KURZPROTOKOLL
MK-7902-011

Öffentlicher Titel	Phase III Studie zu Pembrolizumab als Erstlinientherapie beim Blasenkarzinom
Wissenschaftl. Titel	A Phase 3, Randomized, Double-blind Study to Compare the Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with Lenvatinib (E7080/MK-7902) Versus Pembrolizumab and Placebo as First Line Treatment for Locally Advanced or Metastatic Urothelial Carcinoma in Cisplatin-ineligible Participants Whose Tumors Express PD-L1, and in Participants Ineligible for Any Platinum-containing Chemotherapy Regardless of PD-L1 Expression (LEAP-011)
Kurztitel	MK-7902-011
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase III
Erkrankung	Niere/Harnwege: Harnblasenkrebs: Erstlinie
Einschlusskriterien	- Has a histologically or cytologically confirmed diagnosis of advanced/unresectable (inoperable) or metastatic urothelial carcinoma (UC) of the renal pelvis, ureter (upper urinary tract), bladder, or urethra - Has >=1 measurable target lesion per RECIST 1.1 as assessed by the local site investigator/radiologist - Has provided an archival tumor tissue sample or newly obtained core or excisional biopsy of a tumor lesion not previously irradiated and adequate for Programmed Death-Ligand 1 (PD-L1) evaluation - Has received no prior systemic chemotherapy for advanced or metastatic UC with the following exceptions: Neoadjuvant (prior to surgery) platinum-based chemotherapy for treatment of muscle-invasive bladder cancer with recurrence >12 months from completion of the therapy is permitted. Adjuvant (following surgery) platinum-based chemotherapy following radical cystectomy, with recurrence >12 months from completion of the therapy, is permitted - Meets criteria for either option a or option b (below): a. Has a tumor(s) with PD-L1 combined positive score (CPS) >=10 and is considered ineligible to receive cisplatin-based combination therapy, based on 1 of the following: Eastern Cooperative Oncology Group (ECOG) performance status (PS) score of 2 within 7 days prior to randomization National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 Grade >=2 audiometric hearing loss NCI CTCAE Version 4.0 Grade >=2 peripheral neuropathy OR b. In the opinion of the investigator, is considered ineligible to receive any platinum-based chemotherapy (i.e., ineligible for cisplatin and carboplatin) based on: ECOG PS of 2 within 7 days prior to randomization. and >=1 of the following: Documented visceral metastatic disease NCI CTCAE Version 4.0 Grade >=2 audiometric hearing loss NCI CTCAE Version 4.0 Grade >=2 peripheral neuropathy Other reason for the participant's being unable to receive both cisplatin and carboplatin safely. Additional criteria for platinum ineligibility will be considered and allowed on a case-by-case basis, following consultation with the Sponsor. Note: Participants considered ineligible for any platinum-based chemotherapy are eligible for this study regardless of their tumor PD-L1 status - Has ECOG PS 0, 1, or 2 within 7 days prior to randomization and a life expectancy of >=3 months

- Male participants are eligible to participate if they agree to the following during the treatment period and for >=30 days after the last dose of pembrolizumab or lenvatinib/placebo: Be abstinent from heterosexual intercourse as their preferred and usual lifestyle and agree to remain abstinent, OR Must agree to use contraception unless confirmed to be azoospermic (vasectomized or secondary to medical cause as detailed below: Agrees 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
- A female participant is eligible to participate if she is not pregnant or breastfeeding and if she is not a WOCBP OR is a WOCBP and is using a contraceptive method that is highly effective (with a failure rate of <1% per year) with low user dependency, or is abstinent from heterosexual intercourse as her preferred and usual lifestyle during the intervention period and for >=120 days post pembrolizumab or >=30 days post lenvatinib/placebo
- Has adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as BP <=150/90 mm Hg at screening and no change in antihypertensive medications within 1 week prior to randomization
- Has adequate organ function

Ausschlusskriterien

- Has disease that is suitable for local therapy administered with curative intent (e.g. chemotherapy and radiation for Stage 3 disease)
- Has tumor with any neuroendocrine or small cell component
- Has a history of a gastrointestinal condition or procedure (e.g. gastric bypass, malabsorption) that, in the opinion of the investigator, may affect oral drug absorption
- Has had major surgery within 3 weeks prior to the first dose of study treatment
- Has a pre-existing Grade >=3 gastrointestinal or non-gastrointestinal fistula
- Has radiographic evidence of major blood vessel invasion/infiltration, or has had clinically significant hemoptysis (>=0.5 teaspoon of bright red blood) or tumor bleeding within 2 weeks prior to the first dose of study treatment
- Has had significant cardiovascular impairment within 12 months of the first dose of study treatment, such as history of New York Heart Association (NYHA) >Class II congestive heart failure, unstable angina, myocardial infarction or cerebrovascular accident (CVA)/stroke, cardiac revascularization procedure, or cardiac arrhythmia associated with hemodynamic instability
- Has known intolerance or severe hypersensitivity (Grade >=3) to pembrolizumab or lenvatinib or any of their excipients
- Has received lenvatinib as monotherapy or in combination with a programmed cell death-1/programmed cell death-ligand 1 (PD-1/PD-L1) inhibitor or has previously been enrolled in a clinical study evaluating lenvatinib for bladder cancer, regardless of the treatment received
- Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 inhibitor, indoleamine-pyrrole 2,3 dioxygenase (IDO1) inhibitor, or agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g. cytotoxic T-lymphocyte-associated antigen 4 [CTLA-4], OX 40, CD137), or any other antibody or drug targeting T-cell costimulatory pathways in the adjuvant or advanced/metastatic setting
- Has received prior radiotherapy to a metastatic site without the use of chemotherapy radiosensitization within 3 weeks of the first dose of study treatment, with the exception of palliative radiotherapy to bone lesions, which is allowed if completed 2 weeks before the start of study treatment. Participants must have recovered from all radiation-related toxicities, and must not require corticosteroids
- Has received a live vaccine within 30 days prior to the first dose of study treatment

- In the investigator's judgment, has not recovered from toxicity or other complications from any major surgery prior to starting study treatment
- Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment. Note: Participants who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks after the last dose of the previous investigational agent
- Has history or presence of an abnormal electrocardiogram (ECG) that, in the investigator's opinion, is clinically meaningful
- Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy (at a dose exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior to randomization
- Has had an active malignancy (except locally advanced or metastatic UC) within the past 36 months. Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinoma in situ (e.g. breast carcinoma, cervical cancer in situ) who have undergone potentially curative therapy are not excluded
- Has a history of prostate cancer (T2NXMX or lower with Gleason score <=7) treated with definitive intent (surgically or with radiation therapy) >=1 year prior to study entry is acceptable, provided that the participant is considered prostate cancer-free
- Has central nervous system (CNS) metastases, unless the participant has completed local therapy (e.g. whole brain radiation therapy, surgery, or radiosurgery) and has discontinued use of corticosteroids for this indication for >=4 weeks before starting study treatment. Any signs (e.g. radiologic) or symptoms of CNS metastases must be stable for >=4 weeks before starting study treatment
- Has an active autoimmune disease that has required systemic treatment in the past 2 years (i.e, with disease-modifying agents, corticosteroids, or immunosuppressive drugs)
- Has a history of (non-infectious) pneumonitis that required systemic steroids, or current pneumonitis
- Has an active infection requiring systemic therapy
- Has a known history of human immunodeficiency virus (HIV) infection
- Has a known history of or is positive for active hepatitis B virus (HBV) or has active hepatitis C virus (HCV)
- Has active tuberculosis (TB)
- Is receiving hemodialysis
- Is pregnant or breastfeeding or expecting to conceive or father children within the projected duration of the study, starting with the screening visit through 120 days after the last dose of pembrolizumab and lenvatinib/placebo
- Has had an allogeneic tissue/solid organ transplant

Alter	18 Jahre und älter
Sponsor	MSD Sharp & Dohme
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03898180 (primäres Register) EudraCT 2018-003752-21