CHOA Clinical Trial Master List

RENAL CELL CANCER:

CX-839-005: Randomized, Double-Blind, Placebo-Controlled Phase 2 Study Comparing CB-839 in Combination with Everolimus (Afinitor) (CBE) vs. Placebo with Everolimus (PboE) in Patients with Advanced or Metastatic Renal Cell Carcinoma (RCC)	
Sponsor: Calithera ****Clear Cell Pathology****	Therapy Line: **3rd Line Advanced or Metastatic** Drug Classification: **Glutaminase Inhibitor**
Principal Investigator: James M. Orcutt, MD	**CRC:** Ashley Morrill ext. 291
Basic Enrollment Information Criteria: Karnofsky Performance Score (KPS) ≥ 70% (Attachment 4) Estimated Life Expectancy of at least 3 mo, Documented histological or cytological diagnosis of renal cell carcinoma with a clear-cell component. Measurable Disease per RECIST 1.1 as determined by the Investigator (see Attachment 5) Must have received at least two prior lines of systemic therapy, including at least one VEGFR-targeting TKI (e.g., sunitinib, sorafenib, pazopanib, cabozantinib) For the most recently received VEGFR-targeting TKI there must have been progression of disease as determined by the treating physician either (i) during treatment or (ii) within 6 mo following completion of at least 4 weeks of treatment with the TKI Unless unavailable, must have received at least one of cabozantinib or nivolumab (or other active anti-PD-1/PD-L1 therapy) Prior treatment with other anti-cancer therapies including cytokines, monoclonal antibodies, immunotherapies, and cytotoxic chemotherapy is allowed (except for mTOR inhibitors, see Exclusion Criterion #1). **Exclusion Criteria:** Prior treatment with mTOR inhibitors (everolimus (Afinitor) or temsirolimus (Torisel)) or CB-839 Receipt of any anticancer therapy within the following windows before randomization: -TKI therapy within 2 weeks or 5 half-lives, whichever is shorter. -Any type of anti-cancer antibody within 4 weeks -Cytotoxic chemotherapy within 4 weeks -Investigational therapy within 4 weeks or 5 half-lives whichever is shorter -Radiation therapy for bone metastasis within 2 weeks, any other external radiation therapy within 4 weeks before randomization. Patients with clinically relevant ongoing complications from prior radiation therapy are not eligible. Any other current or previous malignancy within the past three years except a) adequately treated basal cell or squamous cell skin cancer, b) carcinoma *in situ* of the cervix, c) prostate cancer with stable prostate specific antigen (PSA) levels for 3 years, or d) other neoplasm that, in the opinion of the Principal Investigator and with the agreement of the Medical Monitor, will not interfere with study-specific endpoints. Unable to receive medications PO or any condition that may prevent adequate absorption of oral study medication including refractory nausea and vomiting, uncontrolled diarrhea, malabsorption, significant small bowel resection or gastric bypass surgery, use of feeding tubes, Major surgery within 28 days prior to randomization Known brain metastases or CNS cancer unless adequately treated with radiotherapy and/or surgery and stable by symptoms and radiographic imaging and not requiring corticosteroids for at least 2 mo before randomization, Unstable/inadequate cardiac function: Symptomatic ischemia or myocardial infarction within the previous 6 mo., Uncontrolled or clinically significant conduction abnormalities (e.g., ventricular tachycardia on antiarrhythmics are excluded, 1st degree AV block or asymptomatic LAFB/RBBB are eligible) Congestive heart failure (New York Heart Association class III to IV) Known active infection with HIV or Hepatitis B or C virus Chronic treatment with corticosteroids or other immunosuppressive agents except inhaled or topical steroids or replacement dose corticosteroids equivalent to ≤ 10 mg prednisone and (ii) patients receiving physiological doses of hydrocortisone for adrenal insufficiency. Any condition including social, psychiatric or medical (including uncontrolled significant concurrent illness) that in the opinion of the Investigator could interfere with treatment or protocol-related procedures. Patients who are pregnant or lactating.	

REVISED: 19Jun2018 BR

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RENAL CELL CANCER:

<table>
<tr><td colspan="2">USO#16251: Merck-3475-564 (KEYNOTE -564): Phase III, Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Pembrolizumab (MK-3475) as Monotherapy in the Adjuvant Treatment of Renal Cell Carcinoma Post Nephrectomy (KEYNOTE-564)</td></tr>
<tr><td>Sponsor: Merck

Clear Cell Pathology

Tissue Submission required but can be submitted after start of treatment</td><td>Therapy Line: 1st line for Advanced/ Metastatic Clear Cell RCC (see inclusion for M1)
Drug Classification: Humanized monoclonal antibody of the IgG4/Kappa isotype that blocks the interaction between PD-1 & its ligands PD-L1 & PD-L2</td></tr>
<tr><td>Principal Investigator: George Keogh, MD</td><td>CRC: Jacqueline Showalter ext. 293</td></tr>
<tr><td colspan="2">Basic Enrollment Criteria: ECOG of 0 or 1. Have intermediate-high risk, high risk, or M1 NED RCC as defined by the following pathological tumor-node-metastasis and Fuhrman grading status [39] [42] [43]: a) Intermediate-high risk RCC pT2, Gr. 4 or sarcomatoid, N0, M0 pT3, Any Gr., N0, M0 b) High risk RCC pT4, Any Gr. N0, M0 pT Any stage, Any Gr., N+, M0 c) M1 NED RCC (participants who present not only with the primary kidney tumor but also solid, isolated, soft tissue metastases that can be completely resected at the time of nephrectomy) Have received no prior systemic therapy for advanced RCC (except nephrectomy or Metastasectomy). Have undergone a partial nephroprotective or radical complete nephrectomy (and complete resection of metastatic lesion(s) in M1 NED participants) with negative surgical margins. Must have undergone a nephrectomy (and metastasectomy for M1 NED) ≥28 days prior to signing informed consent and must be randomized ≤12 weeks after surgery. Must be tumor-free as assessed by the Investigator and validated by either CT or MRI scan of the brain and CAP and a bone scan ≤28 days from randomization. All baseline scans must be sent to the central imaging vendor and receipt must be confirmed prior to randomization.
Exclusion criteria: Has had major surgery, other than nephrectomy plus resection of pre-existing metastases for M1 NED participants, within 12 weeks prior to randomization. Note: If participants received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment. Has received prior radiotherapy for RCC. Has residual thrombus post nephrectomy in the vena renalis or vena cava. Has a known additional malignancy that is progressing or requires active treatment. Exceptions include early-stage cancers (carcinoma in situ or Stage 1) treated with curative intent, basal cell carcinoma of the skin, squamous cell carcinoma of the skin, insitu cervical cancer, in situ prostate cancer, or in situ breast cancer that has undergone potentially curative therapy. Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent or with an agent directed to another co-inhibitory T-cell receptor (ie, CTLA-4, OX-40, CD137) or has previously participated in a Merck pembrolizumab (MK-3475) clinical trial. Has received prior anticancer therapy, monoclonal antibody, chemotherapy, or an investigational agent or device within 4 weeks or 5 half-lives (whichever is longer) before first dose of study treatment or not recovered (ie, must be ≤Grade 1 or at baseline) from AEs due to previously administered agents. Note: Upon consultation with the Sponsor, denosumab may be allowed for bone protective purposes if dosing has been stable for ≥2 weeks before screening.</td></tr>
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