New Perspectives for Pancreatic Cancer Treatment. Will We Be Able to Ensure Equity to Care?

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Pancreatic ductal adenocarcinoma (PDAC) represents a type of cancer that has a poor prognosis. Standing as the 14th most common cancer globally, it is the seventh leading cause of tumour-related mortality.[1] PDAC was the second leading cause of cancer deaths in the United States in 2018, and, by 2030, it is expected to be the second leading cause of cancer deaths.[2,3]

The need for new therapeutic strategies for treating pancreatic cancer sees the birth of new integrated protocols that combine chemotherapy, radiation therapy, and surgery. Allowing patients with pancreatic cancer to qualify for surgery stands as one of the biggest challenges for the research community, as surgery still appears as the only long-time cure.[2] Nevertheless, such a challenge represents, as of today, an unmet medical need for most patients diagnosed with borderline resectable pancreatic cancer (BRPC).

Recent studies define the use of neoadjuvant chemo and radiotherapy in BRPC patients. In a multicenter, single-arm, phase II study, patients received S1 (40 mg/m2bid) and concurrent radiotherapy (50,4 Gy in 28 fractions). Surgery occurred between 15 and 56 days after the end of chemo and radiotherapy. The primary endpoint of the study was R0 resection rate, met with an encouraging rate of 63%.[4]

So far, four studies have been reported regarding combined chemo-radio neo-adjuvant therapy for BRPC.[4] All studies on new treatments appear particularly challenging due to several variables, including the condition's rarity, the radiological interpretation, the pathological examination.[5] The early results indicate that neoadjuvant treatment seems to be essential for BRPC. While the effectiveness of radiation therapy can be improved, new approaches need to be developed.

A new promising way appears to be the one employing proton- or carbon ion radiotherapy instead of photons. In particular, carbon ion therapy is supposed to be more effective than photon radiotherapy due to a higher relative biological effectiveness and a steep dose-gradient, making dose delivery highly conformal.[6] Today, a few clinical trials aim to apply carbon ion radiotherapy (CIRT) to allow surgical resection of PDAC.[7]

One ongoing prospective, phase II, multicenter, single-arm trial assesses the efficacy and the feasibility of the neoadjuvant administration of 3 cycles of mFOLFIRINOX followed by a short course of CIRT. The so-called PIOPPO study[8] uses CIRT as neoadjuvant therapy to increase the local progression-free survival (L-PFS) and R0 resection rate of BRCP patients.

The use of a particular form of radiotherapy such as CIRT can represent a pioneering step forward in the therapy of BRPC. One of the most interesting aspects to be evaluated is the effect of CIRT on the tissues and the impact on the following surgical procedure. Preliminary data show that after CIRT the pancreatic and peripancreatic tissues are increased in consistency with a certain reduction of the cleavage planes. In the face of greater difficulty in demolition, the reconstruction appears favoured by a fibrotic pancreatic remnant, making pancreatic-jejunal anastomosis easier. However, the intraoperatory effects in irradiated patients represent one open research issue currently under investigation.

Although CIRT seems like one of the most promising options for the pre-surgical treatment of pancreatic cancer, a major issue emerges. At present, CIRT can only be delivered by a few centres worldwide. Despite significant interest from the research community, such a technology is currently available only in 5 countries, and some more are to come due to the high investment required. The very first US CIRT centres are presently under development.[7] Still, thousands of patients affected by BRPC/ medical needs cannot be addressed with only a few therapy centres.

Equity in access to the best possible care opens up the ethical topic of health care disparities. While these

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generally refer to unsatisfactory outcomes regarding limited access to care, poor satisfaction, inadequate treatments, and untimely follow-up, geographic differences also emerge, referring to the proximity to high-volume hospitals or specialized hubs.[9]

In the case of CIRT, suppose the results of the ongoing trials confirm the expected outcomes. Besides the continuous clinical research and scientific dissemination within the oncological and surgical communities, there will be the need to investigate how to make such technology available to a more significant number of patients worldwide to ensure equity in care, offering hope to everyone in need.

Authors' Contributions

LC and FDM conceived the idea of the manuscript and jointly wrote it. They both approved the final version of it.

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