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NCCN Guidelines Panel: Pancreatic Adenocarcinoma

On behalf of The Society of Interventional Oncology, we are grateful to see that the NCCN Pancreatic Adenocarcinoma panel has now included an interventional radiologist on the panel. However, IR procedures are not referenced in the current guidelines.

Interventional radiology (IR) can offer multiple options for the treatment and management of pancreatic cancer. IR is currently being utilized in locoregional control of disease, management of non-IR treatment complications, palliative options, and treatment of metastatic disease. Therefore, we request the consideration of the following changes in the current guideline:

Specific Change 1: Include Locoregional therapies for patients with locally advanced pancreatic cancer

Multiple locoregional therapies (LRT) are available for the treatment and management of patients with pancreatic cancer. These options can be beneficial in select patients and specific clinical scenarios as outlined below:

1. **Locally advanced disease.**
   Irreversible electroporation or IRE technique (percutaneous or open) alone or in combination with systemic therapy. There is strong evidence, including a phase 3 clinical trial, demonstrating that this ablation technique is safe and able to improve progression-free survival (PFS) and overall survival (OS) in pancreatic cancer patients. Current literature supports utilizing IRE as a neoadjuvant treatment in addition to chemoradiation. Moreover, the literature has demonstrated that IRE is able to successfully convert locally advanced patients to surgically resectable patients. We propose to include IRE as one of the treatment options for patients with locally advanced pancreatic cancer. The following articles are relevant to this proposed change:

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Author	Year	Study design	# of pts	Stage of Dx	Primary endpoint
Narayanan G *et al*	2012	Retrospective	14	Locally advanced	Safety
Martin RC *et al*	2013	Prospective	54	Locally advanced	Safety
Martin RC *et al*	2015	Prospective	200	Locally advanced	90-day outcome, OS*
Belfiore MP *et al*	2015	Prospective	29	Locally advanced	OS
Scheffer HJ *et al*	2016	Phase I/II PANFIRE study	25	Locally advanced	Local progression, event-free survival and OS
Mansson C et al	2016	Prospective	24	Locally advanced	Local progression, OS
Narayanan G *et al*	2017	Retrospective	50	Locally advanced	Safety. 2ndary endpoint = OS
Sugimoto K et al	2018	Prospective	5	Locally advanced	Safety. 2ndary endpoint = OS
Leen E *et al*	2018	Prospective	75	Locally advanced	30 day mortality, PFS and OS
Holland MM *et al*	2019	Prospective	152	Locally advanced	PFS**, OS, TTP***
Ruarus AH *et al*	2020	Phase II MCT+	50	Locally advanced	Local recurrence, OS
Yang PC *et al*	2020	Prospective	74	Locally advanced	PFS, OS
Narayanan G *et al*	2021	RCT- On going	528	Locally advanced	PFS, OS

*OS = Overall survival
**PFS = Progression free survival
*** TTP = Time to progression
+ MCT = Multicenter clinical trial

Specific Change 2: Include Locoregional therapies as a palliative or supportive care option in patients with advanced disease.

1. LRT for pain control.

Both IRE and cryoablation have been reported to be very safe and effective in blocking the celiac plexus and relieving pain in patients with advanced pancreatic cancer. Celiac plexus IRE and cryoablation have provided a new treatment option for intractable abdominal pain in these patients.

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Specific Change 3: Include Locoregional therapy for patients with metastatic cancer.

3. Metastatic liver disease:

It is well established that metastatic pancreatic cancer is a systemic disease, and systemic therapy is an essential part of its management. However, locoregional treatments benefit a highly selected group of oligo-metastatic pancreatic cancer patients. Surgical literature has demonstrated improved overall survival following resection of liver metastasis in selected patients. Similar to surgical resection, targeted locoregional therapies have been demonstrated to benefit a selected group of pancreatic cancer patients with liver metastasis. Locoregional liver-directed options include thermal ablation techniques i.e., radiofrequency ablation (RFA) and microwave ablation (MWA), and intra-arterial therapies i.e., selective internal radiation therapy (SIRT), also known as Transarterial radioembolization (TARE). These treatments have demonstrated survival benefits in pancreatic cancer patients with liver metastases. A review of the literature demonstrates that the following patient characteristics are associated with survival benefits after ablation or TARE: younger age, performance status of 0-1, smaller primary tumor size, fewer and smaller tumors in the liver, lower primary tumor stage, liver-only metastasis, liver metastasis in patients with resected primary tumor, neutrophil-to-lymphocyte ratio of less than 2.5, and lower tumor marker CA19-9 levels pre or post-treatment. We propose including these two Locoregional options for this group of patients.

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