AIO-TRK-0320: Thoracic radiotherapy with atezolizumab in small cell lung cancer extensive disease: a randomized, open-label, multicenter phase II study (TREASURE)

AIO-Studie

Studiennummer/-Code:	AIO-TRK-0320 - TREASURE		
Status:	in Rekrutierung		
Rekrutierungszeit:	von: 30.09.2020	bis: Q1.2023	
Anzahl Zentren:	geplant: 18	aktuell initiiert: 18	aktiv rekrutierend: 14
Weitere Zentren:	sind leider nicht möglich		
Anzahl Patienten:	geplant: 104	aktuell eingeschlossen: 53	
Letzte Aktualisierung	22.03.2022		

STUDY TYPE	Investigator-initiated trial (IIT)
PRINCIPAL INVESTIGATOR	Dr. Farastuk Bozorgmehr Prof. Dr. Stefan Rieken Univ.-Prof. Dr. Michael Thomas
TRIAL OFFICE	Department of Thoracic Oncology/ Internal Medicine Thoraxklinik at Heidelberg University Hospital Röntgenstr.1 69126 Heidelberg
SPONSOR	Institut für Klinische Krebsforschung IKF GmbH at Krankenhaus Nordwest Steinbacher Hohl 2-26 60488 Frankfurt am Main
DESIGN	Prospective, randomized, open-label, multicenter, phase II trial.
INDICATION	SCLC extensive disease
OBJECTIVE(S)	Primary objective: The objective of this study is to investigate the treatment efficacy of combining thoracic radiotherapy (TRT) with the IMpower133 regimen in the upfront treatment of ED SCLC patients. Secondary objectives: Additionally, with this study, we aim to determine the safety and tolerability of the combination of immunological and radiological treatment in the first-line setting of advanced SCLC. Furthermore, blood, stool and tissue samples are collected prospectively for the separate translational program.
INTERVENTION(S)	At time of inclusion into the study, all patients must have received four cycles of induction therapy with carboplatin/etoposide and atezolizumab independently of the study as part of standard of care therapy. After 1:1 randomization, eligible patients will receive either atezolizumab (1,200 mg fixed dose, Q3W) and TRT (30 Gy in 10 fractions) in arm A or atezolizumab only (1,200 mg fixed dose, Q3W) in arm B.
OBJECTIVES of OPTIONAL TRANSLATIONAL RESEARCH	An accompanying translational research project will investigate the mechanisms behind potential tumor-specific immune effects that might be induced by the combination of PD-L1 inhibition and radiotherapy and will explore potential biomarkers for such a treatment. To this end, blood and stool samples will be obtained at baseline, on day 1 of the second and the fourth cycle, and at the time of disease progression. Collection of tumor tissue samples will take place at baseline and his highly recommended in case of a re-biopsy after disease progression under study treatment. While the baseline tissue collection is mandatory, collection of all other biomarker samples is optional, i.e. patients can participate in the clinical trials if they do not consent to the collection of biomarker samples.

BACKROUND/RATIONALE	In the past years, immune checkpoint inhibitors have revolutionized the therapeutic landscape for lung cancer. Along this line, the IMpower133 trial showed that the addition of the PD-L1 inhibitor atezolizumab to first-line platinum/ etoposide chemotherapy resulted in improved outcome for patients with advanced small cell lung cancer (SCLC) leading to approval of this regimen. At the same time, accumulating preclinical and clinical data suggest beneficial synergisms of radiotherapy and immunotherapy in cancer patients via the radiation-mediated induction of anti-tumor immunogenicity and establishment of an immunostimulatory environment. Combining the recent findings, the TREASURE clinical trial aims to i.) increase the efficacy of combined atezolizumab- and chemotherapy by adding radiotherapy, ii.) determine the safety and tolerability of the combination of chemotherapeutic, immunological and radiological treatment in the first-line setting of advanced SCLC, and iii.) to collect tumor tissue as well as blood and stool samples for separate biomarker research projects.
KEY EXCLUSION CRITERIA	History of autoimmune disease Prior treatment with immunotherapeutic drugs Prior therapy for limited-stage SCLC with curative intent Prior radiotherapy to lung and mediastinal lymph nodes within the past 5 years before the first dose of study drug History of interstitial lung disease (ILD) (including but not limited to idiopathic pulmonary fibrosis (IPF)/usual interstitial pneumonia (UIP)/cryptogenic fibrosing alveolitis (CFA)), non-infectious pneumonitis, drug-induced pneumonitis, idiopathic pneumonitis. History of active primary immunodeficiency Clinical diagnosis of active tuberculosis Positive testing for hepatitis B virus surface antigen (HBV sAg), hepatitis C virus ribonucleic acid (HCV RNA), or human immunodeficiency virus (HIV) Current use of immunosuppressive medication Any co-existing medical condition that in the investigator's judgement will substantially increase the risk associated with the patient's participation in the study.
KEY INCLUSION CRITERIA	Fully-informed written consent ED SCLC ECOG performance-status score ≤1 Any response after four cycles of induction chemo-immunotherapy defined as CR/PR or thoracic SD with CR/PR of extrathoracic lesions Thoracic treatment volume considered treatable using acceptable radiation fields as judged by a radiation oncologist 28 ± 7 days between last administration of chemo-immunotherapy and randomization. Patients with a history of treated CNS metastases are eligible, if there is no ongoing requirement for corticosteroids as therapy for CNS disease. Patients with asymptomatic brain metastases that do not require local therapy with irradiation (whole brain irradiation) can be included. No previous radiotherapy to lung and mediastinal lymph nodes within the past 5 years before the first dose of study drug Availability of pre-treatment tumor tissue specimen FEV1 ≥ 40% (%Soll) Adequate bone marrow, renal function, and hepatic functions
OUTCOME(S)	Primary endpoint: Overall survival (time to event) Secondary endpoints: 1- and 2-year OS rate PFS according to RECIST 1.1 Response rate according to RECIST 1.1 Intrathoracic tumor control (defined as rate of intrathoracic progression and time to intrathoracic progression) Safety evaluation: Incidence, nature, causal relationship and severity of Adverse Events according to CTC v5.0

	Frequency of abnormal laboratory parameters Feasibility in terms of: Frequency of treatment withdrawal (either due to adverse events or other reasons) Cmpletion of radiotherapy Cancer related quality of life (FACT-L) Collection of biomarker samples for separate biomarker research project
STATISTICAL ANALYSIS	The primary endpoint will be analyzed by performing multivariate cox-regression adjusting for the variable therapy group and the stratification variables. Secondary endpoint analyses will be performed descriptively. Safety analysis will comprise a description of relative and absolute frequencies of treatment-related adverse and serious adverse events. Feasibility will be analyzed by a description of relative and absolute frequencies of treatment withdrawal. Furthermore, a safety interim analysis with the possibility to terminate the trial will be performed in arm A after half of the patients in this arm (n=23) have been followed for three months after the end of TRT.
SAMPLE SIZE	n=92, incl. Drop Out n=104 (52 per arm)
TRIAL DURATION	Duration of recruitment: 24 months starting from FPI Follow-up: 24 months total trial duration: 48 months