KURZPROTOKOLL
PEARLS

Öffentlicher Titel	Phase III Studie zu Pembrolizumab vs Placebo bei NSCLC als adjuvante Therapie
Wissenschaftl. Titel	A randomized, Phase 3 Trial with anti-PD-1 monoclonal antibody pembrolizumab (MK-3475) versus Placebo for patients with early stage NSCLC after resection and completion of Standard adjuvant therapy
Kurztitel	PEARLS
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, doppelblind, zweiarmig
Studienphase	Phase III
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - adjuvant
Ziele	- To prospectively investigate whether adjuvant treatment with pembrolizumab after completion of radical surgery (lobectomy/pneumonectomy) with or without standard adjuvant chemotherapy for stage IB (T 4 cm) -II-IIIA NSCLC patients improves Disease Free Survival (DFS), as assessed locally by the investigator, compared to placebo in the PD-L1 strong positive subgroup and overall population. - To prospectively compare DFS as assessed by the investigator in the PD-L1 positive population - To prospectively determine and compare OS in the PD-L1 strong positive and overall population - To prospectively determine and compare OS in the PD-L1 positive population - To prospectively determine and compare the Lung Cancer Specific Survival (LCSS) in the whole population irrespective of PD-L1 expression status - To prospectively assess the safety of pembrolizumab after radical surgery followed by standard adjuvant chemotherapy
Einschlusskriterien	- Pathological diagnosis of NSCLC confirmed at surgery, any histology is eligible - UICC v7 stage IB (T 4 cm), II-IIIA NSCLC at complete surgical resection with no residual disease (R0) after complete surgical resection (lobectomy/pneumonectomy) - Availability of tumor sample obtained at surgical resection for PD-L1 Immunohistochemistry (IHC) expression assessment - At least 18 years - Written informed consent must be given according to ICH/GCP, and national/local regulations - Adjuvant chemotherapy is not mandatory but considered for patients with stage IB (T 4 cm) and strongly recommended for stage II and IIIA, and will be administered according to national and local guidelines. Patients who received more than 4 cycles of adjuvant therapy are not eligible - ECOG Performance status 0-1 - Adequate organ function performed within 10 days of treatment initiation - Female patients must have a negative urine or serum pregnancy test at screening (within 72 hours of first dose of study medication) irrespectively of their childbearing potential - If of childbearing potential, female patients must be willing to use two adequate barrier methods throughout the study, starting with the screening visit up to 120 days after last dose of chemotherapeutic and investigational agents as specified in the protocol - Male patients with a female partner(s) of child-bearing potential must agree to use two adequate barrier methods throughout the trial starting with the screening visit through 120 days after the last dose of study treatment is received. Males with pregnant partners must agree to use a condom; no additional method of contraception is required for the pregnant partner - Female patients who are breast feeding should discontinue nursing prior to the first dose of study treatment and until 44 months after the last study treatment

	- Absence of severe comorbidities that in the opinion of the Investigator might hamper the participation to the study and/or the treatment administration
Ausschlusskriterien	- Evidence of disease at clinical examination and/or baseline radiological assessment on baseline assessment as documented by contrast enhanced chest/upper abdomen CT scan, brain CT/MRI and clinical examination - Prior or foreseen neoadjuvant or adjuvant radiotherapy and/or neoadjuvant chemotherapy - Prior treatment with an anti-PD-1, anti-PD-L1/2, anti- CD137, CTLA-4 modulators; patients receiving live vaccine within 30 days prior to the first dose of study treatment are not eligible - Current participation or treatment with an investigational agent or use of an investigational device within 4 weeks of the first dose of study treatment - Known history or current evidence of active TB (Bacillus Tuberculosis), Hepatitis B (e.g., HBsAg reactive) or C (e.g., HCV RNA[qualitative] is detected) or Human Immunodeficiency Virus (HIV) (HIV-1/2 antibodies) - Chronic use of immunosuppressive agents and/or systemic corticosteroids or any use in the last 3 days prior to the first dose of trial treatment - History of interstitial lung disease (ILD) OR pneumonitis (other than COPD exacerbation) that has required oral or IV steroids - Active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (i.e., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment and is allowed - History of a hematologic or primary solid tumor malignancy, unless in remission for at least 5 years. A pT1-2 prostatic cancer Gleason score < 6, superficial bladder cancer, non melanomatous skin cancer or carcinoma in situ of the cervix is eligible - Previous allogeneic tissue/solid organ transplant - Active infection requiring therapy - Surgery or chemotherapy related toxicity (toxicity resolved to grade 1 (see Appendix D), with the exception of alopecia, fatigue, neuropathy and lack of appetite /nausea) - if the patient is or has an immediate family member (e.g., spouse, parent/legal guardian, sibling or child) who is investigational site or sponsor staff directly involved with this trial, unless prospective IRB approval (by chair or designee) is given allowing exception to this criterion for a specific subject
Alter	18 Jahre und älter
Prüfzentren	**Universitätsklinikum Frankfurt** (Rekrutierung beendet) Medizinische Klinik I, Pneumologie/Allergologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Jenny Winkler Tel: 069 6307 84301 pneumo.studien@kgu.de
Sponsor	Merck KGaA
Förderer	Merck KGaA
Registrierung in anderen Studienregistern	EudraCT 2015-000575-27 ClinicalTrials.gov NCT02504372