

A Phase III Randomized, Open-Label Study of Docetaxel in Combination with CG1940 and CG8711 versus Docetaxel and Prednisone in Taxane-Naïve Patients with Metastatic Hormone-Refractory Prostate Cancer With Pain

Nontechnical Abstract

Prostate cancer is the most common form of non-skin cell cancer in adult males in the United States. In 2005, the estimated incidence and mortality rates in the USA are 232,090 new cases and 30,350 deaths. Surgical removal of the prostate or radiation treatment may cure early prostate cancer if the tumor has not spread outside the prostate gland. However, in 70% of patients, the cancer will spread, mostly to the bone. At this point, the cancer cannot be cured. Hormone therapy can control advanced cancer temporarily in most patients, but the advanced cancer progresses in nearly all patients. In 2004, the FDA approved a treatment regimen for advanced hormone refractory prostate cancer consisting of docetaxel administered every 3 weeks in combination with oral daily prednisone. Immunotherapy (CG1940 and CG8711) combined with docetaxel chemotherapy is being tested in this proposed trial in order to assess whether patient survival and prostate cancer disease control can be improved over using docetaxel alone. An earlier version of the CG1940/CG8711 vaccine demonstrated a median survival of 26 months in a phase 2 clinical study providing a signal that the vaccine has potential clinical activity against prostate cancer. Combining vaccine with docetaxel is designed around the principal of adding two separate anti-tumor agents in order to utilize a synergistic increased treatment regimen efficacy. Combining GM-CSF secreting whole cell vaccine with docetaxel demonstrated a synergistic increase in survival in preclinical animal models. CG1940 and CG8711 is a vaccine made from cells which were originally taken from the tumors of two patients with advanced prostate cancer. To make the vaccine, the cells are altered by inserting a gene for GM-CSF, (granulocyte-macrophage colony-stimulating factor), a substance made by the body that helps the immune system recognize a tumor and destroy it. The gene for GM-CSF is inserted into the prostate cancer cells using an artificial virus containing parts of a natural virus called "Adeno-associated Virus." The cells are then grown in a laboratory to produce the vaccine. The vaccine cells are treated with radiation so they cannot grow or divide after injection. The cells themselves do not contain virus and are **not** radioactive. The cells are frozen to preserve them until they are administered to the patient.

This is an open label Phase 3 clinical trial that is designed to assess whether the prostate cancer vaccine (GC1940 and CG8711) in combination with docetaxel results in an improved prostate cancer disease control and patient survival compared to docetaxel alone. The objectives of this trial are to compare between the two treatment regimens 1) the duration of survival, 2) the time to disease progression on X-Rays, and 3) the time to pain progression.

Patients in this study must have cancer of the prostate that has spread to the bone or tissues and have failed hormonal therapy. They must be active and able to walk and take care of themselves independently. Patients are required to have moderate or severe cancer-related pain and taking analgesics (ketorolac, opioids, and/or acetaminophen/opioid combinations) for pain management in order to be eligible for the study.

Patients who have received prior gene therapy are not eligible for enrollment in this trial. Patients who have already had chemotherapy are eligible as long as they have not received more than one systemic chemotherapy and they have not received taxane chemotherapy.

In the study, patients are randomly assigned to treatment with chemotherapy in combination with vaccine versus chemotherapy alone. Patients in the vaccine plus chemotherapy arm are treated every three weeks with docetaxel and vaccine (GC1940 and CG 8711) for ten cycles. At the end of the ten-cycle treatment schedule, patients in the vaccine plus chemotherapy arm continue to receive vaccine therapy alone monthly. In the chemotherapy only group, patients are treated with 10 cycles of docetaxel every three weeks and daily oral prednisone. Patients who are not responding to study treatment can stop receiving the vaccine or docetaxel and receive another prostate cancer treatment per recommendation of the treating physician.

Patients will be followed closely in the clinic after and during the time period that they start receiving treatment until one month following administration of the last dose of study drug and will be evaluated by physical examination, blood tests, and X-rays. Patients will be assessed for adverse events. Thereafter, patients will be followed quarterly for the rest of their life for survival and long-term safety assessments.