KURZPROTOKOLL
GO29527

Öffentlicher Titel	Phase III Studie zu Atezolizumab bei nicht-kleinzelligem Lungenkarzinom nach OP
Wissenschaftl. Titel	A Phase III, Open-Label, Randomized Study to Investigate the Efficacy and Safety of Atezolizumab (Anti-PD-L1 Antibody) Compared With Best Supportive Care Following Adjuvant Cisplatin-Based Chemotherapy in Patients With Completely Resected Stage IB -IIIA Non-Small Cell Lung Cancer
Kurztitel	GO29527
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, zweiarmig
Studienphase	Phase III
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - adjuvant
Einschlusskriterien	- Tumor PD-L1 expression of TC3 or IC3, as determined by an IHC assay performed by a central laboratory on a resected tumor tissue previously obtained at screening. A representative formalin-fixed paraffin-embedded (FFPE) tumor specimen in paraffin block (preferred) or a minimum of 15 unstained, freshly cut, serial sections from an FFPE resected tumor specimen is required for participation in this study. This specimen must be accompanied by the associated pathology report - Signed Informed Consent Form - Age >= 18 years - Ability to comply with protocol - ECOG performance status of 0 or 1 - Histological or cytological diagnosis of Stage IB (tumors >= 4 cm)IIIA (T23 N0, T13 N1, T1-3 N2) NSCLC (per the UICC/AJCC staging system, 7th edition) - Patients must have had complete resection of NSCLC 412 weeks (>= 28 days and <= 84 days) prior to enrollment and must be adequately recovered from surgery. Accepted types of resection include any of the following: lobectomy, sleeve lobectomy, bilobectomy, or pneumonectomy. Resection by segmentectomy or wedge resection is not allowed - If mediastinoscopy was not performed preoperatively, it is expected that, at a minimum, mediastinal lymph node systematic sampling will have occurred, though complete mediastinal lymph node dissection (MLND) is preferred. Systematic sampling is defined as removal of at least one representative lymph node at specified levels. MLND entails resection of all lymph nodes at those same levels. For a right thoracotomy, sampling or MLND is required at levels 4 and 7 and for a left thoracotomy, levels 5 and/or 6 and 7. If there is clear documentation in the operative report or in a separately submitted addendum by the surgeon of exploration of the required lymph node areas, the patient will be considered eligible if no lymph nodes are found in those areas. If patients have documented N2 disease in one level (per the UICC/AJCC staging system, 7th edition), not all levels need to be sampled - Eligibility to receive a cisplatin-based chemotherapy regimen - Adequate hematologic and end-organ function, defined by the following laboratory results obtained within 14 days prior to enrollment: -ANC >= 1500/L; -Platelet count >= 100,000/L; -Prothrombin time/INR <= 1.5, or, if patient is receiving therapeutic anticoagulation, prothrombin time/INR < 3.0; -aPTT <= institutional upper limit of normal (ULN) OR, if patient is receiving therapeutic; -anticoagulation, aPTT must be < 1.5 ×ULN; -Total bilirubin <= 1.5 mg/dL; -SGOT (AST) <= 2.5 ×ULN; -SGPT (ALT) <= 2.5×ULN; -Calculated creatinine clearance (CRCL) > 60 mL/min, with use of the standard Cockcroft and Gault formula - For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of <1% per year during the treatment period and for at least 90 days after the last dose of study drug

- A woman is considered to be of childbearing potential if she is postmenarcheal, has not reached a postmenopausal state (>= 12 continuous months of amenorrhea with no identified cause other than menopause), and has not undergone surgical sterilization (removal of ovaries and/or uterus)
- Examples of contraceptive methods with a failure rate of < 1% per year include bilateral tubal ligation, male sterilization, established, proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices
- The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods of contraception
- Women who are not postmenopausal (>= 12 months of nontherapy-induced amenorrhea) or surgically sterile must have a negative serum pregnancy test result within 14 days prior to initiation of cisplatin-based chemotherapy
- For enrollment into the China extension cohort, residence in the People’s Republic of China
- Adequate hematologic and end-organ function defined by the following laboratory results obtained within 14 days prior to randomization: -ANC >= 1500/L (without granulocyte colony-stimulating factor support); -Lymphocyte count >= 500/L; -Platelet count >= 100,000/L; -Hemoglobin >= 9.0 g/dL. Patients may be transfused to meet this criterion; -INR and aPTT <= 1.5 × ULN. This applies only to patients who are not receiving therapeutic anticoagulation; patients receiving therapeutic anticoagulation should be on a stable dose; -AST, ALT, and alkaline phosphatase <= 2.5 × the ULN; -Serum bilirubin <= 1.5 × ULN. Patients with known Gilbert disease who have serum bilirubin level <= 3 × ULN may be enrolled; -Calculated CRCL >= 30 mL/min
- Women who are not postmenopausal (>= 12 months of nontherapy-induced amenorrhea) or surgically sterile must have a negative serum pregnancy test result within 14 days prior to initiation of study drug or BSC

Ausschlusskriterien

- Pregnant and lactating women
- Treatment with prior systemic chemotherapy at any time Methotrexate given in low doses for non-malignant conditions with the last dose at least 14 days prior to date of enrollment will be allowed. Other low-dose chemotherapeutics for non-malignant conditions will be considered after discussion with and approval by the Medical Monitor
- Hormonal cancer therapy or radiation therapy as prior cancer treatment within 5 years before enrollment. Prior surgery, biologic therapy, hormonal therapy, or radiation therapy for a malignancy over 5 years prior to enrollment that is now considered cured is acceptable. Current use of hormone-replacement therapy or oral contraceptives is allowed.
- Treatment with any other investigational agent or participation in another clinical study with therapeutic intent within 28 days prior to enrollment
- Patients with hearing impairment
- Known sensitivity to any component of the chemotherapy regimen the patient will be assigned to, or to mannitol
- Prior treatment with an antiPD-1, antiPD-L1, anti-CD137, or anti-cytotoxic T-lymphocyteassociated antigen-4 antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways)

- Malignancies other than NSCLC within 5 years prior to enrollment, with the exception of those with a negligible risk of metastasis or death (e.g., expected 5-year OS > 90%) treated with expected curative outcome (such as adequately treated carcinoma in situ of the cervix, basal or squamous cell skin cancer, localized prostate cancer treated surgically with curative intent, ductal carcinoma in situ treated surgically with curative intent)
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to biopharmaceuticals produced in Chinese hamster ovary cells or any component of the atezolizumab formulation
- History of autoimmune disease, including but not limited to myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis Patients with a history of autoimmune-mediated hypothyroidism on a stable dose of thyroid replacement hormone may be eligible for this study. Patients with controlled Type I diabetes mellitus on a stable dose of insulin regimen are eligible for this study.
- Positive test for HIV
- Patients with active hepatitis B (chronic or acute; defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or hepatitis C Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (defined as the presence of hepatitis B core (HBc) antibody and absence of HBsAg) are eligible. HBV DNA must be obtained in these patients prior to enrollment. Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA.
- Active tuberculosis
- Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or greater), myocardial infarction within the previous 3 months, unstable arrhythmias, or unstable angina. Patients with known coronary artery disease, congestive heart failure not meeting the above criteria, or left ventricular ejection fraction < 50% must be on a stable medical regimen that is optimized in the opinion of the treating physician, in consultation with a cardiologist if appropriate
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted
- Prior allogeneic bone marrow transplantation or solid organ transplant
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the patient at high risk from treatment complications
- Specific Exclusions for Pemetrexed Treatment: -Patients with squamous cell histology; -Patients who are receiving concurrent nonsteroidal anti-inflammatory agents (NSAIDs) and are unable to discontinue treatment
- Signs or symptoms of infection within 14 days prior to randomization (Severe infection within 28 days prior to randomization), including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia
- Received therapeutic oral or IV antibiotics within 14 days prior to randomization. Patients receiving prophylactic antibiotics (e.g., for prevention of a urinary tract infection or to prevent chronic obstructive pulmonary disease exacerbation) are eligible.

	- Major surgical procedure within 28 days prior to randomization or anticipation of need for a major surgical procedure during the course of the study - Administration of a live, attenuated vaccine within 28 days prior to randomization or anticipation that such a live attenuated vaccine will be required during the study Influenza vaccination should be given during influenza season only (example: approximately October to March in the Northern Hemisphere). Patients must not receive live, attenuated influenza vaccine (e.g., FluMist®) within 28 days prior to randomization or at any time during the study - Treatment with systemic immunostimulatory agents (including but not limited to interferons or interleukin-2) within 6 weeks or five half-lives of the drug, whichever is shorter, prior to randomization Treatment with systemic immunosuppressive medications (including but not limited to corticosteroids, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor [anti-TNF] agents) within 14 days prior to randomization Patients who have received acute, low-dose, systemic immunosuppressant medications (e.g., a one-time dose of a systemic corticosteroid for nausea) may be randomized in the study after discussion with and approval by the Medical Monitor. The use of inhaled corticosteroids for chronic obstructive pulmonary disease; mineralocorticoids (e.g., fludrocortisone), for patients with orthostatic hypotension or low dose supplemental corticosteroids for adrenocortical insufficiency is allowed - Uncontrolled or symptomatic hypercalcemia (> 1.5 mmol/L ionized calcium or calcium > 12 mg/dL or corrected serum calcium >ULN) - For patients who are receiving denosumab prior to randomization, unwillingness or ineligibility to receive a bisphosphonate instead while in the study
Alter	18 Jahre und älter
Sponsor	Hoffmann-La Roche
Registrierung in anderen Studienregistern	EudraCT 2014-003205-15 ClinicalTrials.gov NCT02486718