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Second-line Chemotherapy Options in Metastatic PDAC

Announcer:
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Dr. Dotan:
My name is Efrat Dotan, and I'm a medical oncologist focused on the care of patients with pancreatic cancer. This video will focus on second-line chemotherapy treatments for patients with metastatic pancreatic ductal adenocarcinoma.

As most of you know, pancreatic cancer is usually diagnosed in advanced, incurable stage, and has very poor prognosis, and conventional chemotherapy remains the core therapy that we use and the standard of care for patients with this advanced disease. We have limited treatment option, and that's why it's really important to make sure patients are exposed and have access to all available therapies during their treatment journey, and really pay attention and think about how we sequence these treatment while treating patients with this aggressive cancer.

So multiple factors come into play when we think about second-line therapy, and the choice of the treatment has to take all these factors into account. Number one, we have to think about what patients received in the frontline setting, and that will inform what we should use in the second-line setting. But additional factors include whether the patients have any residual side effects, what is their performance status, comorbidities, symptoms that may affect their ability to tolerate treatment in the second-line setting. Do they have any actionable mutations that were found on NGS testing, which hopefully was done after their diagnosis? And also, what type of tolerance do we expect them to have from this treatment? And what are their goals of care as they embark on the second-line treatment?

So based on the current treatment guidelines, for patients that received a 5-FU-based therapy in the frontline setting, and this could be FOLFIRINOX or NALIRIFOX, the second-line treatment should be a gemcitabine-based treatment, such as gemcitabine and nab-paclitaxel. However, for patients that received gemcitabine-based therapy in the first-line setting, the preferred second-line treatment should be a 5-FU-based therapy, and usually we would use something like 5-FU and liposomal irinotecan or an NALIRI, FOLFIRI, or even FOLFOX.

Thinking about liposomal irinotecan, just so we understand what is the difference about this drug. This drug has an encapsulated liposomal nanoparticles that cover the irinotecan, and the idea is that this would enhance the accumulation of the SN-38, the active metabolite within the tumor, and also prevent the rapid clearance, thereby increasing the efficacy and reducing the side effects. And the benefit of using this drug was published in the NAPOLI-1 study. This was a phase 3 randomized trials that investigated the effect of liposomal irinotecan in patients with metastatic. Pancreatic cancer in the second-line setting, following gemcitabine-based treatment. The patients were randomized to received 5-FU plus NALIRI, NALIRI alone, or 5-FU alone. And the results of this trial showed an improvement in media and overall survival 6.1 months with the combination of 5-FU and liposomal irinotecan, versus 4.2 months with 5-FU alone.

In terms of adverse events, grade 3 or 4 adverse events occurred most frequently were neutropenia, fatigue, diarrhea, and vomiting, and these were managed by dose reduction. And what was interesting is, later on, there was data presented in terms of outcomes for those patients who had dose reduction, and the benefit in terms of overall survival and progression-free survival was maintained in those patients that had dose reduction. So this regimen is approved for use and is recommended for patients that receive gemcitabine-based therapy in the frontline setting for second-line treatment.

So other than using liposomal irinotecan plus 5-FU as an option, another option would be to use oxaliplatin-based therapy. We have two studies that were done looking at oxaliplatin-based therapy in the second-line setting, the CONKO-003 trial, which randomized patients to 5-FU and folinic acid, versus 5-FU, folinic acid, and oxaliplatin. And the PANCREOX study, which randomized patients to FOLFOX versus 5-FU and leucovorin. And the results of the studies are actually conflicting. The CONKO-003 trial demonstrated improvement in overall survival in patient that received the combination of oxaliplatin, folinic acid, and 5-FU. Conversely, the PANCREOX study did not show any benefit from the addition of oxaliplatin. This makes it difficult to really understand what oxaliplatin can provide patients in this setting.

And another important consideration is that if patients receive gemcitabine and nab-paclitaxel in the frontline setting, many of them may have neuropathy, which would make it quite difficult to give them oxaliplatin in the second-line setting. And this is where irinotecan-based treatment may be more tolerable and more beneficial.

We also have to remember that targeted therapy and evaluating the NGS testing of patients with pancreatic cancer comes into play in the second-line setting, and if patients have any targetable mutation, this is where we would consider these targeted therapies. And we hope, with time and potential approval of RAS inhibitors, we will have more treatment options in this setting.

We hope you found this helpful and educational learning about second-line therapy for metastatic pancreatic cancer. You can find more details and download a full set of slide on this topic from the COR2ED website. Thank you.

Announcer:
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