Clinical trial: Combination treatment extends progression-free survival in pancreatic cancers

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Halla Nimeiri, MD, health system clinician of Medicine in the Division of Hematology and Oncology and a member of the Robert H. Lurie Comprehensive cancer center of Northwestern University, was a co-author of the study published in the *Journal of Clinical Oncology*. Credit: Northwestern University

A combination treatment approach using two chemotherapy drugs improved treatment response and progression-free survival in patients with advanced pancreatic neuroendocrine tumors, according to a recent clinical trial published in the *Journal of Clinical Oncology*.

"These results suggest that the combination of capecitabine and temozolomide is a new validated standard of care and is a reasonable comparator control arm in future randomized studies, which are currently underway," said Halla Nimeiri, MD, health system clinician of Medicine in the Division of Hematology and Oncology and a co-author of the study.

Pancreatic neuroendocrine tumors (NETs) form in hormone-making cells in the pancreas, called islet cells. Patients with advanced forms of this cancer have few effective treatment options, and the lack of predictive biomarkers has made developing patient care strategies and new treatments a challenge.

Previous work, however, has suggested that combining the chemotherapy drug capecitabine with another chemotherapy drug called temozolomide, which is typically used to treat brain cancer, may improve treatment response and progression-free survival for patients who generally respond poorly to other treatment options.

"Temozolomide is an alkylating agent that induces DNA methylation at the O6 position of guanine, leading to DNA damage and cell death. Prior to this study, no prospective randomized studies have evaluated the antitumor activity of temozolomide alone or in combination with capecitabine in pancreatic NETs," said Nimeiri, who is also a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

In the current study, more than 130 patients with advanced pancreatic NETs were randomly assigned to receive either temozolomide alone or a combination of capecitabine and temozolomide, with a primary trial endpoint of progression-free survival.

Overall, average progression-free survival was 14.4 months for temozolomide-only group and 22.7 months for the capecitabine and temozolomide combination group. In a final analysis conducted five years after the conclusion of study participant enrollment, average overall survival was 53.8 months for the temozolomide group and 58.7 months for capecitabine and temozolomide group.

Additionally, the investigators found that the deficiency of MGMT, a DNA repair enzyme, was significantly associated with treatment response.

"National Comprehensive Cancer Network guidelines currently align with this efficacy outcome and currently recommend temozolomide plus capecitabine as the preferred regimen when tumor response is urgently needed for symptoms or debulking," Nimeiri said.

More information: Pamela L. Kunz et al, Randomized Study of Temozolomide or Temozolomide and Capecitabine in Patients With Advanced Pancreatic Neuroendocrine Tumors (ECOG-ACRIN E2211), *Journal of Clinical Oncology* (2022). DOI: 10.1200/JCO.22.01013

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