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What is the current status of immunotherapy in pancreatic cancer?

Hi, my name is Dr. Eileen O'Reilly. I am going to discuss the current status of immunotherapy in pancreatic cancer. Many immune strategies have been investigated in pancreas cancer, and today, there has not been a robust signal, but there are certainly early hints. For example, checkpoint inhibitors have been evaluated as single agents, both PD-1 agents, PDL-1 agents, and anti-CTLA-4, and we have some data showing that in a small number of patients, responses are evident. More recently, it has been apparent that MSI-high tumors which probably account for about 1%, maybe 2%, of people with pancreas cancer are a small but important subgroup to identify where there may be a robust signal to an immune therapy. Pembrolizumab has been recently FDA approved for MSI-high tumors, but it is agnostic of tumor type. From the GI perspective, the cancer that we would think of would be colorectal cancer, certainly cholangiocarcinoma, esophagogastric malignancies in terms of frequency of MSI-high, and then pancreas cancer has a small, small subset that needs to be identified. Thus far, it appears that this is overly represented by HNPCC (Hereditary Non-Polyposis Colorectal Cancer) or Lynch individuals who have pancreas cancer where they have a high mutation burden and potential for response to immune checkpoint inhibitors, so a small but important subset.

What else is happening with regard to immune therapy? Single agents, in terms of checkpoints outside the MSI-high setting, for the most part are not cutting it, and the focus has been on developing combination strategies; for example, combining two checkpoint inhibitors together. There are a number of studies that have been completed and yet to be reported in pancreas cancer combining, for example, a checkpoint inhibitor and a vaccine using radiation as an immune modulator combined with a checkpoint. Perhaps a strategy that may have some traction, but again we are awaiting data, is combining cytotoxic therapy and immune therapy in pancreas cancer, recognizing now that there is a precedent in non-small cell lung cancer for the strategy and for pancreas cancer where we are heavily reliant on the value of cytotoxic therapies

for disease control. This particular approach may be relevant moving forward. There are a lot of targets; to give examples of some that are in development in the immune setting, CD40 modulating the microenvironment using vitamin D modulation, pegylated PEGPH20 an enzyme that degrades hyaluronan that may also have some immune properties and is being looked at in combination with checkpoints.

Where do we see an immunotherapy setting in pancreatic cancer? Well, I think there is yet to be an established niche, but a possible context might be in a maintenance setting after disease has been debulked, and symptoms stabilized that may be a setting or possibly in a locally advanced disease context, after again initial disease control has been maintained and has more maintenance strategy for going forward. I think the excitement is that there is a lot happening. There are a lot of studies underway, and while as yet, we have not made the inroads with immunotherapies that are evident in other major solid organ malignancies, there is certainly hope that, with an increased focus on understanding the tumor microenvironment and the immune biology, that we may begin to see some strategies for moving forward in this setting in pancreas cancer.