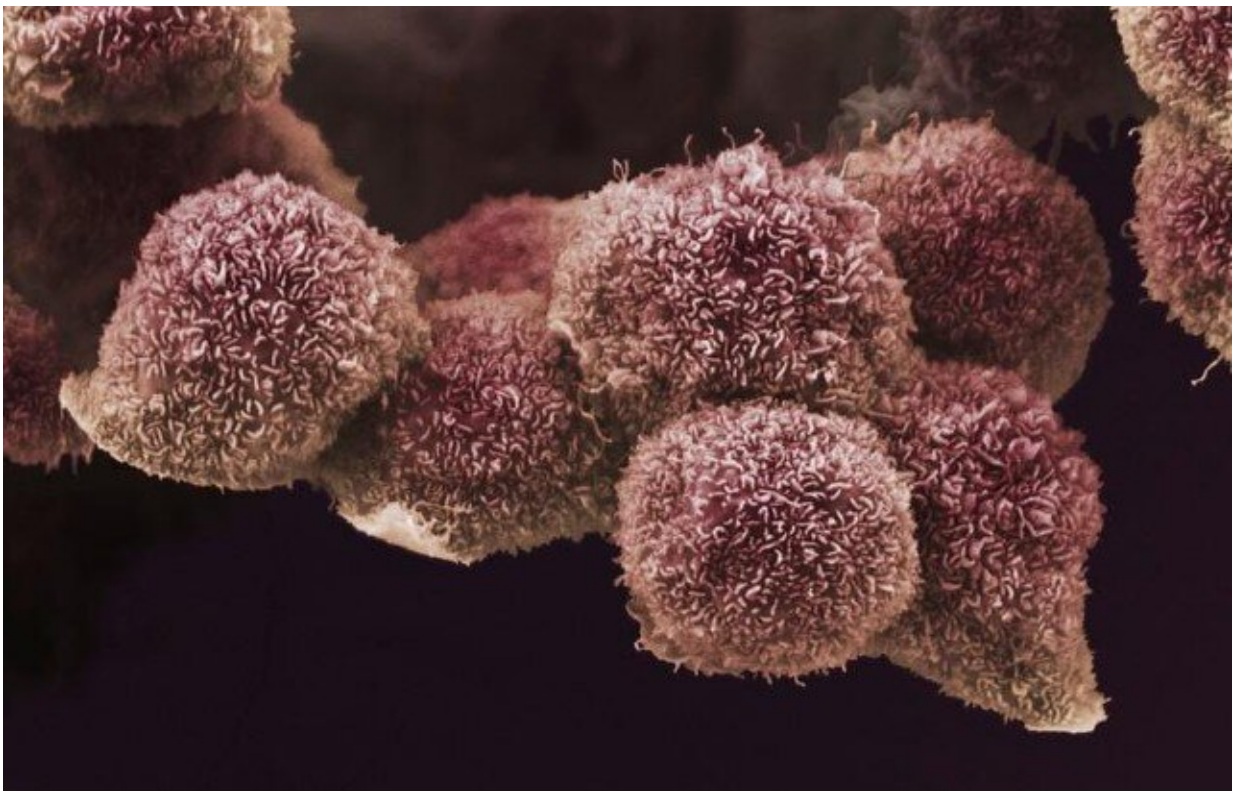


Clinical trial shows combination therapy with vitamin A is safe for patients with pancreatic cancer

September 25 2020, by Joel Winston



Pancreatic cancer cells grown in culture, SEM. Credit: Anne Weston, Francis Crick Institute. Attribution-NonCommercial 4.0 International (CC BY-NC 4.0)

A treatment combination involving the addition of a form of vitamin A

to the current standard treatment regimen for pancreatic cancer is safe for patients, according to an early phase clinical trial led by Queen Mary University of London.

Following the encouraging results of this phase I trial (STARPAC), published today in *Nature Communications*, a second clinical trial called STARPAC2 will now investigate whether the addition of this form of vitamin A, called ATRA, to standard chemotherapy can enhance the efficacy of treatment in patients with [pancreatic cancer](#).

There are around 10,300 new pancreatic cancer cases diagnosed in the UK each year and although this accounts for only 3 percent of the total cancer cases, pancreatic cancer has the lowest survival rate of all common cancers. It sadly claims the lives of approximately 9,200 people each year, and only around 7 percent of those diagnosed with this cancer type survive for five years or more. It is believed that pancreatic cancer will be the second most common cause of cancer mortality (after lung cancer) by 2030.

Chemotherapy and radiotherapy alone are relatively unsuccessful in treating pancreatic cancer, and while surgery to remove the tumor offers the best chance of survival, a lack of symptoms in the early stages of the disease means most patients are diagnosed when the cancer is advanced. A novel approach that is able to target the cancer more effectively is urgently required.

Vitamin A in the fight against pancreatic cancer

STARPAC was launched following research conducted by Professor Kocher's laboratory, which found that using ATRA to treat a particular type of cell, known as [stellate cells](#), within pancreatic tumors, restricted tumor growth. Stellate [cells](#) have an important role in normal tissue formation; however, they become corrupted in cancer and help to form

an impenetrable barrier, known as the stroma, around the pancreatic tumor.

Treating stellate cells with ATRA (a pre-existing drug used for the treatment of acne and some types of leukemia) was found to restore the vitamin A content of the cells, converting them from tumor-promoting cells to cells which have an anti-cancer effect. By combining this drug with chemotherapy in preclinical models, the team were able to disrupt the communication between the cancer cells and the surrounding stromal cells, leading to a reduction in cancer cell proliferation and invasion.

Trial to determine safety

To determine the safety of this treatment combination in the clinic, patients were recruited to the phase I STARPAC trial from Barts Health NHS Trust, Imperial College Healthcare NHS Trust, Guys and St Thomas' NHS Foundation Trust and Cambridge University Hospitals NHS Foundation Trust.

The trial showed that the addition of ATRA to standard chemotherapy had no additional harmful effects in patients when compared with the standard chemotherapy alone, and also demonstrated that the combination does seem to modify the pancreatic cancer stroma in patients.

Hemant Kocher, Professor of Liver and Pancreas Surgery at Queen Mary's Barts Cancer Institute (BCI) and Consultant Liver and Pancreas Surgeon at Barts Health NHS Trust, said: "It is pleasing to demonstrate that changes in the stroma (or scar tissue) surrounding cancer can be used to potentially change pancreatic cancer behavior. This proof-of-principle that the stroma can be targeted in patients is a novel and exciting discovery, and this approach may also be able to be applied to other cancers and diseases where the stroma performs a critical role in

disease progression."

The trial was performed in collaboration with the Institute of Cancer Research, London and the Cancer Research UK Cambridge Institute, and funded by the Medical Research Council (MRC) with support from Celgene Corporation.

New phase II clinical trial for pancreatic cancer

Following on from STARPAC, the MRC is to award £1.5million to fund a phase II clinical trial that will set out to determine whether the addition of ATRA to current standard chemotherapy can improve the treatment outcome in pancreatic cancer. The MRC grant will be accompanied by approximately £1million worth of "drugs in kind" provided by Celgene.

Led by Professor Kocher, the team hope that the STARPAC2 trial could lead to the realization of a vital new treatment option for patients with pancreatic cancer.

The team endeavor for STARPAC2 to be open in at least 16 UK centers to recruit patients with locally advanced [pancreatic](#) cancer, i.e. cases in which the [cancer](#) is too advanced for surgical removal but has not yet spread to other organs. Ultimately, the team hope that for some patients this new treatment combination will shrink the tumor to the point where surgery to remove the remaining tumor is possible.

More information: Hemant M. Kocher et al. Phase I clinical trial repurposing all-trans retinoic acid as a stromal targeting agent for pancreatic cancer, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-18636-w](https://doi.org/10.1038/s41467-020-18636-w)

Provided by Queen Mary, University of London

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