KURZPROTOKOLL
DURATION

Öffentlicher Titel	Durvalumab für frail und ältere Patienten mit nicht-kleinzelligem Lungenkrebs
Wissenschaftl. Titel	Durvalumab (MEDI4736) in frail and elder patients with metastatic NSCLC
Kurztitel	DURATION
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, mehrarmig
Studienphase	Phase II
Erkrankung	Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - Zweitlinie oder höher Lunge: Lungenkrebs: Nicht kleinzelliges Lungenkarzinom (NSCLC) - Erstlinie

Einschlusskriterien

- Written informed consent and any locally-required authorization (EU Data Privacy Directive in the EU) obtained from the subject prior to performing any protocol-related procedures, including screening evaluations
- Age >= 70 years at time of study entry and/or Charlson-Comorbidity-Index (CCI) >1 and/or Performance status ECOG >1
- Histologically confirmed diagnosis of metastatic NSCLC and no targetable molecular alterations (EGFRwt; ALKtransl-) and not amenable to cisplatinum-based standard-combination chemotherapy.
- Patients with measurable disease (at least one uni-dimensionally measurable target lesion not previously irradiated, by CT-scan or MRI) according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1) are eligible.
- A formalin fixed, paraffin-embedded (FFPE) tumor tissue block (archival less than 3 years old or recent) or a minimum of 10 unstained slides of tumor sample (slices must be 2-3 mikrometer in thickness and less than 90 days and collected on Superfrost slides provided by the sponsor) must be available for biomarker (PD-L1) evaluation. Biopsy should be excisional, incisional or core needle 18 gauge or larger. Fine needle aspiration is inappropriate.
- No prior chemotherapy or any other systemic therapy for metastatic NSCLC. Patients who have received prior platinum-containing adjuvant, neoadjuvant, or definitive chemoradiation for locally advanced disease are eligible, provided that progression has occurred >6 months from last therapy.
- Prior radiotherapy and surgery are allowed if completed 4 weeks (for minor surgery and palliative radiotherapy for bone pain: 2 weeks) prior to start of treatment and patient recovered from toxic effects or associated adverse events.
- Adequate blood count, liver-enzymes, and renal function: a) Haemoglobin >= 9.0 g/dL; b) Absolute neutrophil count (ANC) >= 1.5 x 10^9/L (> 1500 per mm3); c) Platelet count >= 100 x 10^9/L (>100,000 per mm^3); d) Serum bilirubin <= 1.5 x ULN. This will not apply to subjects with confirmed Gilbert’s syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of hemolysis or hepatic pathology), who will be allowed only in consultation with their physician; e) AST (SGOT)/ALT (SGPT) <= 2.5 x institutional upper limit of normal unless liver metastases are present, in which case it must be <= 5x ULN; f) Serum creatinine CL>40 mL/min by the Cockcroft-Gault formula (Cockcroft and Gault 1976) or by 24-hour urine collection for determination of creatinine clearance
- Subject is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits, examinations including follow up and appropriate contraception.

Ausschlusskriterien

- Mixed small-cell lung cancer and NSCLC histology
- Mean QT interval corrected for heart rate (QTc) >=470 ms calculated from 3 electrocardiograms (ECGs) using Fredericia’s correction

- History of another primary malignancy except local prostate cancer without need for systemic treatment (e.g. active surveillance, operation without need for adjuvant treatment) and malignancies treated with curative intent and with no known active disease >5 years befor the first dose of study drug and of low potential risk for recurrence, e.g. adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease, adequately treated carcinoma in situ without evidence of disease (e.g. cervical cancer in situ)
- Pre-existing peripheral neuropathy of Grade >= 2
- Brain metastasis or spinal cord compression unless asymptomatic or treated and stable off steroids and anti-convulsants for at least 1 month prior to study treatement.
- Active or prior documented autoimmune disease within the past 2 years. NOTE: Subjects with vitiligo, Grave's disease, or psoriasis not requiring systemic treatment (within the past 2 years) are not excluded.
- Active or prior documented inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis)
- History of primary immunodeficiency
- History of allogeneic organ transplant
- History of hypersensitivity to durvalumab or any excipient
- History of hypersensitivity to any of the comparator agents
- Medication that is known to interfere with any of the agents applied in the trial.
- Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, active peptic ulcer disease or gastritis, active bleeding diatheses including any subject known to have evidence of acute or chronic hepatitis B, hepatitis C or human immunodeficiency virus (HIV), or psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent
- Clinical diagnosis of active tuberculosis
- Receipt of live attenuated vaccination within 30 days prior to study entry or within 30 days of receiving durvalumab
- Male patients of reproductive potential who are not employing an effective method of birth control (failure rate of less than 1% per year)
- Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results
- Participation in another clinical study with an investigational product during the last 30 days before inclusion
- Any previous treatment with a PD-1 or PD-L1 inhibitor, including durvalumab
- Current or prior use of immunosuppressive medication within 28 days before the first dose of durvalumab, with the exceptions of intranasal and inhaled corticosteroids or systemic corticosteroids at physiological doses, which are not to exceed 10 mg/day of prednisone, or an equivalent corticosteroid
- Receipt of the last dose of anti-cancer therapy (chemotherapy, immunotherapy, endocrine therapy, targeted therapy, biologic therapy, tumor embolization, monoclonal antibodies, other investigational agent) <= 21 days prior to the first dose of study drug or <=4 half-lifes of the agent administered, which ever comes first.
- Previous enrollment or randomization in the present study.
- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff of sponsor and study site)
- Patient who might be dependent on the sponsor, site or the investigator

	- Patient who has been incarcerated or involuntarily institutionalized by court order or by the authorities § 40 Abs. 1 S. 3 Nr. 4 AMG. - Patients who are unable to consent because they do not understand the nature, significance and implications of the clinical trial and therefore cannot form a rational intention in the light of the facts [§ 40 Abs. 1 S. 3 Nr. 3a AMG].
Alter	>= 70 Jahre
Molekularer Marker	EGFR wt
Sponsor	AIO-Studien GmbH
Förderer	Astra Zeneca
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03345810 (primäres Register) EudraCT 2016-003963-20