KURZPROTOKOLL
MK-3475-564

Öffentlicher Titel	Phase III Studie zu Pembrolizumab als adjuvante Therapie bei Nierenzellkarzinom
Wissenschaftl. Titel	A Phase III, Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Pembrolizumab (MK-3475) as Monotherapy in the Adjuvant Treatment of Renal Cell Carcinoma Post Nephrectomy (KEYNOTE-564)
Kurztitel	MK-3475-564
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase III
Erkrankung	Niere/Harnwege: Nierenzellkrebs: adjuvant
Einschlusskriterien	- Must have histologically confirmed diagnosis of RCC with clear cell component with or without sarcomatoid features. Diagnosis of RCC with clear cell component is to be made by the investigator and does not require central histology review. - Be >= 18 years of age on day of signing informed consent. - Female participants of childbearing potential must have a negative urine or serum pregnancy test within 72 hours prior to randomization. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. - Female participants of childbearing potential must be willing to use an adequate method of contraception as outlined in the protocol, for the course of the trial through 120 days after the last dose of trial drug must be collected within 10 days prior to randomization. - Male participants of childbearing potential must be willing to use an adequate method of contraception as outlined in the protocol, for the course of the trial through 120 days after the last dose of trial drug. - The participant provides written informed consent/assent for the trial. The participant may also provide consent/assent for Future Biomedical Research; however the participant may participate in the main trial without participating in Future Biomedical Research. - Have intermediate-high risk, high risk, or M1 NED RCC as defined by the following pathological tumor-node-metastasis and Fuhrman grading status: - a)Intermediate-high risk RCC: -pT2, Gr. 4 or sarcomatoid, N0, M0; -pT3, Any Gr., N0, M0 - b)High risk RCC: - pT4, Any Gr. N0, M0; -pT Any stage, Any Gr., N+, M0 - c)M1 NED RCC -participants who present not only with the primary kidney tumor but also solid, isolated, soft tissue metastases that can be completely resected at one of the following: - -> the time of nephrectomy (synchronous) or, - -> <=1 year from nephrectomy (metachronous) - Have received no prior systemic therapy for advanced RCC - Have undergone a partial nephroprotective or radical complete nephrectomy (and complete resection of solid, isolated, soft tissue metastatic lesion(s) in M1 NED participants) with negative surgical margins. - Must have undergone a nephrectomy and/or metastasectomy >=28 days prior to signing informed consent and <=12 weeks prior to randomization. - Must be tumor-free as assessed by the Investigator and validated by either CT or MRI scan of the brain and CAP and a bone scan <=28 days from randomization. All baseline scans must be sent to the central imaging vendor and receipt must be confirmed prior to randomization . - Must have provided adequate tissue per the following: - -> Nephrectomy only: tissue from nephrectomy (required).

- -> Synchronous M1 NED: tissue from nephrectomy (required) AND, metastasectomy issue (if available).
- -> Metachronous M1 NED: tissue from metastasectomy (required) AND, nephrectomy tissue (if available).
- Have an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1.
- Have adequate organ function as defined in the protocol. Specimens

Ausschlusskriterien

- Has had major surgery, other than nephrectomy and/or resection of pre-existing metastases for M1 NED participants, within 12 weeks prior to randomization.
- Has received prior radiotherapy for RCC.
- Has pre-existing brain or bone metastatic lesions.
- Has residual thrombus post nephrectomy in the vena renalis or vena cava
- Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study treatment.
- Has an active autoimmune disease that has required systemic treatment in past 2 years (ie, with use of disease modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.
- Has a known additional malignancy that is progressing or required active treatment <=3 years ago. Exceptions include early-stage cancers (carcinoma in situ or Stage 1) treated with curative intent, basal cell carcinoma of the skin, squamous cell carcinoma of the skin, in situ cervical cancer, in situ prostate cancer, or in situ breast cancer that has undergone potentially curative therapy.
- Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis.
- Has an active infection requiring systemic therapy
- Has a history of, or is currently on, dialysis
- Has a known history of human immunodeficiency virus infection. No human immunodeficiency virus testing is required unless mandated by local health authority.
- Has a known active hepatitis B (hepatitis B surface antigen reactive) or hepatitis C virus (eg, hepatitis C virus [HCV] RNA [qualitative] is detected)
- Has a known history of active tuberculosis (Bacillus tuberculosis).
- Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the participant's participation for the full duration of the trial, or is not in the best interest of the participant to participate, in the opinion of the treating investigator
- Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial in the opinion of the investigator 16.Has had a prior solid organ transplant.
- Has severe hypersensitivity (>=Grade 3) to pembrolizumab and/or any of its excipients.
- A woman of childbearing potential (WOCBP) who has a positive urine pregnancy test within 72 hours before randomization. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. Participants must be excluded/discontinued from the trial in the event of a positive or borderline positive test result.

- Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with the Screening visit through 120 days after the last dose of study treatment.
- Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PDL2 agent or with an agent directed to another co-inhibitory T-cell receptor (ie, CTLA-4, OX-40, CD137) or has previously participated in a Merck pembrolizumab (MK 3475) clinical trial.
- Has received prior anticancer therapy, monoclonal antibody, chemotherapy, or an investigational agent or device within 4 weeks or 5 half-lives (whichever is longer) before first dose of study treatment or not recovered (ie, must be <=Grade 1 or at baseline) from AEs due to previously administered agents.
- Has received a live vaccine within 30 days prior to the first dose of study treatment. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette -Guérin, and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist) are live attenuated vaccines and are not allowed
- Is currently participating in or has participated in a trial of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment.

Alter	18 Jahre und älter
Sponsor	Merck Serono
Registrierung in anderen Studienregistern	EudraCT 2016-004351-75