

# PARP Inhibitor Delays Pancreatic Cancer Recurrence

Most people who received Rubraca maintenance therapy experienced tumor regression or had stable disease.

May 6, 2019 By [Liz Highleyman](#)

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The PARP inhibitor Rubraca (rucaparib) may be a well-tolerated option to replace long-term chemotherapy for people with advanced pancreatic cancer with certain genetic mutations, according to findings from a small study presented at the recent 2019 American Association for Cancer Research (AACR) annual meeting in Atlanta.

“In this interim analysis, we are finding that patients with platinum-sensitive pancreatic cancer appear to benefit from treatment with single-agent rucaparib,” said Kim Reiss Binder, MD, of the University of Pennsylvania in Philadelphia, who gave an overview of the study at an AACR press conference. “Several patients had complete or partial responses with rucaparib treatment, suggesting that this therapy has the potential not only to maintain the disease but also to shrink the tumors in some instances.”

Often diagnosed at a late stage, pancreatic cancer is difficult to treat and has a high mortality rate. Around 5% to 8% of people with pancreatic cancer have BRCA mutations or associated PALB2 mutations, best known for their role in raising the risk of breast and ovarian cancer.

PARP inhibitors work by blocking poly (ADP-ribose) polymerase proteins, which play a role in DNA repair. Inhibiting PARP leads to more DNA breaks in cancer cells, which can halt cell division. People with BRCA mutations do not make proteins that fix this kind of DNA damage, so BRCA-related cancers are particularly susceptible to these drugs.

People with these mutations often respond well to platinum-based chemotherapy using drugs such as cisplatin or oxaliplatin. But ongoing treatment leads to cumulative toxicity that can have a detrimental effect on quality of life, leading researchers to explore better tolerated options for long-term maintenance therapy. Previous studies showed that [Rubraca](#) and another PARP inhibitor, [Lynparza \(olaparib\)](#), work well as maintenance therapy for ovarian cancer, and they are approved by the Food and Drug Administration for this purpose.

This Phase II trial evaluated Rubraca as a single-agent maintenance therapy for people with locally advanced or metastatic pancreatic cancer with BRCA1, BRCA2 or PALB2 mutations whose cancer

had stabilized with no further progression after at least four months of platinum-based chemotherapy. All participants received twice-daily Rubraca tablets until they experienced disease progression or unacceptable side effects.

Reiss Binder presented data from an interim analysis of 19 evaluable patients. Most (84%) were women, more than 90% were white and the median age was 61.

The overall response rate, meaning complete or partial tumor shrinkage, was 37% (or 41% among those with measurable disease when they started Rubraca), which included six partial responses and one complete response. Taking into account both tumor regression and stable disease for at least eight weeks, the disease control rate was 90%. Two people experienced disease progression, Reiss Binder reported.

The median progression-free survival after starting Rubraca, meaning patients were still alive without worsening of disease, was 9.1 months. The median overall survival was not reached because a majority of patients are still alive. Eight study participants have been on Rubraca for more than six months and two others for more than a year, with ongoing responses.

Treatment with Rubraca was generally well tolerated without dose-limiting toxicities, Reiss Binder reported. The most common adverse events considered possibly related to treatment included nausea, taste changes (dysgeusia), fatigue and elevated liver enzymes. No severe (grade 3 or higher) adverse events were reported. She noted that study participants had improved quality of life and were able to resume activities like traveling and teaching after stopping chemotherapy.

“Although this is very preliminary data, the fact that we’re seeing sustained clinical responses in some of these patients is very exciting,” Reiss Binder said in an [AACR press release](#). “Other than the recent tissue-agnostic approval of pembrolizumab [Keytruda] for patients with microsatellite instability-high tumors, there really is no other targeted therapy that has shown promise for patients with pancreatic cancer.”

A bit further along in development, the Phase III POLO trial showed that Lynparza is likewise effective as maintenance therapy for people with pancreatic cancer after platinum-based chemotherapy, according to a [recent announcement](#) by AstraZeneca.

These findings highlight the importance of genetic testing for germline (inherited) and somatic (tumor-specific) mutations in people with pancreatic cancer. “The presence of certain mutations can guide treatment strategies, and patients should know to ask their oncologist about getting tested,” Reiss Binder said.

[Click here](#) to read the AACR study abstract.

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