Öffentlicher Titel
Phase II Studie zu Gefitinib und Chemotherapie als Induktionstherapie bei Patienten mit NSCLC in den Stadien II-IIIb und EGFR-Mutation

Wissenschaftl. Titel
Induction therapy with gefitinib followed by taxane platinum chemotherapy and intercalated gefitinib in NSCLC stages II-IIIB with activating EGFR mutation - A single arm Phase II trial

Kurztitel
NeoIntercal

Studienart
multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig

Studienphase
Phase II

Erkrankung
THORAX: Nicht kleinzelliges Lungenkarzinom: Neoadjuvant

Ziele
- pathologic complete remission rate (pCR rate) [ Time Frame: 12 weeks (after 3 cycles and surgery) after enrollment ] [ Designated as safety issue: No ] The primary objective of the study is to assess the pathologic complete remission rate after induction therapy with gefitinib d-12 to d-1 followed by docetaxel 75 mg/m2 and cisplatin 50 mg/m2 d1+2 q21 and intercalated gefitinib 250 mg d4 to d20 (cycle 1 and 2) and d4-17 (for cycle3), in order to demonstrate feasibility and efficacy of this treatment scheme. It is expected to achieve a pCR 30% regression grade IIB and III (Junker criteria) compared to historical controls in the mediastinal lymph nodes.

- Adverse Events (AEs) / Serious adverse events (SAEs) [ Time Frame: 30 months ] [ Designated as safety issue: Yes ] AEs/SAEs from 21 patients during induction CTx with docetaxel and cisplatin in combination with intercalated gefitinib

- Surgical R0 resection rate [ Time Frame: 30 month ] [ Designated as safety issue: No ] R0 resection rate as assessed according to the German S3 guidelines

- Response: radiologic response based on CT [ Time Frame: 30 month ] [ Designated as safety issue: No ] Response: radiologic response based on CT [ Time Frame: 30 month ] [ Designated as safety issue: No ]

- progression free survival (PFS) [ Time Frame: 30 month ] [ Designated as safety issue: No ] Progression-free survival (PFS) will be defined as the time from enrollment to the time of disease progression or relapse or death, or to the date of last assessment without any such event (censored observation).

- Overall survival (OS) [ Time Frame: 30 month ] [ Designated as safety issue: No ] The duration of overall survival (OS) will be determined by measuring the time interval from enrollment to the date of death or last observation (censored).

- relapse pattern [ Time Frame: 30 month ] [ Designated as safety issue: No ] After the end of treatment will be performed every 3 month (± 14 days) for minimum 12 months in order to collect information on relapse and site of relapse

- quality of life [ Time Frame: 30 month ] [ Designated as safety issue: No ] Explorative analysis of health related quality of life, QoL at various time points throughout the study, to assess the QoL during and after induction therapy with gefitinib, after three cycles of chemotherapy with intercalated gefitinib including pre- and post surgery

- translational research [ Time Frame: 30 month ] [ Designated as safety issue: No ] To collect and store tumor tissue as well as plasma and serum samples for exploratory analyses of potential predictive markers, monitoring of biomarkers during and after treatment

- monitoring of epidermal growth factor receptor (EGFR) mutation status [ Time Frame: 30 month ] [ Designated as safety issue: No ] Analysis of EGFR ctDNA in patient plasma; screening for EGFR mutation status (activating and resistance mutations especially T790M), monitoring of EGFR mutation status by means of Circulating tumor DNA (ctDNA) detection in patient plasma
Einschlusskriterien

- Patients with histologically confirmed non-squamous non-small-cell lung cancer (NSCLC) stage II, IIIA and IIB detected preoperatively by adequate methods and activating EGFR mutation in exons 18-21 and deemed to be able to undergo curative surgery after induction therapy. Stage should be confirmed by PET-CT as well as adequate mediastinal staging. MRI of the brain to exclude CNS metastases is mandatory.
- At least one unidimensionally measurable lesion meeting RECIST criteria (version 1.1);
- Performance status of 0 to 1 on the ECOG scale;
- Estimated life expectancy of at least 12 weeks;
- Patients aged 18 years;
- Adequate organ function including the following: dequate bone marrow reserve: absolute neutrophils (segmented and bands) count (ANC) 1.5x10^9/L; platelets 100x10^9/L; haemoglobin 9 g/dL.
- Adequate organ function including the following: Hepatic: bilirubin 1xULN; alkaline phosphatase (AP); aspartate transaminase (AST) and alanine transaminase (ALT) 2.5xULN.
- Adequate organ function including the following: Renal: serum creatinine < 1.3 mg/dL, glomerular filtration rate 70 mL/min; if GFR is below 70 mL/min, the administration of carboplatin is allowed. If other contraindications against cisplatin exist, carboplatin may also be used;
- Adequate lung function tests as assessed by body plethysmography, diffusion test and if necessary spiro-ergometry.
- Cooperation and willingness to complete all aspects of the study; Written informed consent to participate in the study.

Ausschlusskriterien

- EGFR wild type configuration;
- EGFR resistance mutations (i.e. T790M);
- Significant cardiovascular disease, such as uncontrolled hypertension, myocardial infarction within the last 6 months, unstable angina pectoris, CHF NYHA 2, serious arrhythmia, significant peripheral vascular disease;
- Pre-existing neuropathic grade 2;
- Patients with confirmed HIV infection. HIV testing is not mandatory.
- Prior history of malignancy except for basal cell carcinoma or carcinoma in situ of the cervix, and with the exception of other malignancies after curative treatment with an interval of at least 3 years.
- Lactating or pregnant woman, woman of child-bearing potential who do not agree to the usage of highly effective contraception methods (allowed methods of contraception, meaning methods with a rate of failure of less than 1% per year are implants, injectable contraceptives, combined oral contraceptives, intrauterine devices (only hormonal devices), sexual abstinence or vasectomy of the partner). Woman of childbearing potential must have a negative pregnancy test (serum -HCG) at visit 1.
- Any other chemotherapy at start;
- Treatment with other experimental drugs during the course of the study or within the last 30 days or 7 half-lifes, whatever is of longer duration, prior study start;
- Any psychiatric illness that would affect the patient's ability to understand the demands of the clinical trial;
- Parallel participation in another clinical trial or participation in another clinical trial within the last 30 days or 7 half-lifes, whatever is of longer duration, prior study start;
- Patient has already been included in this trial;
Patients who do not understand the nature, the scope and the consequences of the clinical trial;
- Affected persons who might be dependent on the sponsor or the investigator.

**Alter**
18 Jahre und älter

**Molekularer Marker**
EGFR

**Status**
Geschlossen

**Beginn der Rekrutierung**
01.05.2016

**Fallzahl**
21

**Prüfzentren**
Universitätsklinikum Frankfurt
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