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Zosia Chustecka has disclosed no relevant financial relationships.

From Medscape Medical News Best Survival Data Ever Reported in Metastatic Pancreatic Cancer



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June 11, 2010 (Chicago, Illinois) — Results from a phase 3 study of metastatic pancreatic cancer showing the best survival time ever reported in such a setting have led to calls for a new standard of care in this disease.

Gemcitabine has been a cornerstone of pancreatic cancer treatment for 15 years now, used alone or more recently in combination with erlotinib (*Tarceva*), but the new results suggest that it should be replaced with the FOLFIRINOX combination (5-fluorouracil, leucovorin, irinotecan, and oxaliplatin).

In a phase 3 trial conducted in 342 patients, this combination resulted in an overall survival of 10.4 months, compared with 6.8 months with gemcitabine alone (hazard ratio [HR], 0.57; $P < .0001$). After 1 year, 48.4% of patients who received the combination were still alive, compared with 20.6% of those who received gemcitabine alone. Progression-free survival significantly improved to 6.4 months with the combination, compared with 3.4 months with gemcitabine alone (HR, 0.47; $P < .0001$).

These results were reported by Thierry Conroy, MD, from the Centre Alexis Vautrin, Vandoeuvre les Nancy, France, here at the American Society of Clinical Oncology (ASCO) 2010 Annual Meeting. The trial (known as PRODIGE 4/ACCORD 11) was conducted at 48 centers across France, he said.

Dr. Conroy pointed out that the 10-month overall survival seen with the combination is the longest that has ever been reported in a phase 3 trial in this setting, and concluded that FOLFIRINOX should become the new international standard of care for patients with metastatic pancreatic cancer.

Toxicity of 3-Drug Regimen

He cautioned that this combination should be used only in patients with normal or near normal levels of bilirubin and good performance status. It is more toxic than gemcitabine alone, but "overall it has very manageable toxicity," he said. There was more febrile neutropenia reported in the combination group than in the gemcitabine group (5.4% vs 0.6%). The combination was associated with peripheral neuropathy (9% of patients) and alopecia (11%), whereas gemcitabine use was not associated with these adverse events.

However, emphasizing the adverse effects reported with the combination, which included grade 3 or 4 neutropenia in 46% and fatigue in 25% of patients, discussant Margaret Tempero, MD, from the University of California, San Francisco, described the toxicity as "very concerning."

"I am not sure" that FOLFIRINOX should become the new international standard of care for metastatic pancreatic cancer, she said, and cautioned that "enthusiasm must be tempered by its attendant side effects." Patients receiving this regimen will need access to good supportive care and a capable biliary team, she added.

Nevertheless, Dr. Tempero said this was "ground-breaking work," and added that this approach should now be advanced to "the adjuvant setting, where we can accept a regimen with more toxicity."

Also unsure about whether this combination would become a worldwide standard of care was Charles Blanke, MD, from the University of British Columbia in Vancouver, who chose this study as one of the highlights of the day. He said the study was "very well conducted," but expects that the medical community will want confirmation from a North American trial.

"This trial has got us all talking," said John Marshall, MD, director of clinical research at the Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, in a [video review](#) of ASCO gastrointestinal cancer news for *Medscape Oncology*. He said it looks as if, after 15 years, gemcitabine might be replaced as the standard of care, but he did wonder if all 3 drugs in the FOLFIRINOX regimen were necessary, and whether 2 drugs would work just as well.

The trial was supported by Amgen and grants from the French government and the French league against cancer. Dr. Conroy and colleagues have disclosed no relevant financial relationships. Dr. Marshall reports serving as a consultant/advisor or speaker and receiving research grants and remuneration from Amgen, Genentech, and Roche.

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