POLO trial for advanced pancreatic cancer: a new standard of care

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Hedy Kindler, MD Credit: Robert Kozloff, UChicago

Treatment with the drug olaparib significantly reduced the risk of disease progression or death from metastatic pancreatic cancer, according to findings from the recently completed, international, phase-

III POLO (Pancreas cancer OLaparib Ongoing) trial.

Olaparib (trade name LYNPARZA, jointly developed and commercialized by AstraZeneca and Merck) is a PARP inhibitor. It targets cancer cells that have a defect in DNA damage repair.

Progression-free survival, the primary endpoint in this study, was 7.4 months on the olaparib arm, and 3.8 months on the placebo arm. From 6 months onwards, more than twice the proportion of patients on the olaparib arm were progression-free.

"This is clearly a practice changing trial," said cancer specialist Hedy Kindler, MD, lead author of the study and a professor of medicine at the University of Chicago. "It will change how we think about patients with metastatic pancreatic cancer and who should consider germline testing."

This global study—to be featured at the Plenary Session at ASCO, the annual meeting of the American Society for Clinical Oncology in Chicago, and published online June 2 in the *New England Journal of Medicine*—is the first from a randomized trial to validate a targeted treatment in a biomarker-selected population of pancreatic cancer patients.

Pancreatic cancer tends to be "very resistant to treatment," said Kindler. "There are few drug regimens with significant activity, and most clinical trials of new agents are unfortunately negative."

"This is a devastating disease, with the briefest survival of any solid tumor," Kindler said. Pancreatic cancer will soon become the second leading cause of cancer death in the United States.

The randomized, double-blind, placebo-controlled phase III POLO trial focused on a selected group of patients with metastatic pancreatic cancer

who had inherited mutations in the BRCA 1 and 2 genes.

The study screened 3,315 patients at 119 centers on 4 continents for germline BRCA mutations, which were detected in 7.5 percent of patients. After they received at least 16 weeks of platinum-based chemotherapy, 154 patients were randomized to receive either olaparib or placebo. Treatment continued until radiological exams detected progression of the disease.

Beyond the improvement in progression-free survival, there were no new safety concerns with olaparib. Health-related quality of life was maintained with treatment.

"About a quarter of these patients responded to olaparib for a median of two years, which is truly remarkable in a disease where most patients survive for less than a year," said Kindler, an internationally recognized authority on the treatment of pancreatic cancer and malignant mesothelioma.

"That's almost unheard of," she added. "When we saw the progression-free survival data, my first reaction was a little scream of joy. We finally made real progress in the treatment of a subset of patients with advanced pancreatic cancer."

One of Kindler's patients has been on the study for more than two years. "He's leading a normal life," she said, "feeling fine, living well and taking his pills twice a day."

"In a disease where almost nothing works," she added, "it is truly remarkable to finally have a drug that makes such a difference, even for a small subset of patients."

"A strategic approach of first-line platinum-based chemotherapy

followed by maintenance olaparib treatment should become a new standard of care for patients with metastatic pancreatic cancer who have a germline BRCA mutation," Kindler said.

Provided by University of Chicago Medical Center