ASCO® Guidelines

METASTATIC PANCREATIC CANCER: ASCO GUIDELINE UPDATE		
Clinical Domain	**Recommendation**	**Evidence Rating**
Initial Assessment	A multiphase computed tomography 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 PS, symptom burden, and comorbidity profile of a patient 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 (to include a discussion of an advance directive), patient preferences, as well as support systems should be discussed with every patient with metastatic pancreatic cancer and his or 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
	Early testing for actionable genomic alterations is recommended for patients who are likely to be potential candidates for additional treatment following first-line therapy. Both germline and tumor (somatic) testing are recommended. This includes testing for microsatellite instability/mismatch repair deficiency, BRCA mutations (excluding variants of unknown significance), and NTRK gene fusions. Results of testing can lead to therapies such as PARP inhibitors, PD-1 checkpoint inhibitor therapy, TRK fusion inhibitors, and clinical trials of targeted therapies. Genomic testing is recommended as part of initial assessment to ensure that the results of testing are available at the time of treatment decision-making where applicable after first-line therapy (see Section 3; Treatment Options Following First-line Therapy).	Type: Informal consensus Strength of recommendation: Strong

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	Qualifying Statement. The decision to test for actionable genomic alterations should involve a discussion between the patient and physician regarding frequency of actionable findings, treatment implications of testing results, and genetic counseling related to germline testing. ASCO has previously developed a provisional clinical opinion (PCO) on Evaluating Susceptibility to Pancreatic Cancer that contains recommendations for germline genetic testing.[1]	
	Every patient 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 (leucovorin, fluorouracil, irinotecan, and oxaliplatin) is recommended for patients who meet all of the following criteria: an ECOG PS of 0 to 1, favorable comorbidity profile, patient preference and a support system for aggressive medical therapy, and access to chemotherapy port and infusion pump management services.	Type: Evidence based, benefits outweigh harms Evidence quality: Intermediate Strength of recommendation: Strong
	Gemcitabine plus NAB-paclitaxel is recommended for patients who meet all of the following criteria: an ECOG PS of 0 to 1, a relatively favorable comorbidity profile, and patient preference and a support system for relatively aggressive medical therapy.	Type: Evidence based, benefits outweigh harms Evidence quality: Intermediate Strength of recommendation: Strong
	Gemcitabine alone is recommended for patients who have either an ECOG PS of 2 or a comorbidity profile that precludes more aggressive regimens and who wish to pursue cancer-directed therapy. The addition of nab-paclitaxel or capecitabine or erlotinib to gemcitabine may be offered in this setting, with proactive dose and schedule adjustments to minimize toxicities.	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

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Treatment Options Following First-line Therapy	In patients with tumors harboring NTRK fusions, treatment with larotrectinib or entrectinib is recommended.	Type: evidence-based; 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 dMMR or MSI-H.	Type: evidence-based; benefits outweigh harms Evidence quality: High Strength of recommendation: Strong
	In patients who have a germline BRCA1 or BRCA2 mutation and have received first-line platinum-based chemotherapy without disease progression for at least 16 weeks, options for continued treatment include chemotherapy or PARP inhibitor olaparib.	Type: evidence-based; benefits outweigh harms Evidence quality: Low Strength of recommendation: Moderate
	Qualifying Statement. For the group of platinum-sensitive patients included in recommendation 3.3, the decision to continue treatment with chemotherapy or proceed to maintenance therapy with olaparib should be based on a discussion between the patient and the oncologist, including consideration of whether a maximum response and plateau in response to chemotherapy have been achieved, level of cumulative toxicities associated with chemotherapy treatment, patient preference, convenience, toxicity, goals of care, cost, and clinical evidence, including a lack of overall survival benefit demonstrated in the POLO randomized controlled trial.[2]	
	Gemcitabine plus NAB-paclitaxel may be offered as second-line therapy to patients who meet all of the following criteria: first-line treatment with FOLFIRINOX, an ECOG PS of 0 to 1, a relatively favorable comorbidity profile, and patient preference and a support system for aggressive medical therapy.	Type: Informal consensus, benefits outweigh harms Evidence quality: Low Strength of recommendation: Moderate

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	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: first-line treatment with a gemcitabine-based regimen, an ECOG PS of 0 to 1, a relatively favorable comorbidity profile, patient preference and a support system for aggressive medical therapy, and access to chemotherapy port and infusion pump management services.	Type: Informal consensus, benefits outweigh harms Evidence quality: Low Strength of recommendation: Moderate
	Fluorouracil plus oxaliplatin may be considered as second-line therapy for patients who meet all of the following criteria: first-line treatment with gemcitabine plus NAB-paclitaxel, an ECOG PS of 0 to 1, a relatively favorable comorbidity profile, patient preference and a support system for aggressive medical therapy, and access to chemotherapy port and infusion pump management services.	Type: Informal consensus, benefits outweigh harms Evidence quality: Low Strength of recommendation: Moderate
	Qualifying statement. A phase III trial comparing mFOLFOX6 with FU + LV demonstrated a higher rate of grade 3 or 4 adverse events and significantly reduced OS within the mFOLFOX6 arm of the trial.[3] However, previous phase III data have demonstrated a benefit with the OFF regimen compared with FU + LV.[4,5] 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.	
	Gemcitabine or fluorouracil can be considered as second-line therapy for patients who have either an ECOG PS of 2 or a comorbidity profile that precludes more aggressive regimens and who wish to pursue cancer-directed therapy (the addition of nab-paclitaxel to gemcitabine or nanoliposomal irinotecan to 5-fluorouracil may be offered in this setting, with proactive dose and schedule adjustments to minimize toxicities).	Type: Informal consensus, benefits outweigh harms Evidence quality: Low Strength of recommendation: Moderate

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	No data are available to recommend third-line (or greater) 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 a clinical trial, imaging to assess first response should be offered at 2 to 3 months from the initiation of therapy. Computed tomography 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 scans for the management of patients with pancreatic cancer is not recommended. CA19-9 is not considered an optimal substitute for imaging for the assessment of 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 to hold or terminate cancer-directed therapy.	Type: Informal consensus, benefits outweigh harms Evidence quality: Low Strength of recommendation: Strong

References

1. Stoffel EM, McKernin SE, Brand R, et al: Evaluating Susceptibility to Pancreatic Cancer: ASCO Provisional Clinical Opinion. J Clin Oncol 37:153-164, 2019
2. Golan T, Hammel P, Reni M, et al: Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer. N Engl J Med 381:317-327, 2019
3. Gill S KY, 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: 391403920, 2016
4. Sohal DPS, Kennedy EB, Khorana A, et al: Metastatic Pancreatic Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 36:2545-2556, 2018
5. Oettle H RH, 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: 2423-2429, 2014

