Durvalumab (MEDI4736) in Frail and Elder Patients With Metastatic NSCLC (DURATION)

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03345810	RECRUITING	NOVEMBER 17, 2017	JULY 30, 2018

STUDY DESCRIPTION

Brief Summary

AIO-YMO/TRK-0416 (DURATION) is a open-label, treatment stratified and randomized phase II study of Durvalumab, frail or elderly patients with metastatic non-squamous NSCLC with no targetable molecular alterations (EGFRwt; ALKtransl-) and not amenable to cisplatinum-based standard-combination chemotherapy but eligible for at-least mono-chemotherapy with gemcitabine or vinorelbine.

Condition or Disease: Carcinoma, Non-Small-Cell Lung
Metastatic Lung Cancer
Non Small Cell Lung Cancer
Lung Adenocarcinoma Metastatic
Large Cell Lung Carcinoma Metastatic

Intervention/treatment: Drug: Carboplatin
Drug: Durvalumab
Drug: Vinorelbine
Drug: Gemcitabine
Drug: nab-Paclitaxel

Phase: Phase 2

DETAILED DESCRIPTION

The primary objective is to assess the safety and tolerability of sequential therapy consisting of standard of care mono- or combination chemotherapy followed by durvalumab in comparison to standard of care mono- or combination chemotherapy in frail/elderly patients.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 200 participants

Intervention Model : Parallel Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: Durvalumab (MEDI4736) in Frail and Elder Patients With Metastatic NSCLC (DURATION)

Actual Study Start Date: December 2017

Estimated Primary Completion Date: June 2022

Estimated Study Completion Date: December 2022

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Experimental Arm B Frail or elderly patients with metastatic NSCLC; CARG- Score ≤ 3 Induction:Carboplatin (AUC 5.0; D1) + nab-Paclitaxel (100mg/m2) D1,D8; Q3W [2 cyc] followed by durvalumab (1125 mg; Q3W) [2 cyc] Maintenance:durvalumab (1500 mg) Q4W	Drug: Durvalumab Induction: (1125 mg) cycle Q3W Maintenance: (1500 mg) cycle Q4W Drug: nab-Paclitaxel (100 mg/m2 intravenous infusion over 30 minutes on D1, D8) cycle Q3W Drug: Carboplatin (AUC = 5 mg•min/mL on Day 1) cycle Q3W
Experimental: Experimental Arm C Frail or elderly patients with metastatic NSCLC; CARG- Score > 3 Induction: Vinorelbine (30 mg/m2; D1+D8) Q3W [2 cyc] or Gemcitabine (1000 mg/m2; D1+D8) Q3W [2 cyc] followed by durvalumab (1125 mg) Q3W [2 cyc] Maintenance:durvalumab (1500 mg; Q4W)	Drug: Durvalumab Induction: (1125 mg) cycle Q3W Maintenance: (1500 mg) cycle Q4W Drug: Vinorelbine (30 mg/m2 D1 + D8 as infusion) cycle Q3W Drug: Gemcitabine (1000 mg/m2 D1 + D8 as infusion) cycle Q3W
Active Comparator: Control Arm D Frail or elderly patients with metastatic NSCLC; CARG- Score > 3 Vinorelbine (30 mg/m2; D1+D8) Q3W or Gemcitabine (1000 mg/m2; D1+D8) Q3W	Drug: Vinorelbine (30 mg/m2 D1 + D8 as infusion) cycle Q3W Drug: Gemcitabine (1000 mg/m2 D1 + D8 as infusion) cycle Q3W
Active Comparator: Control Arm A Frail or elderly patients with metastatic NSCLC; CARG- Score ≤ 3 Carboplatin (AUC 5.0; D1) + nab-Paclitaxel (100mg/m2 D1,D8) Q3W	Drug: nab-Paclitaxel (100 mg/m2 intravenous infusion over 30 minutes on D1, D8) cycle Q3W Drug: Carboplatin (AUC = 5 mg•min/mL on Day 1) cycle Q3W

OUTCOME MEASURES

Primary Outcome Measures:	1. Rate of treatment related Grade III/IV adverse events (CTCAE V4.03) [Time Frame: through study completion, an average of 24 months] Comparison of the outcome of sequential therapy consisting of standard of care mono- or combination chemotherapy followed by durvalumab versus standard of care mono- or combination chemotherapy in frail/elderly patients
Secondary Outcome Measures:	1. PFS [Time Frame: approx. 24 months] Progression Free Survival 2. ORR using assessment according to RECIST 1.1 [Time Frame: approx. 24 months] Response Evaluation Criteria In Solid Tumors (RECIST) 3. OS [Time Frame: approx. 60 months] Overall Survival 4. Adverse Events /Serious Adverse Events [Time Frame: approx. 48 months] Adverse Events: Type, incidence, and severity according to NCI CTCAE version 4.03 5. Health related Quality of Life (HR-QoL) [Time Frame: approx. 60 months] as determined with FACT-L (Functional Assessment of Cancer Therapy - Lung) 6. Geriatric assessment [Time Frame: approx. 60 months] G8-questionnaire 7. Geriatric assessment [Time Frame: approx. 60 months] Timed up & go (test of basic functional mobility) 8. Geriatric assessment [Time Frame: approx. 60 months] 6MWT (6 minutes walk test)

ELIGIBILITY CRITERIA

Ages Eligible for Study: 70 Years and older (Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
1. 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
2. Age ≥ 70 years at time of study entry and/or Charlson-Comorbidity-Index (CCI) >1 and/or Performance status ECOG >1
3. Histologically confirmed diagnosis of metastatic NSCLC and no targetable molecular alterations (EGFRwt; ALKtransl-) and not amenable to cisplatinum-based standard-combination chemotherapy.
4. 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.
5. A formalin fixed, paraffin-embedded (FFPE) tumor tissue block (fresh or archival less than 3 years old or recent) or a minimum of 10 unstained slides of tumor sample (slices must be less than 90 days old 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. Fine needle aspiration is inappropriate.
6. 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.
7. 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.
8. Adequate blood count, liver-enzymes, and renal function:
- Haemoglobin ≥ 9.0 g/dL
- Absolute neutrophil count (ANC) ≥ 1.5 x 109/L (> 1500 per mm3)
- Platelet count ≥ 100 x 109/L (>100,000 per mm3)
- 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.
- 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
- 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
9. 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
Exclusion Criteria:
1. Mixed small-cell lung cancer and NSCLC histology
2. Mean QT interval corrected for heart rate (QTc) ≥470 ms calculated from 3 electrocardiograms (ECGs) using Fredericia's correction
3. 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 >2 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)
4. Pre-existing peripheral neuropathy of Grade ≥ 2
5. 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.
6. 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.
7. Active or prior documented inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis)
8. History of primary immunodeficiency
9. History of allogeneic organ transplant
10. History of hypersensitivity to durvalumab or any excipient
11. History of hypersensitivity to any of the comparator agents
12. Medication that is known to interfere with any of the agents applied in the trial.
13. 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
14. Clinical diagnosis of active tuberculosis
15. Receipt of live attenuated vaccination within 30 days prior to study entry or within 30 days of receiving durvalumab
16. Male patients of reproductive potential who are not employing an effective method of birth control (failure rate of less than 1% per year)
17. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results
18. Participation in another clinical study with an investigational product during the last 30 days before inclusion
19. Any previous treatment with a PD-1 or PD-L1 inhibitor, including durvalumab
20. 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
21. 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.
22. Previous enrollment or randomization in the present study.
23. Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff of sponsor and study site)
24. Patient who might be dependent on the sponsor, site or the investigator
25. Patient who has been incarcerated or involuntarily institutionalized by court order or by the authorities § 40 Abs. 1 S. 3 Nr. 4 AMG.
26. 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].

CONTACTS AND LOCATIONS

Contacts

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Contact: Jonas Kuon, Dr jonas.kuon@med.uni-heidelberg.de

Locations

Germany	Gesundheitszentrum St. Marien GmbH	Amberg
Germany	DRK-Kliniken Berlin Mitte	Berlin-Mitte

Germany	Ev. Lungenklinik Berlin	Berlin
Germany	Klinikum Darmstadt	Darmstadt
Germany	Universitätsklinikum Carl-Gustav-Carus	Dresden
Germany	Klinikum Esslingen	Esslingen
Germany	Universitätsklinikum Frankfurt	Frankfurt am Main
Germany	Klinik Schillerhöhe	Gerlingen
Germany	Universitätsmedizin Greifswald	Greifswald
Germany	Onkodoc GmbH	Gütersloh
Germany	Krankenhaus Martha-Maria Halle Dölau	Halle (Saale)
Germany	Department of Thoracic Oncology, Thoraxklinik at Heidelberg University Hospital	Heidelberg
Germany	Lungenklinik Hemer	Hemer
Germany	"Vincentius-Diakonissen-Kliniken gAG	Karlsruhe
Germany	Kliniken der Stadt Köln gGmbH	Köln
Germany	Ortenau-Klinikum Lahr	Lahr
Germany	Ev. Diakonissenkrankenhaus Leipzig	Leipzig
Germany	Klinikum Ludwigsburg	Ludwigsburg
Germany	Klinik Löwenstein gGmbH	Löwenstein
Germany	Klinikum der Universität München	München
Germany	Pius Hospital Oldenburg	Oldenburg
Germany	Krankenhaus Barmherzige Brüder	Regensburg
Germany	"Klinikum Rheine	Rheine
Germany	Marienhospital	Stuttgart
Germany	Krankenhaus der Barmherzigen Brüder	Trier
Germany	Universitätsklinikum Ulm	Ulm
Germany	Schwarzwald-Baar Klinikum	Villingen-Schwenningen
Germany	SHG-Kliniken-Völklingen	Völklingen
Germany	Hämatologisch-Onkologische Praxis Würselen	Würselen
Germany	Klinikum Würzburg Mitte gGmbH	Würzburg

Sponsors and Collaborators

AIO-Studien-gGmbH

AstraZeneca

Celgene

Investigator

Principal Investigator :	Jonas Kuon, Dr	Department of Thoracic Oncology, Thoraxklinik at Heidelberg University Hospital, Heidelberg, Germany

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MORE INFORMATION

Responsible Party :	AIO-Studien-gGmbH
ClinicalTrials.gov Identifier :	NCT03345810
Other Study ID Numbers :	AIO-YMO/TRK-0416, 2016-003963-20, ESR-15-11003, AX-CL-NSCLC-AIO-008260
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Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	No

Studies a U.S. FDA-regulated Drug Product:	No
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by AIO-Studien-gGmbH:	*NSCLC Non small cell lung cancer*
Additional relevant MeSH terms :	*Adenocarcinoma of Lung* *Carcinoma* *Lung Neoplasms* *Carcinoma, Non-Small-Cell Lung* *Adenocarcinoma*