



# Treatment Strategies for Locally Advanced Pancreatic Cancer

Jong-chan Lee

Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea

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Corresponding author: Jong-chan Lee, E-mail: [ljc0316@snuh.org](mailto:ljc0316@snuh.org), <https://orcid.org/0000-0001-6590-2353>

**QUESTION:** A 62-year-old male visited our hospital complaining of weight loss and jaundice. On computed tomographic finding, a 4 cm-sized tumor was found on the head of the pancreas, and the lesion invaded the common hepatic artery (Fig. 1). Histological examination using endoscopic ultrasonography-guided fine needle aspiration revealed pancreatic ductal adenocarcinoma, and FOLFIRINOX treatment was performed. In the first response evaluation, the lesion decreased to 3 cm in size, but in the second response evaluation, the lesion increased to 5.5 cm in size. What is the appropriate action as a next treatment strategy?

**ANSWER:** The patient was recommended to receive



**Fig. 1.** Initial computed tomography finding of the patient.

second-line chemotherapy with gemcitabine with nab-paclitaxel. Although he strongly wanted to receive the local treatment with “heavy ion therapy,” the patient could not be a candidate for the treatment because of long-segment arterial invasion. Now he is considering second-line chemotherapy and discussing the administration schedule.

**REVIEW:** Pancreatic cancer is known to be one of the dismal diseases. This is because about 50% of cases are already metastatic pancreatic cancer (MPC) at the time of first diagnosis due to delayed symptom onset, and locally advanced pancreatic cancer (LAPC) reaches 35% [1]. These advanced pancreatic cancer patients account for 85% of all pancreatic cancer patients, and resectable pancreatic cancer (RPC) patients are known to be about 15% (some patients in the intermediate stage of RPC and LAPC are known as borderline resectable pancreatic cancer. In the case of MPC patients, chemotherapy is the basic strategy. Although LAPC has the same chemotherapeutic strategy at first, there are cases where conversion surgery is possible depending on the progress after treatment, which means chemotherapy and subsequent strategies are somewhat complex.

As of 2023, according to the National Comprehensive Cancer Network (NCCN) Guidelines, in LAPC patients confirmed by histological biopsy, FOLFIRINOX, modified FOLFIRINOX, or gemcitabine with Nab-paclitaxel is recommended [2]. For patients with *BRCA1/2* or *PALB2*



mutations, FOLFIRINOX, modified FOLFIRINOX, or gemcitabine + cisplatin therapy is recommended. However, if the general condition is not good, gemcitabine or capecitabine monotherapy is recommended. The addition of chemoradiation therapy after chemotherapy may vary depending on the case, which will be described later.

If the disease progresses despite 1st-line chemotherapy, the second-line regimen as the crossover between fluoropyrimidine and gemcitabine series was the content until the 2021 NCCN Guidelines. However, the contents of this part were changed in the 2022 NCCN Guidelines. First of all, the existing crossover strategy is pushed back one step to other recommended regimens, and the most recommended preferred regimens are “MSI-H, dMMR, TMB-H ( $\geq 10$  mut/Mb), pembrolizumab is administered, and *NTKR* gene fusion if positive, administer larotrectinib or entrectinib”, indicating that genome testing before chemotherapy has become more routine practice.

Up to this point, the treatment of LAPC and MPC is the same, but when the lesion shows improvement, the strategy of LAPC is slightly different from that of MPC [3]. If resectability is obtained in the tumor evaluation after chemotherapy, surgical treatment can be considered. The concerning points which has not yet been clearly established are as follows: (1) how many cycles the patients receive chemotherapy before surgery; (2) which patients group we select as surgical candidate; (3) which patients should receive adjuvant chemotherapy after surgery; and (4) which regimen and how many cycles should be performed. However, in recent studies, there are cases in which #12 cycles are recommended by combining preoperative anticancer and postoperative anticancer (based on FOLFIRINOX), but many clinical studies suggest a design of switching to surgery after less chemotherapy, so there is still no firm evidence. In addition, surgery is often performed when the tumor size decreases after chemotherapy, when the CA19-9 level decreases significantly, and when the standardized uptake value decreases

significantly in the positron emission tomography scan.

If the lesion continues in a stable disease state, it is divided into cases including discontinuation, maintenance, and chemoradiation, which is a customized treatment strategy by individually determining the patient’s condition. We need to use a tailored approach.

Finally, in the case of LAPC, systemic chemotherapy and local treatment are sometimes performed at the same time, such as radiofrequency ablation, dual suicide adenovirus injection therapy, and stereotactic body radiation therapy has been introduced.

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## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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