KURZPROTOKOLL
GO41892

Öffentlicher Titel	Phase III Studie zu Atezolizumab und Cabozantinib als Zweitlinientherapie beim metastasierten nicht-kleinzelligen Lungekrebs
Wissenschaftl. Titel	A Phase III, Multicenter, Randomized, Open-Label, Controlled Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Atezolizumab Given in Combination With Cabozantinib Versus Docetaxel Monotherapy in Patients With Metastatic Non-Small Lung Cancer Previously Treated With an Anti-PD-L1/PD-1 Antibody and Platinum-Containing Chemotherapy
Kurztitel	GO41892
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, zweiarmig
Studienphase	Phase III
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - Zweitlinie oder höher
Einschlusskriterien	- Histologically or cytologically confirmed metastatic NSCLC - Documented radiographic disease progression during or following treatment with platinum-containing chemotherapy and anti-PD-L1/PD-1 antibody, administered concurrently or sequentially for metastatic NSCLC - Measurable disease per RECIST v1.1 outside CNS as assessed by investigator - Known PD-L1 status or availability of tumor tissue for central PD-L1 testing - ECOG Performance Status score of 0 or 1 - Recovery to baseline or Grade <=1 NCI CTCAE v5.0 from toxicities related to any prior treatments, unless adverse events are clinically nonsignificant and/or stable on supportive therapy in the opinion of the investigator - Adequate hematologic and end-organ function - Negative HIV test at screening - Negative hepatitis B surface antigen (HBsAg) test at screening - Negative total hepatitis B core antibody (HBcAb) test at screening, or positive total HBcAb test followed by a negative hepatitis B virus (HBV) DNA test at screening - Negative hepatitis C virus (HCV) antibody test at screening, or positive HCV antibody test followed by a negative HCV RNA test at screening - For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agreement to refrain from donating eggs - For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods, and agreement to refrain from donating sperm
Ausschlusskriterien	- Prior therapy with the following agents for NSCLC: Cabozantinib, Docetaxel, Combination of an anti-PD-L1/PD-1 antibody concurrently with a vascular endothelial growth factor (VEGF)R targeting tyrosine kinase inhibitor (TKI) - Treatment with investigational therapy within 28 days prior to initiation of study treatment - Documentation of known sensitizing mutation in the EGFR gene or ALK fusion oncogene - Symptomatic, untreated, or actively progressing CNS metastases - History of leptomeningeal disease - Uncontrolled tumor-related pain - Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (more frequently than once monthly) - Severe hepatic impairment

- Uncontrolled or symptomatic hypercalcemia
- Any other active malignancy at the time of initiation of study treatment or diagnosis of another malignancy within 3 years prior to initiation of study treatment that requires active treatment, except for locally curable cancers that have been apparently cured, such as basal or squamous cell skin cancer, incidental prostate cancer, or carcinoma in situ of the prostate, cervix, or breast
- Significant cardiovascular disease within 3 months prior to initiation of study treatment, unstable arrhythmia, or unstable angina
- Stroke, transient ischemic attack, myocardial infarction or other symptomatic ischemic events within 6 months of initiation of study treatment
- Active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment, including, but not limited to, hospitalization for complications of infection, bacteremia, or severe pneumonia
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- Current treatment with anti-viral therapy for HBV
- Major surgical procedure, other than for diagnosis within 4 weeks prior to initiation of study treatment, or anticipation of need for a major surgical procedure during the study
- Pregnant or lactating females, or intention of becoming pregnant during the treatment with atezolizumab in combination with cabozantinib in the experimental arm or during the treatment with docetaxel in the control arm, or within 5 months after the final dose of atezolizumab and/or 4 months after the final dose of cabozantinib, whichever is later
- Ongoing Grade >= 2 sensory or motor neuropathy
- Active or history of autoimmune disease or immune deficiency, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren syndrome, Guillain-Barré syndrome, or multiple sclerosis with the following exceptions: Patients with a history of autoimmune-mediated hypothyroidism who are on thyroid replacement hormone are eligible for the study. Patients with controlled Type 1 diabetes mellitus are eligible for the study. Patients with eczema, psoriasis, lichen simplex chronicus, or vitiligo with dermatologic manifestations only are eligible for the study provided all of following conditions are met: Rash must cover < 10% of body surface area
- Pharmacologically uncompensated, symptomatic hypothyroidism
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- Prior allogeneic stem cell of solid organ transplantation
- Administration of a live, attenuated vaccine within 4 weeks prior to initiation of study treatment or anticipation of need for such a vaccine during atezolizumab treatment or within 5 months after the final dose of atezolizumab
- Treatment with systemic immunostimulatory agents (including, but not limited to, interferon and interleukin 2) within 4 weeks or 5 drug-elimination half-lives (whichever is longer) prior to initiation of study treatment

- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during study treatment, with the following exceptions: Patients who received acute, low-dose systemic immunosuppressant medication or a one-time pulse dose of systemic immunosuppressant medication are eligible for the study after Medical Monitor confirmation has been obtained. Patients who received mineralocorticoids, corticosteroids for COPD or asthma, or low-dose corticosteroids for orthostatic hypotension or adrenal insufficiency are eligible for the study
- History of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to Chinese hamster ovary cell products or to any component of the atezolizumab formulation
- Known allergy or hypersensitivity to any component of the cabozantinib formulation
- History of severe hypersensitivity to docetaxel or to other drugs formulated with polysorbate 80
- Concomitant anticoagulation with oral anticoagulants or platelet inhibitors
- History of risk factors for torsades de pointes
- Corrected QT interval corrected through use of Fridericia's formula (QTcF) > 480 ms per ECG within 14 days before initiation of study treatment
- Uncontrolled hypertension defined as systolic blood pressure > 150 mm Hg or diastolic BP > 90 mm Hg despite optimal antihypertensive treatment
- Tumors invading the GI-tract, active peptic ulcer disease, acute pancreatitis, acute obstruction of the pancreatic or biliary duct, appendicitis, cholangitis, cholecystitis, diverticulitis, gastric outlet obstruction, or inflammatory bowel disease
- Abdominal fistula, bowel obstruction, GI perforation, or intra-abdominal abscess within 6 months before initiation of study treatment
- Known cavitating pulmonary lesion(s) or known endobronchial disease manifestation
- Lesions invading major pulmonary blood vessels
- Clinically significant hematuria, hematemesis, hemoptysis of > 0.5 teaspoon (2.5 mL) of red blood, coagulopathy, or other history of significant bleeding within 3 months before initiation of study treatment
- Serious non-healing wound/ulcer/bone fracture
- Malabsorption syndrome
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption are also excluded
- Requirement for hemodialysis or peritoneal dialysis
- Inability to swallow tablets

Alter	18 Jahre und älter
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Sponsor	Hoffmann-La Roche
Registrierung in anderen Studienregistern	EudraCT 2020-000100-11 ClinicalTrials.gov NCT04471428 (primäres Register)