New drug shows encouraging survival in pancreatic cancer

August 14 2019

Meredith Morgan, Ph.D., Kyle Cuneo, M.D., and Ted Lawrence, M.D., Ph.D.
Credit: University of Michigan Rogel Cancer Center

A clinical trial testing a new drug in pancreatic cancer had promising initial results, report researchers from the University of Michigan Rogel

Cancer Center.

A phase 1 clinical trial looked at AZD1775, an inhibitor designed to block an enzyme called Wee1, which plays a role in DNA damage repair. The trial builds on almost 20 years of research at U-M focused on improving the treatment of pancreatic cancer that is too advanced for surgery.

Radiation and the chemotherapy drug gemcitabine, which are standard treatment for pancreatic cancer, both work by causing damage to DNA. But pancreatic cancer has a way of repairing that damage, which limits how effective these therapies can be. Rogel Cancer Center laboratory researchers, led by Meredith Morgan, Ph.D., found AZD1775 prevents pancreatic cancer from protecting itself against the effects of radiation and gemcitabine, while leaving normal cells relatively unaffected.

"If we can disable the DNA damage response in pancreatic cancer cells, it might eliminate treatment resistance and sensitize the cancer to the effects of both radiation and chemotherapy," says lead study author Kyle Cuneo, M.D., associate professor of radiation oncology at Michigan Medicine.

The trial enrolled 34 patients with locally advanced pancreatic cancer. Patients received AZD1775 in addition to radiation and gemcitabine. The goal of the study was to determine the maximum tolerated dose of AZD1775 in this combination. In the process, the researchers also found that this combination resulted in better than expected overall survival.

Pancreatic cancer is particularly known for spreading to distant parts of the body, part of the reason overall five-year survival is just 9%.

"If we're ever going to cure pancreatic cancer, we're going to need effective systemic treatment as well as local therapy. Our data suggests

that AZD1775 can do both," says senior study author Ted Lawrence, M.D., Ph.D., Isadore Lampe Professor and chair of radiation oncology at Michigan Medicine.

The median overall survival in the study was 22 months, with no progression for a median of nine months. A previous study using gemcitabine alone in a similar group of patients found overall survival of 12-14 months.

"Adding AZD1775 to radiation and gemcitabine was relatively well tolerated with encouraging survival results. Further studies with this promising combination are needed," Cuneo says.

More information: Kyle C. Cuneo et al, Dose Escalation Trial of the Wee1 Inhibitor Adavosertib (AZD1775) in Combination With Gemcitabine and Radiation for Patients With Locally Advanced Pancreatic Cancer, *Journal of Clinical Oncology* (2019). DOI: 10.1200/JCO.19.00730

Provided by University of Michigan