新たな化学療法レジメンは膵がんの生存率を改善する(Abstract LBA4001)

新たな化学療法レジメンは膵がん患者の生存期間を20か月近く延長させる

Chemotherapy regimen extends life by nearly 20-months for people with pancreatic cancer

第III相ランダム化試験において、膵がんを外科的に切除されmFOLFIRINOX（オキサリプラチン、ロイコボリン、イリノテカン、および5-フルオウラシルを含む化学療法）を施行された患者は、現在の標準治療であるゲムシタビンを投与された患者に比べ無病生存期間が有意に長かった。追跡期間中央値33.6か月の時点で、mFOLFIRINOX群における無病生存期間中央値は21.6か月であったのに対し、ゲムシタビン群では12.8か月であった。全生存期間中央値はmFOLFIRINOX群で54.4か月であったのに対し、ゲムシタビン群では35.0か月であった。mFOLFIRINOXの有益性は全てのサブグループにおいて認められた。この試験結果は、2018 ASCO Annual Meetingで取り上げられた。

Full Text

In a randomized phase III trial people with surgically removed pancreatic cancer who received mFOLFIRINOX, a chemotherapy regimen containing four different medicines, lived a median of 20 months longer and were cancer-free nine months longer than those who received the current standard of care, gemcitabine.

The study was featured at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

"For the first time, our trial shows a large benefit from adjuvant FOLFIRINOX chemotherapy over standard chemotherapy with gemcitabine, showing we can help patients with pancreatic cancer live much longer," said lead study author Thierry Conroy, MD, a medical oncologist and director of the Institut de Cancerologie de Lorraine in Nancy, one of the UNICANCER comprehensive cancer centers in France. "In addition, we were encouraged to see that the results were better than expected when we planned this trial."

After pancreatic cancer surgery, adjuvant chemotherapy with gemcitabine can substantially prolong survival compared to surgery alone, as well as increase the number of patients who are cured at 5 years (about 21% with gemcitabine vs. 10% with surgery alone). Gemcitabine has been the standard adjuvant therapy for the past 10 years.

The PRODIGE 24/CCTG PA.6 trial enrolled patients with non-metastatic pancreatic ductal adenocarcinoma (PDAC) who had surgery that removed all or nearly all of the tumor (no cancer cells were visible to the surgeon after surgery, but microscopic tumoral cells may have remained). PDAC is the most common type of pancreatic cancer and accounts for 90% of all cases. Surgery is possible in only 10-20% of patients with pancreatic cancer overall.

Three to 12 weeks after surgery, 493 patients were randomly assigned in France and in Canada to receive either gemcitabine or mFOLFIRINOX for six months. The mFOLFIRINOX regimen combines four chemotherapy medicines: oxaliplatin, leucovorin, irinotecan, and 5-fluorouracil. A very similar regimen is already used as an initial treatment for metastatic pancreatic cancer, and this study shows FOLFIRINOX can also benefit patients with earlier-stage disease.

At a median follow-up of 33.6 months, the median disease-free survival was much longer in the mFOLFIRINOX group than in the gemcitabine group (21.6 months vs. 12.8 months), as was the median overall survival (54.4 months with mFOLFIRINOX vs. 35.0 months with gemcitabine). The benefit of the mFOLFIRINOX is observed in all subgroups of patients. mFOLFIRINOX also markedly extended the time until metastases appeared (median 30.4 months vs. 17.0 months with gemcitabine).

Overall, more patients experienced severe side effects (mainly hematologic) in the mFOLFIRINOX group than in the gemcitabine group (76% vs. 53%), but the side effects were manageable, according to the authors. One treatment- related death occurred in the gemcitabine group, and none in the mFOLFIRINOX group.

The types of side effects also differed between the two groups. The most common side effects of gemcitabine were headache, fever, flu-like symptoms, swelling, and low white blood cell counts. Patients who received mFOLFIRINOX had more diarrhea, nausea, vomiting, and fatigue. There was no difference in the risk of febrile neutropenia between the two groups.

Past medical history of ischemic heart disease represents a risk with either regimen, but particularly mFOLFIRINOX.

"Pancreatic cancer is notoriously aggressive and typically has a poor prognosis, so it is a major win to find that a new treatment regimen significantly improves survival for patients with this disease," said ASCO Expert Andrew Epstein, MD.

The next step will be to explore the timing of chemotherapy. Patients may benefit from neoadjuvant chemotherapy to shrink the tumor, to destroy undetectable micrometastases and increase the chance that the tumor can be completely removed through surgery. Dr. Conroy noted that mFOLFIRINOX appears to be a good candidate for neoadjuvant chemotherapy. Another option is to give half the cycles of chemotherapy before, and the other half after surgery. Ongoing clinical trials are already testing both of these approaches.

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