KURZPROTOKOLL
MM-121-01-02-09

Öffentlicher Titel	Phase II Studie zu MM-121 bei Patienten mit Heregulin positivem fortgeschrittenem oder metastasiertem NSCLC
Wissenschaftl. Titel	A Phase 2 Study of MM-121 in Combination with Docetaxel or Pemetrexed versus Docetaxel or Pemetrexed Alone in Patients with Heregulin Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer
Kurztitel	MM-121-01-02-09
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig
Studienphase	Phase II
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - Zweitlinie oder höher
Ziele	- To determine whether the combination of MM-121 plus docetaxel or MM-121 plus pemetrexed is more effective than docetaxel or pemetrexed alone based on Overall Survival (OS) in HRG positive patients (defined as HRG ISH score of 1+) - To determine whether the combination of MM-121 plus docetaxel or MM-121 plus pemetrexed is more effective than docetaxel or pemetrexed alone in HRG positive patients (defined as HRG ISH score of 1+) for the following clinical outcome parameters: o Investigator Assessed - Progression-Free Survival (PFS) o Independent Central Review – PFS o Objective Response Rate (ORR) based on RECISTv1.1 o Time to Progression (TTP) - To describe the safety profile of MM-121 in combination with docetaxel or pemetrexed - To assess health-related quality of life (HRQOL) in NSCLC - To characterize the pharmacokinetic (PK) profile of MM-121 when given in combination with docetaxel or pemetrexed and of docetaxel or pemetrexed when given in combination with MM-121. - Exploratory Objective: To evaluate if mechanistically linked exploratory biomarkers from tumor tissue or blood samples correlate with clinical outcomes
Einschlusskriterien	- To be eligible for participation in the study, patients must meet the following criteria. Patients who are assessed to be HRG negative do not complete any screening procedures beyond HRG assessment. - 1) Patients with cytologically or histologically documented NSCLC that is presenting as either: o Stage IV (metastatic disease) or o Stage IIIB disease not amenable to surgery with curative intent or o Recurrent or progressive disease following multimodal therapy (chemotherapy, radiation therapy, surgical resection or definitive chemoradiation therapy for locally advanced or metastatic disease) - 2) Disease progression or evidence of recurrent disease during or after the last systemic therapy as documented by radiographic assessment - 3) Received one prior platinum-based chemotherapy regimen for advanced or metastatic disease - 4) Received nivolumab or other approved anti-PD-1 or anti-PD-L1 therapy where available and clinically indicated - 5) Clinically eligible for intended chemotherapy, docetaxel or pemetrexed, once every three weeks per the investigator’s judgment - 6) Must have: o Available recent tumor specimen, collected following completion of most recent systemic therapy OR o A lesion amenable to either core needle biopsy or fine needle aspiration - 7) A positive in-situ hybridization (ISH) test for heregulin with a score of 1+, as determined by centralized testing - 9) Screening ECG without clinically significant abnormalities

- 10) Women of childbearing potential, as well as fertile men and their partners, must be willing to abstain from sexual intercourse or to use an effective form of contraception (an effective form of contraception is an oral contraceptive or a double barrier method or as defined by country-specific guidelines) during the study and for 90 days following the last dose of study drug(s), or greater, as in accordance with the label requirements or institutional guidelines for docetaxel/pemetrexed
- 11) 18 years of age
- 12) Able to provide informed consent, or have a legal representative able and willing to do so To be eligible for randomization, patients must not meet any of the following criteria: 1) Known Anaplastic Lymphoma Kinase (ALK) gene rearrangement 2) For adenocarcinoma patients only: Presence of exon 19 deletion or exon 21 (L858R) substitution of the EGFR gene 3) Pregnant or lactating 4) Prior radiation therapy to >25% of bone marrow-bearing areas 5) Received >3 prior systemic anti-cancer drug regimens for locally advanced and/or metastatic disease o Any type of maintenance therapy, e.g. pemetrexed maintenance following first line treatment with cisplatin and pemetrexed, is not considered a separate line of therapy

Ausschlusskriterien

- 1) Prior treatment with an anti-ErbB3 antibody
- 2) Patients who have received prior docetaxel for advanced/ metastatic disease are not eligible for the docetaxel-containing chemotherapy backbone
- 3) Patients who have received prior pemetrexed for advanced/metastatic disease and/or maintenance therapy are not eligible for the pemetrexed-containing chemotherapy backbone
- 4) Received other recent antitumor therapy including: o Investigational therapy administered within the 28 days or 5 half-lives, whichever is shorter, prior to the first scheduled day of dosing in this study o Radiation or other standard systemic therapy within 14 days prior to the first scheduled dose in this study, including, in addition (if necessary), the timeframe for resolution of any actual or anticipated toxicities from such radiation
- 5) CTCAE grade 3 or higher peripheral neuropathy for patients considered for the docetaxel backbone
- 6) Presence of an unexplained fever > 38.5°C during screening visits that does not resolve prior to the first day of dosing. If the fever and active infection have resolved prior to randomization, the patient will be eligible. At the discretion of the investigator, patients with tumor fever may be enrolled.
- 7) Clinically active CNS metastasis
- 8) Use of strong CYP3A4 inhibitors for patients considered for the docetaxel backbone
- 9) Any other active malignancy requiring systemic therapy
- 10) Known hypersensitivity to any of the components of MM-121 or previous CTCAE grade 3 or higher hypersensitivity reactions to fully human monoclonal antibodies
- 11) History of severe hypersensitivity reactions to docetaxel or pemetrexed
- 12) Known hypersensitivity to polysorbate (Tween) 80 or arginine
- 13) Inadequate bone marrow reserve as evidenced by: o ANC < 1,500/l or o Platelet count < 100,000/l or o Hemoglobin < 9 g/dL
- 14) Serum/plasma creatinine > 1.5 x ULN for patients receiving docetaxel or a creatinine clearance < 45 mL/min for patients receiving pemetrexed
- 15) For patients receiving pemetrexed: Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 2.5 x ULN (> 5 x ULN if liver metastases are present)
- 16) For patients receiving docetaxel: o Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) > 1.5 x ULN concomitant with Alkaline phosphatase (AP) > 2.5 x ULN o Serum/plasma total bilirubin > ULN

	- 17) Clinically significant cardiac disease, including: symptomatic congestive heart failure, unstable angina, acute myocardial infarction within 12 months of planned first dose, or unstable cardiac arrhythmia requiring therapy (including torsades de pointes) - 18) Uncontrolled infection requiring IV antibiotics, antivirals, or antifungals; or active human immunodeficiency virus (HIV) infection, active hepatitis B infection or active hepatitis C infection - 19) Patients who are not appropriate candidates for participation in this clinical study for any other reason as deemed by the investigator
Alter	18 Jahre und älter
Molekularer Marker	ALK wt ERBB3 EGFR wt
Fallzahl	560
Sponsor	Merrimack Pharmaceuticals
Förderer	Merrimack Pharmaceuticals
Registrierung in anderen Studienregistern	EudraCT 2014-003673-42 ClinicalTrials.gov NCT02387216