PAN1: Evaluating a potential predictive biomarker in the treatment of pancreatic cancer

The AGITG PAN1 trial was designed to assess whether a biomarker called hENT1 might be useful for selecting treatments for patients with advanced pancreatic cancer who would respond well to gemcitabine chemotherapy treatment.

Unfortunately, the study was closed due to lower than expected recruitment into the trial. Only 16 of the planned 80 patients were enrolled. Although promising results were seen, the number of patients was too small to draw any valid conclusions. Future larger-scale trials are necessary to establish a definitive answer to this question.

We appreciate the part played by those who volunteered to participate in this trial, their participation will help to improve the medical treatment of patients diagnosed with pancreatic cancer in the future. Here is a summary of the trial and results.

What was the trial about?

When the PAN1 study began, gemcitabine, a single chemotherapy was the main treatment for patients with locally advanced or metastatic pancreatic cancer. This treatment was only modestly effective. At this time, recent research had shown that some patients had abnormally low levels of hENT1, a protein involved in the transport of gemcitabine into tumour tissue cells and that this group of patients did not respond well to gemcitabine treatment.

Also, at this time, research on combination chemotherapy treatments, such as FOLFOX (oxaliplatin, 5-fluorouracil and leucovorin) had begun to be tested in patients diagnosed with pancreatic cancer. This treatment had been shown to increase their survival, although there were concerns around the toxicity of these treatments. The PAN1 study aimed to establish whether hENT1 could be used as a guide to determine whether patients would respond to gemcitabine, or should receive a combination therapy. A modified FOLFOX (mFOLFOX) treatment schedule was chosen as the combination therapy to be tested. This treatment had been shown to be acceptable and effective in pancreatic cancer patients in previous trials.

Comparing both treatments and hENT1 levels would allow researchers to determine the value of hENT1 as a predictive biomarker for selecting better treatment and as a prognostic marker, an indicator of expected results for pancreatic cancer patients.

How was the effect of treatment measured?

There were two measures of the effectiveness of the treatment compared with hENT1. The main measure was PFS (Progression-Free Survival), the time from beginning the study treatment to the return of the cancer. The other measure was overall survival, the time from beginning the study to the time the patient died from the cancer. Also recorded was the response rate, the number of participants whose tumours shrank or disappeared during treatment and any side effects experienced by the participants.

Was the new treatment better?

Of the 16 patients enrolled in this study; analysis of the results showed that those patients with high levels of hENT1 who were treated with gemcitabine survived for longer than those with low levels of hENT1.

For the patients who received mFOLFOX, there was no difference in survival time when high and low levels of hENT1 were compared.

Although these results are encouraging, given the small sample size, this may be due to chance. Larger studies are needed to allow a definitive conclusion to be made.
What were the side-effects of the treatment?

There were no unexpected side effects for either treatment.

How will the results help patients and doctors in future?

The results of the PAN1 study support further evaluation of hENT1 as a biomarker to help guide treatment selection for advanced pancreatic cancer.

What will the researchers do next?

The PAN1 trial has closed, and the AGITG will no longer be collecting information about patients. However, the results of this trial will inform the design of future studies in this area.

Where can I find out more about the trial?

The results have been presented at an international conference

Chua YJ, and others. Human equilibrative nucleoside transporter 1 (hENT1) in gemcitabine and FOLFOX (oxaliplatin, 5-fluorouracil and leucovorin)-treated patients with metastatic pancreatic cancer: The randomized phase II PAN1 study, at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium in San Francisco in January 2014.

Trial registration

Australian New Zealand Clinical Trials Registry

www.anzctr.org

Registration number ACTRN12610001047088

Australasian Gastro-Intestinal Trials Group

agitg.org.au