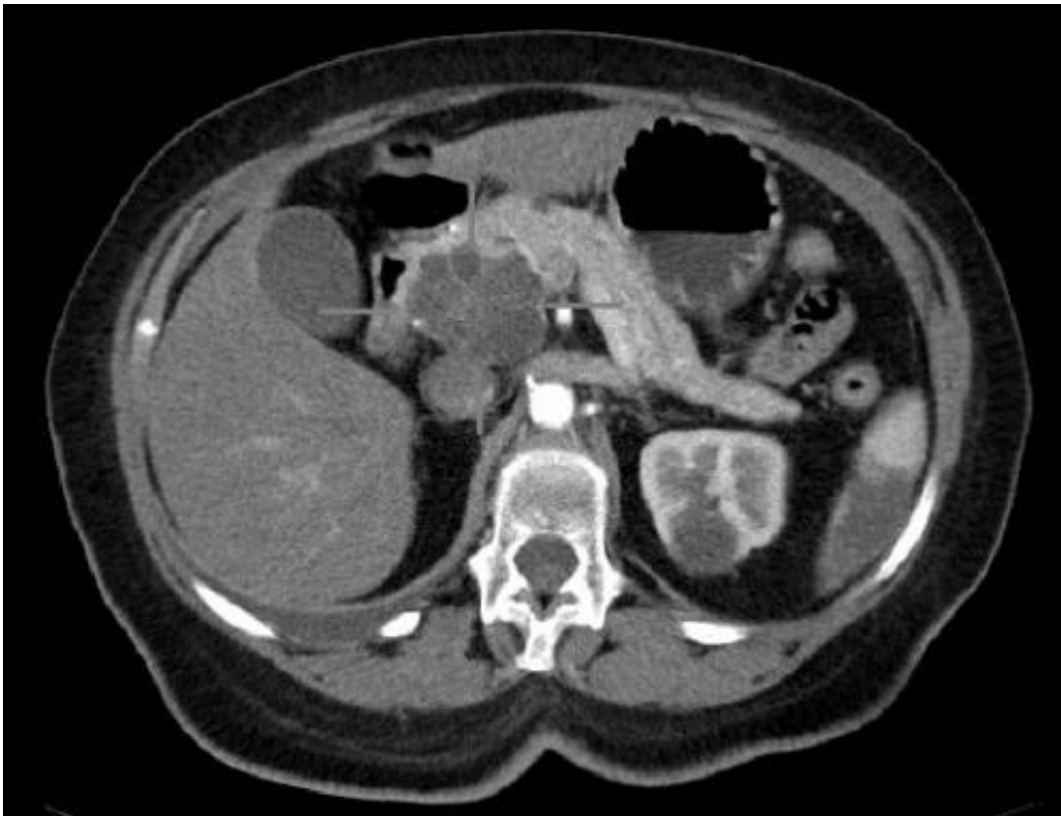


The past, present and future of pancreatic cancer research and treatment

April 23 2015



Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

The oncologists Manuel Hidalgo, Director of the Clinical Research Programme of the Spanish National Cancer Research Centre (CNIO), and Ignacio Garrido-Laguna, member of the Experimental Therapeutics

Program at Huntsman Cancer Institute of the University of Utah (USA), have recently published a review of state-of-the-art clinical treatments for pancreatic cancer—including the most current therapies and innovative research—in the prestigious scientific journal *Nature Reviews Clinical Oncology*.

In their study, which reviews around 200 scientific articles published over the past 30 years, the authors issue a reminder that, despite the fact that over the last decade advances have been made in our understanding of the biology of this type of tumour, no therapeutic targets have been discovered to date that can be successfully translated into better therapies. This is one of the reasons why pancreatic cancer continues to be one of the most deadly cancers. However, researchers are now approaching the subject from a different angle, namely the potential application of immunotherapy together with other treatments that may significantly increase patient [survival rates](#); this could also lead to a reconsideration of the nature of this illness and help to guide future therapeutic strategies.

A possible systemic origin for pancreatic cancer

Hidalgo and Garrido-Laguna raise two questions to bear in mind: on the one hand, there are still no current effective screening methods for detecting pancreatic cancer in its initial phases. On the other hand, despite the advances made in surgical techniques, the 5-year survival rate of patients undergoing surgery continues to be as low as ever, at around 15-20%.

The fact that the initial stages are asymptomatic makes early diagnosis and, therefore, a better chance of survival, difficult. But there could be something else: "Recent research suggests that this is a systemic illness, even during its early stages, in other words, it could involve other organs and not just the pancreas," explains Manuel Hidalgo. "If this hypothesis

is confirmed, the 5-year survival rate could well be improved with the design of systemic adjuvant treatments that go beyond and complement other solutions such as surgery. Another fundamental implication of this hypothesis is that the diagnostic techniques would have to be implemented at an extremely early stage as the illness could be spreading to other organs even during its initial phases."

Immunotherapy and adjuvant treatments

A number of research projects overturn past beliefs. "This was the case, for example, with the application of chemoradiotherapy [a treatment that combines radiotherapy with chemotherapy], a strategy whose benefits have been questioned for treating non-metastatic tumours", says Hidalgo. "Nevertheless, a study is being carried out investigating the possibility that patients that have non-mutated SMAD4 gene would be the most receptive to this type of treatment; this will help oncologists when it comes to making decisions."

On the other hand, if in the past pancreatic cancer was considered as being resistant to immunotherapy, recent research carried out on patients with metastasis has provided positive results in this direction. One example of this is the GVAX vaccine, which contains tumour cells that stimulate the patient's immune system.

Further evidence could provide new therapeutic approaches: some studies point, for example, to the decisive role played by the supporting tissues of the pancreas (the stroma) in the development of this type of tumour. Furthermore, it is believed that neoadjuvant treatments could improve the effects of chemotherapy and radiotherapy and would enable treatment of metastatic [pancreatic cancer](#) at an early stage.

Specifically speaking, a statistically significant improvement of the survival rate of patients suffering from metastatic cancer has been

achieved with the administration of FOLFIRINOX as well as with the combination treatment of nab-paclitaxel plus gemcitabine. The CNIO's Gastrointestinal Cancer Clinical Research Unit, led by Manuel Hidalgo, has contributed to the development of the combination therapy in several scientific studies. "We believe that one of the reasons why this drug combination works is because it selectively eliminates elements that are part of tumour stroma, but this is a laboratory hypothesis that we have to study in more detail," says the oncologist.

A rare but very aggressive cancer

Pancreatic cancer is rare (it represents 2.1% of all tumours), but its incidence has increased since the middle of the 20th century. Furthermore, over 80% of patients experience a recurrence following surgery (60% of them within 6 months).

In Spain, almost 4,000 new cases are recorded every year—53% in men and 44% in women—most of whom are diagnosed between the ages of 65 and 75. Each year this illness kills around 2,400 men and 2,000 women in our country.

More information: Pancreatic cancer: from state-of-the-art treatments to promising novel therapies. Ignacio Garrido-Laguna, Manuel Hidalgo. *Nature Reviews Clinical Oncology* (2015). [DOI: 10.1038/nrclinonc.2015.53](https://doi.org/10.1038/nrclinonc.2015.53)

Provided by Centro Nacional de Investigaciones Oncológicas

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