's Syndrome [unconjugated hyperbilirubinaemia] or liver metastases
- g. Serum creatinine >1.5 times ULN concurrent with creatinine clearance <60 mL/min [calculated by Cockcroft and Gault equation]—confirmation of creatinine clearance is only required when creatinine is >1.5 times ULN.
- h. INR <= 1.4 or aPTT <= 40 sec during the last 7 days before chemotherapy [Subjects under therapeutic anticoagulation are permitted.]
- 11. Women who are pregnant or breast-feeding

Alter	18 Jahre und älter
Molekularer Marker	EGFR
Prüfzentren	**Innere Medizin 2** (Aktiv) Hämatologie / Medizinische Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Studienkoordination PACE-LUNG goekbuget@em.uni-frankfurt.de
Sponsor	Goethe-Universität Frankfurt
Förderer	Astra Zeneca
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT05281406 EudraCT 2019-004757-88 (primäres Register)
Links	Studiendokumente zum Download (roXtra) Weiterführende Informationen Weiterführende Informationen

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