

# Encouraging Outcomes in Pancreatic Cancer with Multimodal Approach

BY ED SUSMAN

**S**AN FRANCISCO—A treatment regimen that includes chemotherapy, focused radiation therapy, and surgery appears to offer hope to selected patients with pancreatic cancer—with progression-free survival extended to about two years, researchers reported here at the American Society for Radiation Oncology Annual Meeting.

“These are definitely very encouraging results, but we do require larger studies to validate the findings,” said Kimmen Quan, MD, a Radiation

stereotactic ablative radiotherapy treatments would be given over the course of one week and then the patients were re-imaged again four weeks after having completed radiosurgery. A multidisciplinary discussion would then take place with a radiation oncologist and medical oncologist as to whether the patient would be a surgical candidate. Patients who were not candidates for surgery would then go on to have further chemotherapy.

In the interim analysis of the Phase II study, 10 of 18 patients who had

been diagnosed with borderline resectable pancreatic cancer were able to undergo surgery, as were

two of 16 patients who had been diagnosed with locally advanced pancreatic cancer.

Quan said that of the patients who went on to surgery, 92 percent had no evidence of disease following resection—“meaning that it was a successful surgery.” Importantly, he said that the quality of life of the patients did not appear to be negatively affected by the

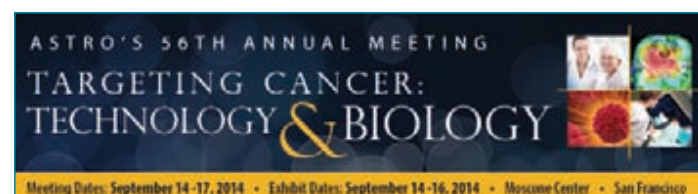


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kinds of encouraging results,” he said. “We only offer this treatment to a certain subset of patients.”

Following surgery, the levels of CA 19-9, a serum marker of tumor-associated antigens, decreased from a mean of 867 units/mL before chemotherapy to 177 units/mL after stereotactic radiotherapy—a normal level is less than 37 units/mL, Quan



Oncologist at the University of Pittsburgh Cancer Center, in presenting the new data at a news conference. The treatment protocol resulted in 40 percent of patients becoming eligible for possible curative surgery, he reported.

He and his colleagues recruited 34 patients who were diagnosed with either locally advanced or borderline resectable pancreatic cancer and used different anti-cancer modalities to reduce the cancer burden to the point where Whipple surgery could be successfully completed.

The patients first underwent four 21-day cycles with gemcitabine plus capecitabine chemotherapy. They then were given a computer-assisted tomography (CT) scan. If there was no tumor progression, the patients would be offered radiosurgery. Three

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course of the therapy. The average age of the patients was 71; and about 56 percent were women.

Three of the patients did not complete chemotherapy—one died after consent but prior to chemotherapy; one died during chemotherapy because of an arterial occlusion; and one had a myocardial infarction prior to completion of the four courses of chemotherapy.

The median disease-free survival for the borderline resectable patients was 25.5 months, and the median disease-free survival for the patients with locally advanced pancreatic cancer was 22.5 months. Local progression-free survival was 100 percent at one year for patients with locally advanced cancer after completing the regimen and 86 percent at one year for patients with borderline resectable cancer.

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explained. “What we showed here is that the treatment is working to decrease these values to a significant level.

“Chemotherapy followed by stereotactic ablation radiotherapy is an attractive treatment option with low toxicity. It addresses potential microscopic spread of disease early, allows for selection of patients who are best suited for local therapy, gives less radiation to other organs, and quality of life appears promising.”

Future studies with pancreatic cancer patients, though, will likely involve newer, more potent chemotherapy regimens, he noted.

## Shorter Time Frame, Increasing Quality of Life

The moderator of a news conference that featured the study, Theodore DeWeese, MD, Chief of Radiation Oncology at Johns Hopkins Medical

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Institutions, said, “The study showed that using combinations of more highly focused, short-course, cancer-killing radiation and chemotherapy increases the likelihood that patients with more advanced pancreatic cancer can have surgery as an important part of cure.

“This shows that radiation can not only be done in a more conformal manner with less side effects, but that it can be done in less time, which gets the patient back to his or her life in a shorter time frame, increasing their quality of life.”

He said the trial was important because about 80 percent of patients with pancreatic cancer present with either locally advanced or borderline resectable disease.

‘Real Strength of the Study...’

Also commenting on the study in an interview, Theodore S. Hong, MD, Director of the Gastrointestinal Service in the Department of Radiation Oncology at Massachusetts General Hospital, and Associate Professor of Radiation Oncology at Harvard Medical School, said that better medical protocols may even improve on these outcomes: “Now that these researchers have demonstrated the safety of this regimen, it will be interesting to see if they can further downstage patients to allowing for surgery with the more potent chemotherapy regimens—that is where the real strength of this study lies. This radiation approach warrants further investigation.

“Clearly, though, in comparing this study to historical controls where the standard of care

involves single-agent gemcitabine and conventional radiation, these numbers are certainly encouraging,” he said. “I think where there remains a lot to learn in the ability to downstage patients to R0 surgery involves better understanding the role of newer chemotherapy regimens that were not evaluated in this study. For example, FOLFIRINOX [leucovorin, fluorouracil, irinotecan, and oxaliplatin] produces markedly more response than the regimen used in this study.

“These results are reflective of a very rapidly changing landscape,” Hong con-

tinued. He said the new research may also help standardize radiation therapy for these patients: “There remains no clear standard for radiation therapy.

“Usual care now is five to six weeks of conventionally fractionated radiation with single-agent chemotherapy, but there is a great deal of interest in their stereotactic regimens preoperatively that better acknowledges the high metastatic risk of these patients and their limited long-term survival. Certainly from a patient satisfaction point-of-view, there is a lot of potential upside with these shorter regimens.”

Caveat about Risk of Selection Bias

He did raise a caution in interpreting the results, though: “In a single-arm study, there is a risk of selection bias. Other single-arms studies have not been borne out in Phase III trials. If the results do hold up following a trial with FOLFIRINOX, then we could move on to a Phase III trial using a hypofractionated radiation schedule. I think that would be a feasible next step.

“With these systemic treatments and shorter radiation schedule, I think things are starting to change in pancreatic cancer,” he said. □