KURZPROTOKOLL
CA209-214

Öffentlicher Titel	Phase III Studie zu Nivolumab in Kombination mit oder ohne Ipilimumab in Patienten mit Nierenzellkarzinom
Wissenschaftl. Titel	A Phase 3, Randomizid, Open-Label Study of Nivolumab Combined with Ipilimumab Versus Sunitinib Monotherapy in Subjects with Previosuly Untreated, Advanced or Metastatic Renal Cell Carcinoma (CheckMate 214; CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 2014)
Kurztitel	CA209-214
Studienart	multizentrisch, prospektiv, randomisiert, offen/unverblindet, Pharma-Studie, zweiarmig
Studienphase	Phase III
Erkrankung	Niere/Harnwege: Nierenzellkrebs: Erstlinie
Ziele	- The purpose of this study is to compare the progression free survival and the overall survival of nivolumab combined with ipilimumab to sunitinib monotherapy in patients with previously untreated Renal Cell Cancer. - Secondary objectives of the trial: 1.Progression-free survival 2.Overall survival 3.Objective response rate 4.Duration of objective response 5.Overall safety & tolerability 6.Disease related symptom progression 7.Health related quality of life 8.Healthcare resource utilization
Einschlusskriterien	- Histological confirmation of RCC with a clear-cell component - Advanced (not amenable to curative surgery or radiation therapy) or metastatic (AJCC Stage IV) RCC - No prior systemic therapy for RCC with the following exception: - a) One prior adjuvant or neoadjuvant therapy for completely resectable RCC if such therapy did not include an agent that targets VEGF or VEGF receptors and if recurrence occurred at least 6 months after the last dose of adjuvant or neoadjuvant therapy. - Karnofsky Performance Status (KPS) of at least 70% - Measurable disease as per RECIST 1.1 - Tumor tissue (formalin-fixed paraffin-embedded (FFPE) archival or recent acquisition) must be received by the central vendor (block or unstained slides) in order to randomize a subject to study treatment. (Note: Fine Needle Aspiration [FNA] and bone metastases samples are not acceptable for submission). - Patients with favorable, intermediate and poor risk categories will be eligible for the study. Patients must be categorized according to favorable versus intermediate/poor risk status at registration. - To be eligible for the Intermediate and Poor-Risk cohort, at least one of the following prognostic factors as per International Metastatic RCC Database Consortium (IMDC) must be present: - a) KPS equal to 70 - b) Less than 1 year from diagnosis to randomization - c) Hemoglobin less than the LLN - d) Corrected calcium concentration greater than 10 mg/dL - e) Absolute neutrophil count greater than the ULN - f) Platelet count greater than the ULN - If none of the above factors are present, subjects are only eligible for the favorable-risk cohort. The favorable-risk cohort may close to enrollment earlier than the intermediate- or poor-risk cohort.
Ausschlusskriterien	- Any history of or current CNS metastases. Baseline imaging of the brain is required within 28 days prior to randomization.

- Prior systemic treatment with VEGF or VEGF receptor targeted therapy (including, but not limited to, sunitinib, pazopanib, axitinib, tivozanib, and bevacizumab).
- Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways.
- Any active or recent history of a known or suspected autoimmune disease or recent history of a syndrome that required systemic corticosteroids (> 10 mg daily prednisone equivalent) or immunosuppressive medications except for syndromes which would not be expected to recur in the absence of an external trigger. Subjects with vitiligo or type I diabetes mellitus or residual hypothyroidism due to autoimmune thyroiditis only requiring hormone replacement are permitted to enroll.
- Any condition requiring systemic treatment with corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days prior to first dose of study drug. Inhaled steroids and adrenal replacement steroid doses > 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease.
- Uncontrolled adrenal insufficiency.
- Ongoing symptomatic cardiac dysrhythmias, uncontrolled atrial fibrillation, or prolongation of the Fridericia corrected QT (QTcF) interval defined as > 450 msec for males and > 470 msec for females, where QTcF = QT / 3RR
- Poorly controlled hypertension (defined as systolic blood pressure (SBP) of  150 mmHg or diastolic blood pressure (DBP) of  90 mmHg), despite antihypertensive therapy
- History of any of the following cardiovascular conditions within 12 months of enrollment: cardiac angioplasty or stenting, myocardial infarction, unstable angina, coronary artery by-pass graft surgery, symptomatic peripheral vascular disease, class III or IV congestive heart failure, as defined by the New York Heart Association
- History of cerebrovascular accident including transient ischemic attack within the past 12 months
- History of deep vein thrombosis (DVT) unless adequately treated with low molecular weight heparin.
- History of pulmonary embolism within the past 6 months unless stable, asymptomatic, and treated with low molecular weight heparin for at least 6 weeks.
- History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within the past 6 months.
- Serious, non-healing wound or ulcer.
- Evidence of active bleeding or bleeding susceptibility; or medically significant hemorrhage within prior 30 days.
- Any requirement for anti-coagulation, except for low molecular weight heparin.
- Prior malignancy active within the previous 3 years except for locally curable cancers that have been apparently cured, such as basal or squamous cell skin cancer, superficial bladder cancer, or carcinoma in situ of the prostate, cervix, or breast.
- Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).
- Any positive test for hepatitis B or hepatitis C virus indicating acute or chronic infection.
- Known medical condition (eg, a condition associated with diarrhea or acute diverticulitis) that, in the investigator’s opinion, would increase the risk associated with study participation or study drug administration or interfere with the interpretation of safety results.

	- Major surgery (eg, nephrectomy) less than 28 days prior to the first dose of study drug. - Anti-cancer therapy less than 28 days prior to the first dose of study drug or palliative, focal radiation therapy less than 14 days prior to the first dose of study drug.
Alter	18 Jahre und älter
Fallzahl	1355
Sponsor	Bristol-Myers Squibb
Förderer	Bristol-Myers Squibb
Registrierung in anderen Studienregistern	EudraCT 2014-001750-42 ClinicalTrials.gov NCT02231749