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Phase 3 Trial of Immunotherapy for Metastatic Prostate Cancer Terminated

Nick Mulcahy | October 17, 2008

October 17, 2008 — A phase 3 clinical trial of an immunotherapy in patients with asymptomatic metastatic hormone-refractory prostate cancer has been terminated by its corporate sponsor, Cell Genesys, Inc, of South San Francisco, California, because of a lack of effect on survival, the company announced.

The trial was fully enrolled in 2007 with 626 patients and compared GVAX immunotherapy with docetaxel (*Taxotere*, Sanofi-Aventis) chemotherapy plus prednisone.

"I have not lost my conviction that immunotherapy will play a role in the treatment of this disease," said Stephen A. Sherwin, MD, chair and chief executive officer of Cell Genesys, in a press conference call with reporters. "There's a huge amount of preclinical and early clinical data suggesting the activity of this platform [GVAX], and that's why I remain optimistic."

In speculating about the failure of trial, Dr. Sherwin said: "Perhaps metastatic prostate cancer, even though it's less aggressive than other cancers, is simply just too tough a target for a slow-acting immunotherapy such as GVAX."

Dr. Sherwin also wondered if the company had "raised the bar too high in these phase 3 trials when we put GVAX up against an active chemotherapy drug."

The company ended the trial based on the results of an unplanned futility analysis conducted by the study's Independent Data Monitoring Committee (IDMC), which indicated that the trial had less than a 30% chance of meeting its prespecified primary end point of an improvement in survival.

The termination of the VITAL-1 phase 3 clinical trial of GVAX immunotherapy follows the termination, on August 27, 2008, of VITAL-2, another phase 3 trial involving the therapy.

In contrast to the VITAL-1 study, the VITAL-2 study was conducted in patients with symptomatic metastatic hormone-refractory prostate cancer and compared the combination of GVAX immunotherapy plus docetaxel to docetaxel plus prednisone (the control group).

When the VITAL-2 study was terminated, the IDMC reported an imbalance in deaths between the 2 treatment groups that was observed during a routine safety-monitoring meeting of the committee. Of 114 deaths at the time of the IDMC review, 67 occurred in the group receiving GVAX immunotherapy plus docetaxel, and 47 occurred in the group receiving docetaxel plus prednisone. A total of 408 patients had been enrolled in the study up to that point.

Cell Genesys has now conducted an initial analysis of the incomplete VITAL-2 dataset that was reviewed by the IDMC in August, and Dr. Sherwin provided an update during the press conference. The analysis has revealed no imbalance in patient baseline characteristics with respect to demographic and disease prognostic factors. In addition, no significant toxicities were observed with GVAX immunotherapy plus docetaxel that could explain the imbalance in deaths. The vast majority of deaths in both treatment groups were reported as being due to the progression of prostate cancer.

Notably, fewer treatment cycles with docetaxel were administered to patients receiving GVAX immunotherapy than to those receiving prednisone, said Dr. Sherwin, and the difference was statistically significant.

GVAX immunotherapy, an intradermal injection administered on an outpatient basis for prostate cancer, is comprised of 2 prostate tumor cell lines that have been modified to secrete granulocyte-macrophage colony-

stimulating factor (GM-CSF), an immune-stimulatory cytokine that plays a key role in stimulating the body's immune response, and then irradiated for safety. Dr. Sherwin called GM-CSF a "powerful cytokine," and noted that it is used "across the board in immunotherapy trials as an adjunctive therapy" because of its potency.

Cell Genesys has put on hold the further development of GVAX immunotherapy for prostate cancer pending a review of the program with its collaborator, Takeda Pharmaceutical Co. Ltd.

Dr. Sherwin thanked the patients in the study during his press conference. "On behalf of the Cell Genesys management team, I would like to express my deep gratitude to the courageous patients who participated in this study, as well as to our committed clinical-trial investigators and their teams."

As a result of the terminated clinical trials, Cell Genesys will reduce its staff of 290 by approximately 75% by year-end, with further reductions anticipated in the first half of 2009 as additional activities are phased out, according to Dr. Sherwin.

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