KURZPROTOKOLL
CLEAR

Öffentlicher Titel	Phase III Studie zu Lenvatinib und Everolimus/Pembrolizumab vs Sunitinib zur Erstlinientherapie bei Nierenkrebs
Wissenschaftl. Titel	A Multicenter, Randomized, Open-Label, Phase3 Trial to Compare the Efficacy and Safety of Lenvatinib in Combination with Everolimus or Pembrolizumab Versus Sunitinib Alone in First-Line Treatment of Subjects with Advanced Renal Cell Carcinoma
Kurztitel	CLEAR
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, dreiarmig
Studienphase	Phase III
Erkrankung	Niere/Harnwege: Nierenzellkrebs: Erstlinie
Einschlusskriterien	- Histological or cytological confirmation of RCC with a clear-cell component (original tissue diagnosis of RCC is acceptable). - Documented evidence of advanced RCC. - At least 1 measurable target lesion according to RECIST 1.1 meeting the following criteria: - -> Lymph node (LN) lesion that measures at least 1 dimension as >=1.5 cm in the short axis - -> Non-nodal lesion that measures >=1.0 cm in the longest diameter - -> The lesion is suitable for repeat measurement using computerized tomography/magnetic resonance imaging (CT/MRI). Lesions that have had external beam radiotherapy (EBRT) or locoregional therapy must show radiographic evidence of disease progression based on RECIST 1.1 to be deemed a target lesion. - Male or female subjects age >=18 years (or any age greater than 18 years of age if that age is considered to be an adult per the local jurisdiction) at the time of informed consent - Karnofsky Performance Status (KPS) of >=70. - Adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as BP <=150/90 mmHg at Screening and no change in antihypertensive medications within 1 week before the Cycle 1/Day 1. - Adequate renal function as creatinine <=1.5× upper limit of normal (ULN); or for subjects with creatinine >1.5×ULN, the calculated creatinine clearance >=30 mL/min (per the Cockcroft-Gault formula) is acceptable. - Adequate bone marrow function defined by: - -> Absolute neutrophil count (ANC) >=1500/mm³ - -> Platelets >=100,000/mm³ - -> Hemoglobin >=9 g/dL - -> NOTE: Criteria must be met without erythropoietin dependency and without packed red blood cell (pRBC) transfusion within the previous 2 weeks - Adequate blood coagulation function defined by International Normalized ratio (INR) <=1.5 unless participant is receiving anticoagulant therapy, as long as INR is within therapeutic range of intended use of anticoagulants. - Adequate liver function defined by: - -> Total bilirubin <=1.5×ULN except for unconjugated hyperbilirubinemia of Gilbert's syndrome. - -> Alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) <=3×ULN (in the case of liver metastases <=5×ULN), unless there are bone metastases. Subjects with ALP values >3×ULN and known to have bone metastases can be included. - Provide written informed consent

- Willing and able to comply with all aspects of the protocol

Ausschlusskriterien

- Subj. who have received any systemic anticancer therapy for RCC, including anti-VEGF therapy, or any systemic investigational anticancer agent. Prior adjuvant treatment with an investigational anticancer agent is not allowed unless the investigator can provide evidence of subject's randomization to placebo arm.
- Subj. with CNS metastases are not eligible, unless they have completed local therapy (eg, whole brain radiation therapy [WBRT], surgery or radiosurgery) and have discontinued the use of corticosteroids for this indication for at least 4 weeks before starting treatment in this study.
- Active malignancy (ex. for RCC, definitively treated basal or squamous cell carcinoma of the skin, and carcinoma in-situ of the cervix or bladder) within the past 24 months. Subjects with history of localized & low risk prostate cancer are allowed in the study if they were treated with curative intent if no PSA recurrence within the past 5 years.
- Prior radiation therapy within 21 days prior to start of study treatment with the exception of palliative radiotherapy to bone lesions, which is allowed if completed 2 weeks prior to study treatment start.
- Subj. who are using other investigational agents or who had received investigational drugs <=4 weeks prior to study treatment start.
- Received a live vaccine within 30 days of planned start of study treatment (Cycle 1/Day 1). Examples of live vaccines include, measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette–Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist) are live attenuated vaccines and are not allowed.
- Subj. with proteinuria >1+ on urine dipstick testing will undergo 24-h urine collection for quantitative assessment of proteinuria. Subj. with urine protein >=1 g/24 h will be ineligible
- Fasting total cholesterol >300 mg/dL (or >7.75 mmol/L) and/or fasting triglycerides level >2.5 x ULN. NOTE: these subjects can be included after initiation or adjustment of lipid-lowering medication.
- Uncontrolled diabetes as defined by fasting glucose >1.5 times the ULN. Note: these subjects can be included after initiation or adjustment of glucose-lowering medication.
- Prolongation of QTc interval to >480 ms.
- Subj.who have not recovered adequately from any toxicity and/or complications from major surgery prior to starting therapy.
- Gastrointestinal malabsorption, gastrointestinal anastomosis, or any other condition that might affect the absorption of lenvatinib, everolimus, and/or sunitinib.
- Bleeding or thrombotic disorders or subjects at risk for severe hemorrhage. The degree of tumor invasion/infiltration of major blood vessels (eg, carotid artery) should be considered because of the potential risk of severe hemorrhage associated with tumor shrinkage/necrosis following lenvatinib therapy.
- Clinically signif. hemoptysis or tumor bleeding within 2 weeks prior to the first dose of study drug.
- Signif. cardiovascular impairment within 12 months of the first dose of study drug: history of congestive heart failure greater than New York Heart Association (NYHA) Class II, unstable angina, myocardial infarction, cerebrovascular accident (CVA), or cardiac arrhythmia associated with hemodynamic instability. The following is also excluded:
- -> Left ventricular ejection fraction (LVEF) below the institutional normal range as determined by MUGA or echocardiogram.
- Active infection (any infection requiring systemic treatment).

	- Subjects known to be positive for Human Immunodeficiency Virus (HIV). 18. Known active Hepatitis B (eg, HBsAg reactive) or Hepatitis C (eg, HCV RNA [qualitative] is detected). - Known history of, or any evidence of, interstitial lung disease - Has a history of (non-infectious) pneumonitis that required steroids, or current pneumonitis - Any medical or other condition that in the opinion of the investigator(s) would preclude the subject's participation in a clinical study. - Subjects with a diagnosis of immunodeficiency or who are receiving chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of study treatment. - Active autoimmune disease (with the exception of psoriasis) that has required systemic treatment in the past 2 years. - Females who are breastfeeding or pregnant at Screening or Baseline - Females of childbearing potential who do not agree to use a highly effective method of contraception for the entire study period and for 120 days after study discontinuation - Males who have not had a successful vasectomy and do not agree to use condom + spermicide OR have a female partner who does not meet the criteria above. - Known intolerance to any of the study drugs (or any of the excipients).
Alter	18 Jahre und älter
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Sponsor	Eisai
Registrierung in anderen Studienregistern	EudraCT 2016-000916-14 ClinicalTrials.gov NCT02811861 (primäres Register)
Links	Studiendokumente zum Download (roXtra)