Pancreatic Cancer Vaccine Improves Survival Rates

ARTICLES BY FRAN LOWRY
Orlando Bureau

ORLANDO — A therapeutic, investigational vaccine given in combination with chemoradiotherapy after surgery was associated with improved survival in patients with resected pancreatic adenocarcinoma, according to a phase II trial presented at a symposium on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

The median overall survival for patients who received the vaccine was 26.8 months, compared with 20 months for historic controls, said Dr. Daniel A. Laheru of the department of oncology at Johns Hopkins University, Baltimore.

Of the 60 patients who received the vaccine, 88% survived for 1 year and 76% survived for 2 years. These results compare very favorably with those of previous studies, in which patients treated with surgery alone had an average 1-year survival rate of 63% and a 2-year survival rate of 42%, Dr. Laheru said at the symposium, which was also sponsored by the AGA Institute, the American Society for Therapeutic Radiology and Oncology, and the Society of Surgical Oncology.

Most of the participants (52 of 60) were considered to be at high risk because their cancer had spread to the regional lymph nodes.

The vaccine, known as GVAX immunotherapy, boosts the patient's own immune system to help it recognize cancer cells throughout the body and destroy them. GVAX is made up of lethally irradiated lines of pancreatic cancer cells that were engineered to secrete granulocyte macrophage colony stimulating factor (GM-CSF).

"The GM-CSF molecule attracts immune cells to the vaccine site, where the immune cells encounter pancreas cancer antigens. They then patrol the rest of the patient's body in a kind of seek and destroy mission, to destroy pancreas tumor cells possessing the same antigen profile," Dr. Laheru explained. The vaccine does not prevent cancer, he added.

Patients who were deemed to be free of cancer 30 days after their surgery were eligible to receive the vaccine. The first infusion was given 8-10 weeks after pancreatic resection.

This was followed by treatment with a standard regimen of 5-fluorouracil–based chemotherapy plus radiation.

Patients who were disease free 1 month after chemoradiotherapy received three additional vaccine doses, 1 month apart, followed by a fifth booster 6 months later.

The vaccine immunotherapy was well tolerated. Side effects included transient vaccine injection site reactions, such as itching, redness, and swelling. These typically resolved within 10 days.

"Pancreatic cancer is the fourth leading cause of cancer-related death [in the United States]. Surgery is the only known cure for early pancreatic cancer, but most patients [have a recurrence] even after optimal resection. We are optimistic about the results from this study, which suggest that the vaccine could provide additional benefit over chemoradiotherapy, but prospective randomized trials are needed to confirm this observation," Dr. Laheru said.

He and the Johns Hopkins investigators also plan to study whether the vaccine is most effective in combination with chemotherapy alone or with chemotherapy plus radiation.

Dr. Laheru disclosed that he received research funding from Cell Genesys Inc., which developed the vaccine. ■

Teaching Hospitals More Aggressive In Treating Pancreatic Cancer

ORLANDO — Teaching hospitals offer state-of-the-art multimodal therapy for pancreatic cancer, but community hospitals not affiliated with academic centers tend to treat with pancreatic resection only, according to a poster presented at a symposium on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

Offering stage-specific treatment to the appropriate patients will improve cancer care in the community, Dr. Karl Y. Bilimoria of Northwestern University, Chicago, said at the symposium, which was also sponsored by the AGA Institute, the American Society for Therapeutic Radiology and Oncology, and the Society of Surgical Oncology.

Dr. Bilimoria led a retrospective study that evaluated various aspects of pancreatic cancer treatment in the United States over a 19-year period. "The morbidity and mortality after pancreatic surgery has decreased in recent years, and several trials have shown improved outcomes with multimodal therapy, which includes chemotherapy, radiation, and surgery.

Academic centers were significantly more likely to offer pancreatectomy and adjuvant chemoradiation therapy than were community institutions.

But national practice patterns in the management of pancreatic cancer were poorly defined, and we wanted to shed some light on the use of treatment relative to hospital characteristics," he explained at the poster presenting their work.

The investigators used the National Cancer Data Base to analyze treatment patterns for 301,033 patients with pancreatic cancer from 1,667 institutions during two time periods: 1985-1994 and 1995-2003.

They found that the cancer stage at presentation did not differ for the two time periods, but that the percentage of patients receiving treatment for their cancer increased significantly (*P* less than .0001), from 45.1% in the first time period (57,188 patients out of a total of 126,891) to 51.8% (90,222 patients out of a total of 174,172) in the second time period.

The analysis also revealed the following shifts in treatment patterns (all of the changes were significant at *P* less than .0001):

- Pancreatectomy for localized stage I and II disease increased from 36.9% to 49.3%.
- Chemotherapy after curative resection increased from 4.1% to 5.7%.
- Radiation therapy after curative resection decreased, from 7.0% to 4.6%.
- Adjuvant chemoradiation increased from 26.8% to 38.7%.
- Surgery alone decreased from 62.1% to 49.9%.

High-volume academic centers were significantly more likely to offer pancreatectomy and adjuvant chemoradiation therapy than were community institutions (*P* less than .0001), Dr. Bilimoria reported.

"We were not surprised by this finding, but it was important to document the disparity in treatment so that we can go back and say to the community hospitals that perhaps they should look more closely at utilization rates of adjuvant chemoradiation therapy at their institutions," Dr. Bilimoria said in an interview.

It is possible that community hospitals may be seeing older patients or sicker patients, and these factors may be influencing their utilization of adjuvant treatments. "They may, in fact, be treating appropriately, so we need to do more work to investigate this," he said.

Dr. Bilimoria added that one of the more interesting findings of the study was that the National Comprehensive Cancer Network institutions used multimodal therapy significantly more often than did academic centers (*P* less than .0001).

"The NCCN centers have dedicated resources to give state-of-the-art therapy for pancreatic cancer, and they also tend to have special patient populations who come especially to them for their treatment. But we need to identify utilization patterns that we can also bring to community hospitals, without having to talk about regionalization of care. This would definitely improve outcomes at community hospitals," he said. ■

Bevacizumab Disappoints in Pancreatic Cancer

ORLANDO — Hopes that the addition of bevacizumab to gemcitabine would improve survival in patients with advanced pancreatic cancer have been dashed by the disappointing results of CALGB 80303, a phase III randomized trial presented at a symposium on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

An earlier phase II trial of gemcitabine—the standard drug for advanced pancreatic cancer—plus bevacizumab in 52 patients showed responses in 21% and a median survival of 8.8 months. These results were far better than the 5%-10% response rate and 5-6 month survival expected with gemcitabine alone, and prompted the current trial, said lead author, Dr. Hedy Lee Kindler, director of gastrointestinal oncology at the University of Chicago. Unfortunately, the study did not confirm the promising data of its predecessor, she said.

The CALGB (Cancer and Leukemia Group B) 80303 trial randomized 602 patients with advanced pancreatic cancer to gemcitabine plus bevacizumab or gemcitabine plus placebo, and followed them for overall survival, objective response rate, progression-free survival, and toxicity.

The patients were enrolled from June 2004 to April 2006, and weeks later, the CALGB Data Safety Monitoring Board determined that a significant difference in survival between the treatment arms would be unlikely. As a result, all patients on treatment were notified and unblinded, and those who were thought to be benefiting from bevacizumab were allowed to continue the drug with informed consent, Dr. Kindler said at the symposium also sponsored by the AGA Institute, the American Society for Therapeutic Radiology and Oncology, and the Society for Surgical Oncology.

There were no statistically significant differences in survival (5.7 months for gemcitabine plus bevacizumab vs. 6.0 months for gemcitabine alone) or progression-free survival (4.8 months for gemcitabine plus bevacizumab vs. 4.3 months for gemcitabine alone). Treatment with gemcitabine plus bevacizumab resulted in a very slight increase in the rate of tumor shrinkage and stable disease, compared with gemcitabine plus placebo (54% vs. 47%, respectively), Dr. Kindler reported.

However, bevacizumab was associated with grade 3 and 4 hypertension and proteinuria.

The encouraging results in the earlier study may have occurred because that smaller study had proportionally more patients with good prognostic factors, Dr. Kindler said. She added that ongoing companion studies of CALGB 80303 may provide key insights into the biology of pancreatic cancer.

Dr. Charles A. Staley, chief of surgical oncology at Emory University, Atlanta, commented that the treatment of pancreatic cancer continues to be frustrating. "It's a little disappointing—bevacizumab has had a great run in most diseases—but again, this just points out the complexity of drug interactions and what actually happens in the host environment." ■