[News * Analysis * Commentary * Controversy]

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Fatigue: The Forgotten Symptom?

BY HEATHER LINDSEY

A new study shows that few oncologists are following the National Comprehensive Cancer Network guidelines for treating cancer-related fatigue in their patients with advanced disease. Here's the surprising news about the probable reasons. *Page 26*

ASH Annual Meeting: Highlights & Perspective pp.10,20,23,29

Remembering Pioneering Hematopathologist Costan Berard p.5

Pancreatic Cancer Advances from the GI Cancers Symposium pp.6,8

[ALSO]

PERIODICALS

Pancreatic Cancer: Adjuvant S-1 'Significantly' Prolongs Overall Survival

BY RABIYA S. TUMA, PHD

"For the first time we now have another option that looks superior to gemcitabine in this setting."

SAN FRANCISCO—Patients treated with S-1 chemotherapy after resection for pancreatic cancer have significantly better overall survival compared with patients who received gemcitabine, researchers reported during a news conference for the Gastrointestinal Cancers Symposium (***Abstract 145***).

In the Phase III randomized controlled trial, two-year overall survival in S-1 treated patients was 70 percent compared with 53 percent for gemcitabine-treated patients, said the lead investigator, Katsuhiko Uesaka, MD, PhD, Medical Deputy Director at the Shizuoka Cancer Center Hospital in Japan.

"S-1 may be considered the new standard treatment for resected pancreatic cancer patients, at least in Japan," he concluded.

When asked whether these data are likely to be transferable to the U.S. patient population, he noted that prior studies indicate that Caucasian patients have different responses to S-1 compared with Asian patients, including a substantially higher rate of diarrhea in Caucasian individuals. For example, he said, that while S-1 is approved for use in Europe for the treatment of gastric cancer, it is used at a lower dose (25 mg/m^2 twice daily for three weeks, followed by one week off) relative to the dose used in the current pancreatic cancer trial (40-60 mg based on body surface twice daily for four weeks, followed by two weeks off).

"If the dose and schedule are optimized, I expect someday it will be applicable for Caucasian patients with pancreatic cancer," Uesaka said.

'Very Impressive, Incredibly Promising'

"The data speak for themselves," said pancreatic cancer specialist Kenneth Yu, MD, Assistant Professor at Memorial Sloan-Kettering Cancer Center. "The results that were presented are very impressive and, I think, will lead to a lot more discussion about whether or not S-1 can be developed in the U.S. population. But certainly these are incredibly promising results."

The trial, called JASPAC 01, enrolled a total of 385 patients who had undergone potentially curative resection for pancreatic cancer. Within 10 weeks of surgery, patients were randomly assigned to receive either gemcitabine (at 1,000 mg/m^2 on days 1, 8, and 15 every four weeks for six courses) or S-1 (four six-week cycles).

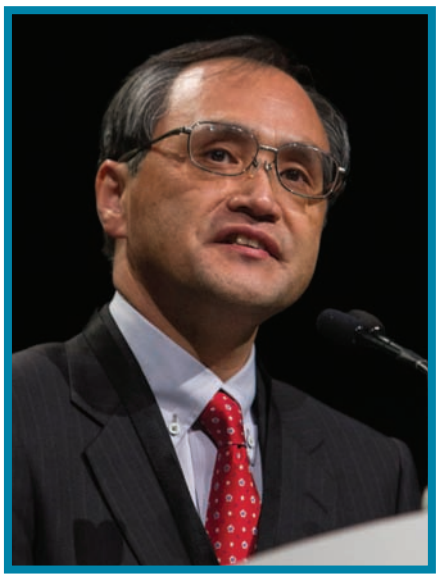
The prespecified boundary for the non-inferiority trial was 1.25, with an expected hazard ratio of 0.87. Patients were enrolled between April 2007 and June 2010.

The data safety monitoring board recommended immediate publication of the data given the magnitude of the survival benefit.

Following a preplanned interim analysis in August 2011, the data safety monitoring board recommended immediate publication of the data given the magnitude of the survival benefit. The results are statistically significant for both non-inferiority and superiority, based on a log-rank test.

There were substantial differences in adverse events between the two arms. Patients in the gemcitabine arm experienced more hematologic side effects, whereas patients in the S-1 arm had more gastrointestinal side effects.

The most common grade 3/4 non-GI adverse event was leukopenia, which occurred in about 39 percent of patients in the gemcitabine arm and about nine percent in the S-1 arm, followed by anemia (17% vs. 13%), thrombocytopenia (9% vs. 4%), elevated AST (5% vs. 1%) and elevated ALT (4% vs. 0.5%).



KATSUHIKO UESAKA, MD, PHD: "If the dose and schedule are optimized, I expect someday the results will also be applicable for Caucasian patients."

The most common grade 3/4 GI side effect was diarrhea (0% in the gemcitabine arm vs. about 5% in the S-1 arm) followed by stomatitis (0% vs. 3%), and vomiting (1.0% vs. 2%). Anorexia was more common in the gemcitabine arm than in the experimental arm (about 6% vs. 8.0%); fatigue was more common in the S-1 arm (4.7% vs. 5.4%).

"Pancreatic cancer remains highly lethal worldwide, but one-third of patients can undergo resection with curative intent," said the moderator of the news conference, Neal J. Meropol, MD, Chief of the Division of Hematology and Oncology in the Department of Medicine at University Hospitals Case Medical Center and Case Western Reserve University School of Medicine. "Among these patients, we've viewed gemcitabine as the standard adjuvant therapy to improve survival over surgery alone.

"For the first time we now have another option that looks superior to gemcitabine in this setting—improving the cure rate for pancreatic cancer that is resectable."

→NAB-PACLITAXEL

continued from page 6

considered. "Patients with very good performance status—those with PS0—have the option of either FOLFIRINOX or nab-paclitaxel plus gemcitabine, whereas those with the lesser PS may be more suited for the nab-paclitaxel plus gemcitabine."

The decision will also depend on patient preferences, he added. For example, if patients are particularly concerned about fatigue or do not want to carry an infusion pump for 48 hours every two weeks, they may prefer nab-paclitaxel plus gemcitabine.

At the end of his discussion, Philip emphasized the need for more progress in pancreatic cancer. "Nab-paclitaxel alone with gemcitabine or in combination with other agents must be considered for further development in earlier-stage disease and as a backbone for adding in biologicals," he said.

This trial "is [only] the fourth positive trial in pancreatic cancer in more than four decades. We really need to do better."

For his part, Von Hoff said he thinks this new regimen will help further progress in the field because it stabilizes patients. And that, he told *OT*, is critical for testing other agents and seeing the effect of other agents in these patients. "If we get the tumors to shrink, we have the opportunity to do other things for these patients."

The study was funded by Celgene. Von Hoff has received honoraria and research funding from the company and has served as a paid consultant for the company. His coauthors on the study reported similar information. Philip reports receiving funds or being a consultant for several companies, but did not report any association with Celgene.