

TYPE OF CANCER: Clear Cell Renal Cell Carcinoma
TYPE OF TRIAL: Phase I
TRIAL SPONSOR: Medarex

PRINCIPAL INVESTIGATOR: Wolfram Samlowski, M.D.
CONTACT PERSON: Therica Miller
(702) 822-5293

STUDY SUMMARY

A Phase 1, Open-label, Dose-escalation, Multidose Study of MDX-1411 Administered Every 14 Days in Subjects with Advanced or Recurrent Clear Cell Renal Cell Carcinoma

TREATMENT OVERVIEW

- Subjects will receive MDX-1411 every 14 days for a total of 3 infusions at the dose they were administered during the initial cycle.
- Each cycle (42 days) consists of 3 infusions on Days 1, 15, and 29 with a response assessment within Days 38 to 42 (results of assessments must be reviewed prior to administering the first dose of the next cycle).
- The maximum study treatment is 2 years.

PRETREATMENT ASSESMENT

- Informed consent
- Inclusion/exclusion criteria
- Demographics/ Medical history
- Physical Examination
- Vital signs (height, weight, ECOG)
- Tumor Evaluation [CT / MRI Chest/ abdomen/ pelvis]
- EKG/ECG
- Hematology
- Serum chemistry
- Urinalysis
- Flow cytometry
- Bone Scan (if clinically indicated)
- Pregnancy test
- Concomitant medications
- Adverse events

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

Inclusion Criteria

1. Subjects must be 18 years of age or older;
2. Life expectancy \geq 12 weeks;
3. Subjects must have histologically confirmed diagnosis of RCC (clear cell component) with advanced or recurrent disease that is not amendable to cure by surgery or other means and must have failed at least 1 prior systemic therapy, including but not limited to treatment with Sunitinib, Temsirolimus, Sorafenib, IL-2, and/or chemotherapy;
4. Subjects must have measurable disease with at least 1 unidimensional measurable lesion per RECIST guidelines with modifications (see Appendix 2);
5. Subjects may have been treated with up to 3 prior systemic therapies for advanced/recurrent disease or have become intolerant to a systemic therapy;
6. Subjects with treated brain metastases must be without MRI evidence of progression for at least 8 weeks and off steroids for at least 4 weeks to be eligible;
7. Subjects may have been treated with radiation therapy (RT) provided there are measurable lesions outside the field of RT;
8. At least 28 days since the last chemotherapy, immunotherapy, biological or investigational therapy, radiation, or at least 2 weeks from approved TKI therapy (Sunitinib, Sorafenib) prior to the first dosing of MDX-1411 and have recovered from any toxicity associated with such treatment;
9. At least 28 days prior to the first dose of MDX-1411 since any major surgery;
10. ECOG Performance Status 0 to 1 (Appendix 2);
11. Screening laboratory values must meet the following criteria:
 - WBC \geq 3000/ μ L
 - Neutrophils \geq 1500/ μ L
 - Platelets \geq 100,000/ μ L
 - Hemoglobin \geq 9.0 g/dL (may have been transfused)
 - Creatinine $<$ 1.5 mg/dL X ULN or creatinine clearance \geq 50 mL/min
 - AST \leq 2.5 X ULN
 - ALT \leq 2.5 X ULN
 - Bilirubin $<$ 1.5 mg/dL (unless diagnosed with Gilbert's syndrome)
 - No known positivity for human immunodeficiency virus (HIV), Hepatitis B, or Hepatitis C (no laboratory testing is required);

12. Women must meet 1 of the following criteria: post-menopausal for at least 2 years; surgically incapable of bearing children (have had a hysterectomy or bilateral oophorectomy); or utilizing a reliable form of contraception;

13. Men must agree to the use of male contraception for at least 70 days after the last dose of study drug.

Exclusion Criteria

Subjects who fulfill any of the following criteria listed below at Screening will not be eligible for admission into the study:

1. Previous treatment with any other anti-CD70 antibody;
2. Any other malignancy, excluding basal or squamous cell carcinoma of the skin, cervical carcinoma in situ, or localized prostate cancer, from which the subject has not been disease-free for at least 5 years;
3. Active infection (viral, bacterial, or fungal) requiring i.v. systemic therapy within 28 days of enrollment;
4. Evidence of bleeding diathesis or coagulopathy;
5. Active autoimmune disease requiring immunosuppressive therapy;
6. Known current drug or alcohol abuse;
7. Apparent active or latent tuberculosis (TB) infection (purified protein derivative [PPD] test is not required) as indicated by any of the following: PPD recently converted to positive; chest x-ray with evidence of infections infiltrate; recent changes in fever/chill patterns;
8. Pregnant or nursing;
9. Any underlying medical condition which, in the Principal Investigator's opinion, will make the administration of MDX-1411 hazardous or obscure the interpretation of adverse events;
10. Psychiatric illness or social situation that would preclude study compliance.