Improving Quality of Life for Patients with Metastatic Pancreatic Cancer

Reduced Chemotherapy Regimen Shown as Effective but Less Toxic than Standard Dosing

BY ED SUSMAN

SAN FRANCISCO—Patients with metastatic pancreatic cancer appear to have similar outcomes but less adverse events if they are given a reduced regimen of standard gemcitabine and nab-paclitaxel, according to data reported here at the Gastrointestinal Cancers Symposium (***Abstract 366***).

The meeting is co-sponsored by the American Gastrointestinal Association Institute, the American Society of Clinical Oncology, the American Society for Radiation Oncology, and the Society of Surgical Oncology.

"A less intense regimen of gemcitabine plus nab-paclitaxel maintains efficacy while significantly reducing toxicity and cost among patients with metastatic pancreatic cancer," said Kavya Krishna, MD, a fellow in hematology/oncology at Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

"Instead of three weeks of treatment and one week off, we are treating patients every other week," she said in an interview at her poster study. "We are reducing the amount of gemcitabine and nab-paclitaxel by one-third."

In the Phase III clinical trial by Daniel von Hoff, MD, et al published in October in the *New England Journal of Medicine* (***369:1691-1703***) showing increased survival for combined gemcitabine and nab-paclitaxel, progression-free and overall survival times were 5.5 and 8.7 months, respectively. Survival times in the new study were 4.8 months for median survival and 11.1 months for overall.

"We are suggesting that our regimen is equivalent to the standard treatment. Patients seem to have a sustained response and we have patients on this therapy tolerate it well going to several cycles. We treat until there is disease progression or unacceptable toxicity," Krishna said.

"Based on data suggesting that biweekly administration of gemcitabine-based combinations preserves efficacy and improves the toxicity profile, our institution adopted a modified regimen of gemcitabine plus nab-paclitaxel. We adapted the every-other-week regimen of giving gemcitabine from our clinical experience with patients who would skip a week and seemed to do as well as patients treated every three weeks before taking off one week. And there are clinical trials that indicate that-every-other-week nab-paclitaxel is effective in treating diseases such as lung cancer."

The regimen was better tolerated and resulted in less hematological toxicity (known to be a particular problem with gemcitabine)—"In the metastatic setting we have been using the every-other-week gemcitabine even before we adopted this regimen," Krishna said.

"The most commonly used regimen is to treat with gemcitabine on Days 1, 8, and 15 of a 28-day cycle. The gemcitabine plus nab-paclitaxel regimen uses the same treatment schedule. Now we administer gemcitabine plus nab-paclitaxel on Day 1 and Day 15. We have dose-delay and dose-reduction data, but we didn't record discontinuation data because it is a smaller patient population and most of the patients went off therapy because the disease progressed."

Regarding the apparent increase in median overall survival of 11.1 months, she said: "Another factor in this patient population was that they didn't get beat up by the chemotherapy. They still had a pretty reasonable performance status so once they progressed they were able to go on to second-line and third-line therapies. That's why the overall survival is so much better than progression-free survival."

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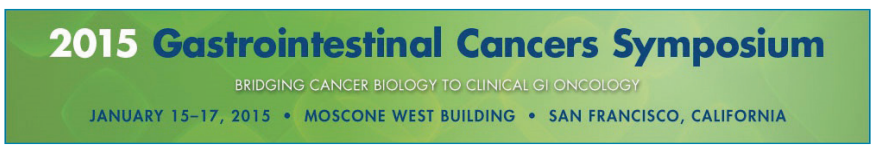

"A less intense regimen of gemcitabine plus nab-paclitaxel maintains efficacy while significantly reducing toxicity and cost among patients with metastatic pancreatic cancer."

"Pancreatic cancer is an especially difficult diagnosis, so weighing the survival benefit of available treatments against how treatment side effects will impact a patient's remaining life is a critically important part of the treatment-planning process."

Not Ready to Use Routinely

Asked for his perspective, Tony Philip, MD, an attending physician in hematology/oncology at North Shore-Long Island Jewish Cancer Institute and Assistant Professor of Medicine at Hofstra North Shore-LIJ School of Medicine, said: "This study gives me another option if I had a patient who was older or frail and wanted to give a less-intensive chemotherapy regimen. However, I don't think we have enough information now to use it routinely with people who are in good performance status.

"This is a single-institution study, and it is not compared with anything. I think we need to take these results with a grain of salt. There needs to be a prospective randomized trial comparing every-other-week treatment with three weeks on, one week off therapy."

Cost Savings

The researchers pointed out that a switch to an every-other-week

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Ramucirumab Slows Progression of Advanced Colorectal Cancer

BY ED SUSMAN

SAN FRANCISCO—The addition of the targeted agent ramucirumab modestly extends the progression-free survival of patients with advanced colorectal cancer when the new drug is administered in a second-line setting, researchers reported here at the Gastrointestinal Cancers Symposium (***Abstract 512***).

The meeting is co-sponsored by the American Gastroenterological Association Institute, American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology.

While the Phase III international trial, called RAISE, which included 1,072 patients, achieved its statistical goal, the actual median survival improvement was just 1.6 months—about six weeks—when ramucirumab was added to FOLFIRI (fluorouracil, leucovorin and irinotecan) when compared with the FOLFIRI treatment alone, Josep Tabernero, MD, PhD, Director of the Vall d'Hebron Institute of Oncology in Barcelona, Spain, said in an ASCO telephone briefing for reporters earlier this week.

"The RAISE study met its primary endpoint. A statistically significant overall survival benefit was observed for ramucirumab plus FOLFIRI versus FOLFIRI in metastatic colorectal cancer after progression on first-line therapy. Ramucirumab is an effective new treatment option for second-line treatment, including patients with poor prognosis."

In the study, which received funding from Eli Lilly, patients assigned to ramucirumab achieved a median overall survival of 13.3 months compared with 11.7 months for patients assigned to the FOLFIRI combination alone. That difference represented a 16 percent reduction in the risk of death and was statistically significant (P=0.0219), he said.

Ed Susman

JOSEP TABERNERO, MD: "It is very encouraging that we now have another safe option that adds benefit to standard chemotherapy in this second-line setting."

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> "Overall, treatment with ramucirumab plus FOLFIRI was well tolerated, and the adverse events were manageable."

Progression-free survival was also improved with ramucirumab, increasing from a median of 4.5 months with FOLFIRI alone to a median of 5.7 months with the addition of ramucirumab—a difference of 1.2 months.

Tabernero reported that objective responses to treatment were observed in 13.4 percent of the patients assigned to ramucirumab compared with 12.5 percent of patients receiving just the FOLFIRI regimen, but that was not statistically significantly different.

Patients Seen in Everyday Practice

"Advanced colorectal cancer is an incurable disease, and it is particularly difficult to treat after initial therapy stops working," he said. "Our study also

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MODIFIED GEMCITABINE/ NAB-PACLITAXEL

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regimen also results in substantial cost savings—an estimated $5,500 per patient per month of treatment. "That figure does not include the cost for growth factors used in treating neutropenia," Krishna said. "Neulasta [pegfilgrastim] is pretty expensive too. In the clinical trial the rate of growth factor use was 26 percent, but in our experience with the every-other-week regimen, just eight percent of patients required growth factors.

"The combination of gemcitabine and nab-paclitaxel in pancreatic cancer is one of the most recent advances in pancreatic cancer treatment and has been shown to improve survival when compared with gemcitabine alone. But this improved survival comes with increased toxic side effects that can affect quality of life."

Study Specifics

She and her colleagues identified 69 patients with pancreatic cancer who received the modified regimen of gemcitabine and nab-paclitaxel. Forty nine had previously untreated metastatic pancreatic cancer and the remaining 20 had either progressed on other chemotherapy treatments or had locally advanced or borderline resectable disease. The patients' median age was 65.

Overall, less than two percent of patients had severe neurological toxicities compared with 17 percent in the previous Phase III study using the three-week-on, one-week-off schedule; 10 percent of patients had severe low white blood cell counts compared with 38 percent of patients in the Phase III study.

Gives Immune System Time to Recover

The study's senior author, Tanios Bekaii-Saab, MD, Section Chief of Gastrointestinal Oncology at the James and Associate Professor of Medicine, explained that shifting to a regimen of every other week gives the immune system time to recover between chemotherapy sessions and results in less overall toxicity. It is also more convenient for patients since it means fewer visits to the infusion center to receive chemotherapy.

"Pancreatic cancer is an especially difficult diagnosis, so weighing the survival benefit of available treatments against how treatment side effects will impact a patient's remaining life is a critically important part of the treatment planning process," Krishna said.