New treatments for pancreatic cancer

FOLFIRINOX, a combination chemotherapy regimen consisting of oxaliplatin (Eloxatin, generics), irinotecan (Camptosar, generics), fluorouracil (Adrucil, generics), and leucovorin (Fusilev, generics), was more effective than standard gemcitabine (Gemzar, generics) in increasing survival and delaying disease progression in patients with metastatic pancreatic cancer.

As the nation’s fourth-leading cause of death from cancer in 2010, pancreatic adenocarcinoma carries a grim prognosis: a 5-year survival rate of 6% in the United States as well as in Europe. Gemcitabine became the reference regimen after a randomized trial, published in 2003, showed the agent to improve median overall survival over fluorouracil (5.6 months vs 4.4 months), and subsequent trials of gemcitabine yielded median overall survival of 5.0 to 7.2 months. However, combining the drug with a variety of cytotoxic and targeted agents had not significantly increased patient survival.

Noting that oxaliplatin, irinotecan, fluorouracil, and leucovorin all had some activity against pancreatic cancer and no overlapping toxic effects, Thierry Conroy, MD, of France’s Nancy University and Centre Alexis Vautrin, and colleagues conducted phase 1 and phase 2 trials of FOLFIRINOX that demonstrated responses in persons with advanced pancreatic cancer. The current project is a phase 2-3 trial in which the combination therapy is further compared against single-agent gemcitabine in persons with metastatic pancreatic cancer.

As Conroy and associates described in the New England Journal of Medicine (2011;364[19]:1817), 342 people with metastatic pancreatic cancer were randomized to FOLFIRINOX or gemcitabine for 6 months. Median overall survival was 11.1 months in the FOLFIRINOX group compared with 6.8 months for the gemcitabine group. Median progression-free survival was 6.4 months and 3.3 months, respectively.

FOLFIRINOX did have a less favorable safety profile; however, the regimen significantly increased time to definitive deterioration of quality of life.

NEW DRUG INDICATIONS IMPROVE PROGNOSIS

The FDA has approved indications for two drugs for a rare, slow-growing pancreatic cancer known as PNET (progressive neuroendocrine tumors located in the pancreas).

Everolimus (Afinitor), an mTOR inhibitor, is approved for use in renal cell carcinoma and subependymal giant cell astrocytoma. Its new indication is for PNET in persons whose tumors have metastasized or cannot be removed surgically. The most commonly reported side effects in the treatment group were stomatitis, rash, diarrhea, fatigue, edema, abdominal pain, nausea, fever, and headache.

Sunitinib (Sutent) is also already on the market for late-stage renal cell carcinoma and for GI stromal tumor. The most commonly reported side effects were diarrhea, nausea, vomiting, fatigue, anorexia, high BP, asthenia, abdominal pain, changes in hair color, stomatitis, and neutropenia.
IN WOMEN undergoing treatment for low-risk gestational trophoblastic neoplasia (GTN), one dose of dactinomycin (Cosmegen) every 2 weeks results in a higher complete response rate than a weekly dose of methotrexate (Trexall, generics), the more commonly used drug.

Whereas cervical or endometrial cancers develop from uterine cells, GTNs start in cells that would normally develop into the placenta during pregnancy. These highly curable tumors include hydatidiform moles, which are caused by overproduction of placental tissue, and choriocarcinoma, a fast-growing form of cancer in the uterus. With no consensus on the best regimen for the primary treatment of low-risk GTNs, a research team compared the two commonly used single-drug regimens in 216 patients over the course of 8 years.

Both regimens were well-tolerated, but biweekly IV dactinomycin 1.25 mg/m² was statistically superior to weekly intramuscular methotrexate 30 mg/m², with complete response rates of 70% and 53%, respectively, in women without choriocarcinoma and with a risk score of 0 to 4. The investigators noted that both regimens were less effective if the risk score was 5 or 6 or if the diagnosis was choriocarcinoma (J Clin Oncol. 2011;29[7]:825).

“Both chemotherapy drugs are effective in treating this kind of neoplasia, but this trial proved that dactinomycin is the best first-line regimen,” remarked coinvestigator David Scott Miller, MD, head of gynecologic oncology at the University of Texas Southwestern Medical Center in Dallas.

Nevertheless, “The study … does not change standard practice at this time,” according to an accompanying editorial (J Clin Oncol. 2011;29[7]:786). “Most treating physicians will continue to use single-agent methotrexate … and will reserve the use of dactinomycin … for methotrexate resistance or toxicity.”

In other news:

Cognitive problems are long lasting in HCT patients

ALTHOUGH many people who undergo allogeneic hematopoietic cell transplantation (HCT) recover significant cognitive function posttransplantation, more than 40% of survivors evaluated in one recent study still experienced deficits 5 years later.

Research has demonstrated that patients experience cognitive problems both before and after high-dose treatment followed by HCT, with partial recovery by the 1-year mark. Karen L. Syrjala, PhD, of the Fred Hutchinson Cancer Research Center in Seattle, Washington, led a team that prospectively examined the trajectory and extent of long-term cognitive dysfunction in patients 1 to 5 years after treatment.

The investigators administered standardized neuropsychological tests to measure information-processing speed, verbal memory, executive function, and motor dexterity and speed in 92 survivors of HCT. The subjects were retested 80 days, 1 year, and 5 years posttransplantation. A total of 66 case-matched controls also were tested at the 5-year time point.

Survivors recovered significant cognitive function from 80 days to 5 years posttransplantation in all tests except verbal recall. In the 1-to-5-year time frame, verbal fluency and executive function improved, but motor dexterity remained below that of controls.

Global deficit score (GDS; representative of overall impairment) indicated that 41.5% of survivors and 19.7% of controls had mild or greater deficits. “Although neurocognitive function improved from 1 to 5 years after HCT, deficits remained for more than 40% of survivors,” affirmed the researchers in the Journal of Clinical Oncology. “Risk factors, mechanisms, and rehabilitation strategies need to be identified for these residual deficits.”
Cancer toll is greater on bisexual and gay adults

HOMOSEXUAL men were 1.9 times more likely to report a cancer diagnosis than were heterosexual men, and lesbian and bisexual women who survived the disease were at least twice as likely to report fair or poor health than were heterosexual female survivors.

The analysis yielding these findings was undertaken by a team headed by Ulrike Boehmer, PhD, of the Boston (Massachusetts) University School of Public Health, to address what the investigators deemed an information gap. “Lesbian, gay, and bisexual populations are not part of cancer surveillance, resulting in scarce information about the cancer survivorship of these populations,” they noted in the journal Cancer.

Data culled from the 2001, 2003, and 2005 California Health Interview surveys revealed that 7,252 women and 3,690 men had received a cancer diagnosis as adults. Although more homosexual men than heterosexual men reported a cancer diagnosis, the two groups had similar assessments of their health status in survivorship.

Conversely, no significant differences in cancer prevalence according to sexual orientation were seen among the women, but lesbian and bisexual female survivors were 2.0 and 2.3 times more likely, respectively, than female heterosexual survivors to report fair or poor health.

Risk for left-sided CRCs is higher

IN A LARGE study of older adults, the risk of new or missed left-sided colorectal cancers (CRCs) jumped from 4% after colonoscopy to 12% after flexible sigmoidoscopy.

This quadrupling of the new/missed CRC rate was noted by Yize Richard Wang, MD, PhD, of the Mayo Clinic in Jacksonville, Florida, and collaborators. In research presented at the Digestive Disease Week conference, held May 7-10, 2011, in Chicago, Illinois, the investigators examined data from all patients in the Surveillance, Epidemiology, and End Results Medicare (SEER-Medicare) who were at least 67 years old when undergoing a lower endoscopy from 1998 to 2005 and who were subsequently diagnosed with CRC within 3 years.

After excluding high-risk patients with preexisting inflammatory bowel disease, family history of GI malignancy, or personal history of colonic polyps, Yang and colleagues included 52,236 men and women in the study. Among them, 3,523 flexible sigmoidoscopies and 57,412 colonoscopies were performed within 36 months prior to CRC diagnosis.

Detected CRCs were defined as those diagnosed within 6 months after a lower endoscopy.

Further research is needed to determine whether bowel preparation or endoscopist attributes were factors.

- New or missed CRCs were defined as those diagnosed 6 to 36 months after a lower endoscopy.

For flexible sigmoidoscopy, the study sample was limited to left-sided CRCs distal to the splenic flexure. Within the 12% rate of new or missed left-sided CRCs recorded after flexible sigmoidoscopy, the highest rate was seen in the descending colon.

“Among older patients, the risk of new or missed left-sided CRCs quadrupled after flexible sigmoidoscopy compared with colonoscopy,” stated the authors, and suggested that further research is needed to determine whether bowel preparation or endoscopist attributes were factors.

In the News

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In the News

Most common cancers among men

156.9 Prostate cancer cases per 100,000
80.5 Lung cancer cases per 100,000
52.7 Colorectal cancer cases per 100,000