KURZPROTOKOLL
MK-7902-006-03

Öffentlicher Titel	Phase III Studie zu Lenvatinib in der Erstlinientherapie des metastasierten nicht-kleinzelligen Lungenkrebs
Wissenschaftl. Titel	A Phase3 Randomized, Placebo-controlled Study to Evaluate the Safety and Efficacy of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) with or without Lenvatinib (E7080/MK-7902) as First-line Intervention in Participants with Metastatic Nonsquamous Non-small Cell Lung Cancer (LEAP-006)
Kurztitel	MK-7902-006-03
Studienart	multizentrisch, prospektiv, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase III
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - Erstlinie
Einschlusskriterien	- Histologically or cytologically confirmed diagnosis of Stage IV (American Joint Committee on Cancer [AJCC], nonsquamous NSCLC - Confirmation that Epidermal Growth Factor Receptor (EGFR), ALK Receptor Tyrosine Kinase (ALK), or ROS1 Receptor Tyrosine Kinase (ROS1)-directed therapy is not indicated as primary treatment (documentation of absence of tumor-activating EGFR mutations AND absence of ALK and ROS1 gene rearrangements OR presence of a Kirsten Rat Sarcoma (KRAS) gene mutation) - Have measurable disease based on RECIST 1.1. Note: Lesions that appear measurable, but are situated in a previously irradiated area, can be considered measurable (eligible for selection as target lesions) if they have shown documented growth since the completion of radiation - Provided an archival tumor tissue sample or newly obtained core or excisional biopsy of a tumor lesion (not previously irradiated) - Life expectancy of at least 3 months - Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 within 7 days prior to the first dose of study intervention but before randomization - Male participants must agree for at least 30 days after the last dose of lenvatinib/matching placebo and up to 180 days after the last dose of chemotherapeutic agents to: Refrain from donating sperm PLUS either Be abstinence from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis) and agree to remain abstinent OR Must agree to use contraception unless confirmed to be azoopsermic (vasectomized or secondary to medical cause) as detailed below Agree to use a male condom plus partner use of an additional contraceptive method when having penile-vaginal intercourse with a woman of childbearing potential (WOCBP) who is not currently pregnant Note: Men with a pregnant or breastfeeding partner must agree to remain abstinent from penile-vaginal intercourse or use a male condom during each episode of penile-vaginal penetration Note: 30 days after lenvatinib/matching placebo is stopped, if the participant is on pembrolizumab only and is greater than 180 days post chemotherapy, no male contraception measures are needed - Female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies Is not a WOCBP OR Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), with low user dependency, or be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis), during the intervention period and for at least 120 days post pembrolizumab and/or 30 days post-lenvatinib/matching placebo, and up to 180 days post last dose of chemotherapeutic agents, whichever occurs last - Adequate organ function

- Adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as BP <= 150/90 mm Hg and no change in antihypertensive medications within 1 week prior to randomization. Note: Participants must not have a history of uncontrolled or poorly-controlled hypertension, defined as >150/90 mm Hg for >4 weeks despite standard medical management.

Ausschlusskriterien

- Known untreated central nervous system (CNS) metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable, clinically stable, and have not required steroids for at least 14 days prior to the first dose of study intervention
- History of (noninfectious) pneumonitis that required systemic steroids or current pneumonitis/interstitial lung disease
- Radiographic evidence of intratumoral caviations, encasement, or invasion of a major blood vessel. Additionally, the degree of proximity to major blood vessels should be considered because for exclusion because of the potential risk of severe hemorrhage associated with tumor shrinkage/necrosis after lenvatinib-therapy. (In the chest, major blood vessels include the main pulmonary artery, the left and right pulmonary arteries, the 4 major pulmonary veins, the superior or inferior vena cava, and the aorta)
- Known history of an additional malignancy, except if the participant has undergone potentially curative therapy with no evidence of that disease recurrence for at least 3 years since initiation of that therapy. Note: The time requirement also does not apply to participants who underwent successful definitive resection of basal cell carcinoma of the skin, superficial bladder cancer, squamous cell carcinoma of the skin, in situ cervical cancer, or other in situ cancers
- Active autoimmune disease that has required systemic treatment in the past 2 years (i.e., with use of disease-modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is allowed
- Diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (doses exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study intervention
- Has had allogeneic tissue/solid organ transplant
- Known history of human immunodeficiency virus (HIV) infection HIV testing is not required unless mandated by the local health authority
- Known history of Hepatitis B. No testing for Hepatitis B or Hepatitis C is required unless mandated by the local health authority
- History of a gastrointestinal condition or procedure that in the opinion of the investigator may affect oral drug absorption
- Active hemoptysis (at least 0.5 teaspoon of bright red blood) within 2 weeks prior to the first dose of study intervention
- Significant cardiovascular impairment within 12 months prior to the first dose of study intervention, including history of congestive heart failure greater than New York Heart Association (NYHA) Class II, unstable angina, myocardial infarction, cerebrovascular accident (CVA)/stroke, or cardiac arrhythmia associated with hemodynamic instability
- Known history of active tuberculosis
- Active infection requiring systemic therapy
- Has not recovered adequately from any toxicity and/or complication from major surgery prior to the first dose of study intervention
- Previously had a severe hypersensitivity reaction to treatment with a monoclonal antibody or has a known sensitivity to any component of lenvatinib or pembrolizumab, or as applicable, carboplatin, cisplatin, or pemetrexed

- A WOCBP who has a positive urine pregnancy test within 24 hours prior to randomization or treatment allocation. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required
- Has preexisting >= Grade 3 gastrointestinal or non-gastrointestinal fistula
- Received prior systemic chemotherapy or other targeted or biological antineoplastic therapy for their metastatic NSCLC. Note: Prior treatment with chemotherapy and/or radiation as part of neoadjuvant/adjuvant therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of metastatic NSCLC
- Received prior treatment with pembrolizumab or any other anti-programmed cell death (PD)-1, anti-PD-L1, anti-PD-L2 agent, with lenvatinib or any other receptor tyrosine kinase inhibitor (RTKi), or with an agent directed to another stimulatory or co-inhibitory T cell receptor
- Received radiotherapy within 14 days prior to the first dose of study intervention or received lung radiation therapy of >30 Gy within 6 months prior to the first dose of study intervention. Note: Participants must have recovered from all radiation-related toxicities to Grade <=1, not required corticosteroids, and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (<=2 weeks of radiotherapy) to non-CNS disease
- Received systemic steroid therapy (in doses exceeding 10 mg daily of prednisone equivalent) within 7 days prior to the first dose of study intervention
- Received a live vaccine within 30 days prior to the first dose of study intervention
- Currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks prior to the first dose of study intervention
- History or presence of an abnormal electrocardiogram (ECG) that, in the investigator's opinion, is clinically meaningful
- Left ventricular ejection fraction (LVEF) below the institutional (or local laboratory) normal range as determined by multigated acquisition scan (MUGA) or echocardiogram (ECHO)

Alter	18 - 99 Jahre
Prüfzentren	**Krankenhaus Nordwest GmbH** (Rekrutierung beendet) Klinik für Onkologie und Hämatologie Steinbacher Hohl 2-26 60488 Frankfurt am Main Dr. med. Akin Atmaca atmaca.akin@khnw.de
Sponsor	MSD Sharp & Dohme
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03829319 EudraCT 2018-003824-35