Destruction caused by the 1986 Chernobyl nuclear power plant explosion in Ukraine.

The results also quantify molecular aspects of the cancers, including the relative rates of driver alterations. "It's not a breakthrough in the sense that it's all novel," he says, "but it's very definitive with the answers that it provides." *–Catherine Caruso* ■

More PARP Inhibitors in Pancreatic Cancer?

The treatment options for patients with germline *BRCA*-mutated pancreatic cancer expanded 18 months ago when the FDA approved olaparib (Lynparza; AstraZeneca) as a maintenance therapy for patients who initially responded to platinum-based chemotherapy.

But the PARP inhibitor was approved only for patients with metastatic adenocarcinomas harboring inherited mutations in *BRCA1* or *BRCA2*, genes involved in homologous recombination repair (HRR). People with other HRR deficiencies, and those with nondisseminated disease or other tumor histologies, were left with standard, more toxic chemotherapeutic regimens.

New trial data now suggest that PARP blockade may benefit more patients with HRR-related vulnerabilities. "This really is a big and important step forward for the field of pancreatic cancer," says James Cleary, MD, PhD, of Dana-Farber Cancer Institute in Boston, MA, who was not involved in the study.

The single-arm trial involved 42 patients with pancreatic cancer who, after responding to chemotherapy for a sustained period—typically 16 weeks or longer—switched to maintenance treatment with the PARP inhibitor rucaparib (Rubraca; Clovis Oncology). Clinical responses occurred in 42% of participants with measurable disease. These included not only patients with germline *BRCA* mutations—confirming the olaparib findings—but also one person with a somatic *BRCA2* alteration and several individuals with inherited mutations in *PALB2*, another gene involved in DNA repair.

Also, the trial included patients with locally advanced disease, revealing a trend toward greater clinical benefit among those with the lowest disease burden. Plus, one study participant with squamous cell carcinoma, a rare subtype of pancreatic cancer, had a complete response. Median progression-free survival was about 13 months; median overall survival was nearly 2 years (J Clin Oncol 2021 May 10 [Epub ahead of print]).

"We hope that this study will now open the door for a small additional number of patients to receive a drug that might work for them," says Kim Reiss, MD, of the University of Pennsylvania's Abramson Cancer Center in Philadelphia, who led the trial.

Looking to further expand indications for PARP inhibitors, Reiss is now leading a 152-person, placebo-controlled trial to evaluate olaparib as an adjuvant treatment for patients with *BRCA1/2* or *PALB2* mutations whose tumors have been surgically removed.

She and others are also evaluating PARP inhibitors as maintenance therapy for patients with a broader range of HRR deficiencies—focusing on genes such as *RAD51C* and *BRIP1* that, when mutated, seem to confer sensitivity to maintenance chemotherapy.

Can those individuals be safely switched over to a PARP inhibitor? To find out, "we really need to drill down on these genes," says Eileen O'Reilly, MD, of Memorial Sloan Kettering Cancer Center in New York, NY.

Several research teams are testing that idea in patients with somatic or germline mutations in more than a dozen HRR genes. Individuals who lack known mutations but show exceptional responses to first-line platinum-based therapy, making them likely to benefit from PARP blockade, are often eligible to enroll. Many of these trials are also combining PARP inhibitors with immunotherapy because the genomic instability wrought by HRR deficiencies may make pancreatic cancers more receptive to checkpoint blockade.

If PARP inhibition benefits patients in these situations, it could become an option for 15% to 20% of those with pancreatic cancer. *–Elie Dolgin* ■

NOTED

Bristol Myers Squibb announced that **the FDA approved the PD-1 inhibitor nivolumab (Opdivo) for patients with esophageal or gastroesophageal junction cancer** who have residual pathologic disease after surgery and neoadjuvant chemoradiotherapy. The approval was based on the phase III CheckMate-577 trial in which nivolumab extended the median disease-free survival by 11.4 months compared with a placebo.

The U.S. Supreme Court declined to review a federal appeals court decision to include two U.S. scientists on immunotherapy patents describing the PD-1 pathway. The scientists—Gordon Freeman, PhD, of Dana-Farber Cancer Institute in Boston, MA, and Clive Wood, PhD, of Boehringer Ingelheim—will be added to the patents, which were initially issued to Ono Pharmaceutical and Tasuku Honjo, MD, PhD, of Kyoto University in Japan.

The TROP2-directed antibody–drug conjugate **datopotamab deruxtecan (DS-1062; AstraZeneca/Daiichi Sankyo) may be active in patients with metastatic triple-negative breast cancer** (TNBC) who have received other therapies. In a phase I trial, five of 21 evaluable patients responded to the drug, and four more responses await confirmation; 11 patients experienced stable disease. Findings were presented at the 2021 European Society of Medical Oncology Breast Cancer Virtual Congress.

Genentech's BRAF inhibitor **vemurafenib (Zelboraf) and anti-CD20 agent rituximab (Rituxan) may lead to durable responses in hairy-cell leukemia** (N Engl J Med 2021;384:1810–23). In a phase II trial, the drug elicited complete responses in 26 of 30 patients with relapsed/refractory disease, and 85% of patients who responded were relapse-free at a median follow up of 34 months.

African American women with TNBC may have a higher mortality rate than their white counterparts (JAMA Oncol 2021 May 13 [Epub ahead of print]). Researchers conducted a retrospective analysis of 23,123 women diagnosed with nonmetastatic TNBC between 2010 and 2015, 25.3% of whom were African American. They found that African American women had a 28% increased risk of death compared with white women, in part due to lower rates of surgery and chemotherapy.

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