

## **“A Phase II Evaluation of EMD 121974 (NSC 707544, Cilengitide) in Patients with Non-Metastatic Androgen Independent Prostate Cancer”**

### **An Evaluation of Treatment in Patients with Non-Metastatic Androgen Independent Prostate Cancer**

Investigator Initiated Trial: David Agus, Principal Investigator  
IRB No. 7895

#### **Contact**

Mana Saedi  
(310) 423-7600; [pcc@cshs.org](mailto:pcc@cshs.org) or [prostate@cshs.org](mailto:prostate@cshs.org)

#### **Description**

Prostate cancer is a common and important health issue facing American men. The initial treatment for prostate cancer often includes medical or surgical treatments that deprive the tumor of male hormones required for growth. Although this treatment is successful for many patients, the cancer may eventually return in others. Recurrent prostate cancer may be treated with additional hormonal agents, but these agents usually do not result in long-term control of the disease. Eventually most patients with recurrent prostate cancer progress to a state where the cancer grows despite very low level of circulating male hormones known as androgen-independent prostate cancer (AIPC). Clinical experience indicates that they majority of patients with this type of disease will continue to get worse and their cancer will eventually become visible on scans. Currently, no standard treatment has been found to delay the growth and spread of the disease. Therefore, we are continually looking for more effective treatments against this disease.

Integrins are a kind of protein, which are known to be important for cancer cell attachment and the formation of new blood vessels, which allow cancer to grow. EMD 121974 (NSC 707544, Cilengitide) is a biologic compound that is a potent inhibitor of integrins. The purpose of this study is to determine if EMD 121974 is an effective treatment for non-metastatic prostate cancer (cancer that is has not spread to you organs or bones).

This research study is designed to test the safety and effectiveness of the investigational drug [EMD 121974 (Cilengitide)]. Investigational drugs are ones that are being evaluated and have not yet been approved by the U.S. Food and Drug Administration (FDA).

#### **Objectives**

The primary purpose of this study is to assess the rate of Prostate Specific Antigen response associated with EMD 121974 therapy in patients with non-metastatic androgen-independent prostate cancer. The secondary purposes are to: (1) to evaluate the safety of EMD 121974 in patients with non-metastatic AIPC; (2) to assess the change in the slope of Prostate Specific Antigen associated with EMD 121974 in patients with non-metastatic androgen-independent prostate cancer; (3) to assess response duration, time to progression, and survival.

#### **Patient Eligibility**

##### **Inclusion Criteria**

- 1) A histologic or cytologic diagnosis of prostate cancer.
- 2) No evidence of metastatic disease, or local progression.
- 3) PSA-only progression despite androgen deprivation therapy and antiandrogen withdrawal (28 days for flutamide and 42 days for bicalutamide or nilutamide). PSA progression is defined as 3 consecutive rising levels, with an interval of >1 week between each determination. The last determination must have a minimum value of  $\geq 2$  ng/mL and be determined within 2 weeks prior to registration. If the third confirmatory value is less than

- the previous value, the patient will still be eligible if a repeat value (No. 4) is found to be greater than the second value.
- 4) Patients must be off steroids or other hormonal agent, except LHRH agonists, for 4 weeks. Please see above for antiandrogens.
  - 5) ECOG performance status of 0-2.
  - 6) No prior EMD 121974 therapy is allowed.
  - 7) No investigational or commercial agents or therapies may be administered with the intent to treat the patient's malignancy.
  - 8) Testosterone < 50 ng/dL. Patients must continue primary androgen deprivation with an LHRH agonist, if they have not undergone orchiectomy.
  - 9) Four weeks must have elapsed since major surgery.
  - 10) Age  $\geq$  18 years.
  - 11) Life expectancy of greater than 6 months.
  - 12) Patients must have normal organ and marrow function as defined below obtained within 14 days prior to registration:
    - a. ANC  $\geq$  1500/ $\mu$ L
    - b. Platelet count  $\geq$  100,000/ $\mu$ L
    - c. Creatinine  $\leq$  1.5 x upper limits of normal
    - d. Bilirubin within normal limits
    - e. SGOT (AST)  $\leq$  2.5 x upper limits of normal
    - f. SGPT (ALT)  $\leq$  2.5 x upper limits of normal
    - g. PSA  $\geq$  2 ng/mL
  - 13) The effects of EMD 121974 on the developing human fetus at the recommended therapeutic dose are unknown. For this reason and because antiangiogenic agents are known to be teratogenic, men must agree to use adequate contraception prior to study entry and for the duration of study participation.
  - 14) Ability to understand and the willingness to sign a written informed consent document that is approved by the Institutional Human Investigation Committee (HIC).

#### **Exclusion Criteria**

- 1) Patients may continue on a daily Multi-Vitamin, but all other herbal, alternative, and food supplements (i.e. PC-Spes, Saw Palmetto, St. John Wort, etc.) must be discontinued before registration.
- 2) Patients on stable doses of bisphosphonates which has been started no less than 6 weeks prior to protocol therapy, that show subsequent tumor progression, may continue on this medication, however patients are not allowed to initiate bisphosphonate therapy immediately prior or during the study.
- 3) Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
- 4) Patients with a "currently active" second malignancy other than non-melanoma skin cancers are not eligible. Patients are not considered to have a "currently active" malignancy if they have completed therapy and are now considered without evidence of disease for 2 years.

#### **Schema**

Patients will undergo a screening procedure to determine eligibility of trial. If the patient is eligible, he will be monitored for 4 weeks with no treatment and have PSA done at 2 weeks and 4 weeks after registration. Treatment will be in "treatment cycles" with each "cycle" being 4 weeks (28 days). There will be no planned breaks between cycles.

EMD 121974 will be given in the outpatient infusion center. The patient will receive an hour-long IV infusion twice weekly on a Monday/Thursday or Tuesday/Friday schedule.

Patients will be seen by a doctor for a physical exam on the first week of every cycle of treatment. Blood will be drawn for routine blood counts, serum chemistry, and PSA on the

**IRB No: Pro00007895/ CR00001938**

**Approval Date: 8/1/2007      Expiration Date: 7/31/2008**

first week of each cycle. Blood for circulating cells will be collected on the first week of every cycle for the first 3 treatment cycles and at the time that the patient comes off the trial. Patients will have imaging studies (Bone scan, CT scan or MRI of the abdomen and pelvis) every 3 cycles of treatment (every 12 weeks) in order to assess response to treatment.

Additional testing (blood testing, scans, and/or x-rays) may be performed if clinically indicated.

**Potential Toxicities**

Based on the initial studies the investigational treatment, common toxicities include: nausea, fatigue, loss of appetite, vomiting, and diarrhea.