ASCO® Guidelines

METASTATIC PANCREATIC CANCER: ASCO CLINICAL PRACTICE GUIDELINE UPDATE		
Clinical Domain	**Recommendation**	**Evidence Rating**
Initial Assessment	A multiphase computed tomography (CT) scan of the chest, abdomen and pelvis should be performed to assess extent of disease. Other staging studies should be performed only as dictated by symptoms.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
	The baseline performance status, symptom burden, and comorbidity profile of a patient diagnosed with metastatic pancreatic cancer should be evaluated carefully.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
	The goals of care (including a discussion of an advance directive), patient preferences, as well as support systems should be discussed with every person diagnosed with metastatic pancreatic cancer and his/her caregivers.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
	Multidisciplinary collaboration to formulate treatment and care plans and disease management for patients with metastatic pancreatic cancer should be the standard of care.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
	Every person with pancreatic cancer should be offered information about clinical trials, which include therapeutic trials in all lines of treatment, as well as palliative care, biorepository/biomarker, and observational studies.	Type: informal consensus, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
First-line Treatment	FOLFIRINOX is recommended for patients who meet ***all*** of the following criteria: ECOG PS 0-1 Favorable comorbidity profile*	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong

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METASTATIC PANCREATIC CANCER: ASCO CLINICAL PRACTICE GUIDELINE UPDATE		
Clinical Domain	**Recommendation**	**Evidence Rating**
	Patient preference and support system for aggressive medical therapy	
	Access to chemotherapy port and infusion pump management services.	
	Gemcitabine plus nab-paclitaxel is recommended for patients who meet ***all*** of the following criteria:	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
	ECOG PS 0-1	
	Relatively favorable comorbidity profile*	
	Patient preference	
	Support system for relatively aggressive medical therapy.	
	Gemcitabine alone is recommended for patients who either have an ECOG PS 2 or have a co-morbidity profile precluding more aggressive regimens, and the wish to pursue cancer-directed therapy. The addition of either capecitabine or erlotinib to gemcitabine may be offered in this setting.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: moderate
	Patients with an ECOG PS ≥ 3 or with poorly controlled comorbid conditions despite ongoing active medical care should be offered cancer-directed therapy only on a case by case basis. The major emphasis should be on optimizing supportive care measures.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: moderate
Second-line Treatment	Routine testing for deficiency in mismatch repair or high microsatellite instability is recommended, using IHC, PCR, or NGS for patients who are considered to be candidates for checkpoint inhibitor therapy.	Type: informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: moderate
	PD-1 immune checkpoint inhibitor pembrolizumab is recommended as second-line therapy for patients who have tested positive for mismatch repair deficiency or high microsatellite instability.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: moderate
	Gemcitabine plus nab-paclitaxel can be offered as second-line therapy for patients who meet ***all*** of the following criteria:	Type: informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: moderate
	First-line treatment with FOLFIRINOX	
	ECOG PS 0-1	
	Relatively favorable comorbidity profile*	

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Clinical Domain	**Recommendation**	**Evidence Rating**
	Patient preference	
	A support system for aggressive medical therapy	
	Fluorouracil plus nanoliposomal irinotecan, or fluorouracil plus irinotecan where the former combination is unavailable, is preferred as second-line therapy for patients who meet ***all*** of the following criteria:	Type: informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: moderate
	First-line treatment with gemcitabine plus nab-paclitaxel	
	ECOG PS 0-1	
	Relatively favorable comorbidity profile*	
	Patient preference and a support system for aggressive medical therapy	
	Access to chemotherapy port and infusion pump management services	
	Fluorouracil plus oxaliplatin may be considered as second-line therapy for patients who meet ***all*** of the following criteria:	Type: informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: moderate
	First-line treatment with gemcitabine plus nab-paclitaxel	
	ECOG PS 0-1	
	Relatively favorable comorbidity profile*	
	Patient preference and a support system for aggressive medical therapy	
	Access to chemotherapy port and infusion pump management services	
	Qualifying statement: A recent phase III trial comparing mFOLFOX6 with fluorouracil and leucovorin (FU/LV) demonstrated a higher rate of grade 3 or 4 adverse events and significantly reduced overall survival within the mFOLFOX6 arm of the trial.[1] However, previous phase III data have demonstrated a benefit with the OFF regimen compared to FU/LV.[2] Considering the inconsistency of these results, although fluorouracil plus nanoliposomal irinotecan is preferred, the Expert Panel continues to support the use of fluorouracil plus oxaliplatin as an option where the availability of fluorouracil plus nanoliposomal irinotecan is limited or where residual toxicity from first-line therapy or comorbidities preclude the use of fluorouracil plus nanoliposomal irinotecan.	

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Clinical Domain	**Recommendation**	**Evidence Rating**
	Gemcitabine or fluorouracil can be considered as second-line therapy for patients who either have an ECOG PS of 2 or have a co-morbidity profile precluding more aggressive regimens, and wish to pursue cancer-directed therapy.	Type: informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: moderate
	There are no available data to recommend third (or greater)-line therapy with a cytotoxic agent. Clinical trial participation is encouraged.	Type: informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: moderate
Palliative Care	Patients with metastatic pancreatic cancer should have a full assessment of symptom burden, psychological status, and social supports as early as possible, preferably at the first visit. In most cases, this assessment will indicate a need for a formal palliative care consult and services.	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
Treatment of Pain and Symptoms	Patients with metastatic pancreatic cancer should be offered aggressive treatment of the pain and symptoms of the cancer and/or the cancer-directed therapy	Type: evidence based, benefits outweigh harms Evidence quality: intermediate Strength of recommendation: strong
Follow up/Surveillance	For patients on active cancer-directed therapy outside of a clinical trial, imaging to assess first response should be offered at 2 to 3 months from the initiation of therapy. CT scans with contrast are the preferred modality. Thereafter, clinical assessment, conducted frequently during visits for cancer-directed therapy, should supplant imaging assessment. The routine use of positron emission tomography (PET) scans for management of patients with pancreatic cancer is not recommended. CA19-9 is not considered an optimal substitute for imaging for assessing treatment response.	Type: Informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: strong
	No data exist on the duration of cancer-directed therapy. An ongoing discussion of goals of care, and assessment of treatment response and tolerability, should guide decisions to continue or hold/terminate cancer-directed therapy.	Type: Informal consensus, benefits outweigh harms Evidence quality: low Strength of recommendation: strong

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*Definitions: A favorable comorbidity profile is loosely defined as hemoglobin ≥10 g/dL and platelet count ≥ 100,000/mL without transfusion support; absolute neutrophil count ≥ 1,500/mL; bilirubin and international normalized ratio ≤ 1.5 times the upper limit of normal; albumin ≥ 3 g/dL; creatinine clearance ≥ 60 mL/min/1.73 m^2; and absence of comorbid conditions that require ongoing active medical care, such as congestive heart failure, chronic obstructive pulmonary disease, uncontrolled diabetes mellitus, and neurologic disorders.
A relatively favorable comorbidity profile is loosely defined as hemoglobin ≥ 9 g/dL and platelet count ≥ 75,000/mL without transfusion support; absolute neutrophil count ≥ 1,500/mL; bilirubin and international normalized ratio ≤ 1.5 times the upper limit of normal; albumin ≥3 g/dL; creatinine clearance ≥60 mL/min/1.73m^2; and absence of poorly controlled comorbid conditions, such as congestive heart failure, chronic obstructive pulmonary disease, uncontrolled diabetes mellitus, and neurologic disorders.

References

1. Gill S, Ko YJ, Cripps C, et al: PANCREOX: A Randomized Phase III Study of Fluorouracil/Leucovorin With or Without Oxaliplatin for Second-Line Advanced Pancreatic Cancer in Patients Who Have Received Gemcitabine-Based Chemotherapy. J Clin Oncol 34:3914-3920, 2016

2. Oettle H, Riess H, Stieler JM, et al: Second-line oxaliplatin, folinic acid, and fluorouracil versus folinic acid and fluorouracil alone for gemcitabine-refractory pancreatic cancer: outcomes from the CONKO-003 trial. J Clin Oncol 32:2423-9, 2014

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