# Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline

www.asco.org/guidelines/MetPC 

# Introduction

- Pancreatic ductal adenocarcinoma is a disease associated with poor prognosis and an increasing impact on cancer-related mortality in the United States and worldwide.

- The focus of this clinical practice guideline is to help with clinical decision making, including determining the appropriate treatment for people with metastatic pancreatic cancer and how to help patients and their families to access and use palliative care services.

# ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

- a systematic literature review by ASCO guidelines staff
- an expert panel provides critical review and evidence interpretation to inform guideline recommendations
- final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at:
www.asco.org/guidlines/MetPC

# Clinical Questions

1. After a histopathologic confirmation of pancreatic adenocarcinoma diagnosis, what initial assessment is recommended before initiating any therapy for metastatic pancreatic cancer?

2. What is the appropriate first-line treatment for patients with metastatic pancreatic cancer?

3. What is the appropriate therapy for patients with metastatic pancreatic cancer who experience either disease progression or intolerable toxicity on prior regimen(s) for metastatic pancreatic cancer?

4. When should the concept of palliative care be introduced?

5. For people with metastatic pancreatic cancer, what are the recommended strategies for relief of pain and symptoms?

6. What is the recommended frequency of follow-up care/surveillance for people with metastatic pancreatic cancer?

# Target Population and Audience

**Target Population**

People diagnosed with metastatic pancreatic cancer.

**Target Audience**

Medical oncologists, radiation oncologists, surgeons, gastroenterologists, and other caregivers

# Summary of Recommendations

**CLINICAL QUESTION 1**

After a histopathologic confirmation of pancreatic adenocarcinoma diagnosis, what initial assessment is recommended before initiating any therapy for metastatic pancreatic cancer?

***Recommendation 1.1***

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)

***Recommendation 1.2***

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)

# Summary of Recommendations

***Recommendation 1.3***

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)

***Recommendation 1.4***

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)

***Recommendation 1.5***

Every person with pancreatic cancer should be offered information about clinical trials - 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)

# Summary of Recommendations

**CLINICAL QUESTION 2**

What is the appropriate first-line treatment for patients with metastatic pancreatic cancer?

***Recommendation 2.1***

FOLFIRINOX is recommended for patients who meet ***all*** of the following criteria:

- ECOG PS 0-1
- Favorable comorbidity profile
- Patient preference and support system for aggressive medical therapy
- Access to chemotherapy port and infusion pump management services

(Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong)

***Recommendation 2.2***

Gemcitabine plus nab-paclitaxel is recommended for patients who meet ***all*** of the following criteria:

- ECOG PS 0-1
- Relatively favorable comorbidity profile
- Patient preference and support system for relatively aggressive medical therapy

(Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong)

# Summary of Recommendations

***Recommendation 2.3***

Gemcitabine alone is recommended for patients who either have an ECOG PS of 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)

***Recommendation 2.4***

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)

# Summary of Recommendations

**CLINICAL QUESTION 3**

What is the appropriate therapy for patients with metastatic pancreatic cancer who experience either disease progression or intolerable toxicity on prior regimen(s) for metastatic pancreatic cancer?

***Recommendation 3.1***

Gemcitabine plus nab-paclitaxel can be offered as second-line therapy for patients who meet ***all*** of the following criteria:

- First-line treatment with FOLFIRINOX,
- ECOG PS 0-1
- Relatively favorable comorbidity profile
- Patient preference and a support system for aggressive medical therapy

(Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate)

# Summary of Recommendations

***Recommendation 3.2***

Fluorouracil plus oxaliplatin, irinotecan, or nanoliposomal irinotecan can be offered as second-line therapy for patients who meet ***all*** of the following criteria:

- 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

(Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate)

***Recommendation 3.3***

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)

# Summary of Recommendations

***Recommendation 3.4***

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)

**CLINICAL QUESTION 4**

When should the concept of palliative care be introduced?

***Recommendation 4.1***

People 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 will indicate a need for a formal palliatve care consult and services. (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong)

**CLINICAL QUESTION 5**

For people with metastatic pancreatic cancer, what are the recommended strategies for relief of pain and symptoms?

***Recommendation 5.1***

People with metastatic pancreatic cancer should be offered aggressive treatment for 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)

# Summary of Recommendations

**CLINICAL QUESTION 6**

What is the recommended frequency of follow-up care/surveillance for people with metastatic pancreatic cancer?

***Recommendation 6.1***

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)

***Recommendation 6.2***

There are no data 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)

# Patient and Clinician Communication

- People with pancreatic cancer are faced with making difficult treatment decisions while being presented with complex medical information and a life-threatening diagnosis.

- Clear communication with people with pancreatic cancer and their caregivers about the diagnosis, treatment options, and goals of care is key for patient understanding. The clinician is also responsible for offering ancillary support services, including offering referral to a palliative care consult and services.

- Clinicians should clearly explain all potential treatment options, the potential outcomes of each, and possible adverse events/side effects so patients can understand benefits and drawbacks of each and make an informed decision. Treatment discussions should include relevant clinical trials at every stage of treatment.

# Patient and Clinician Communication

- Clinicians should also consider and proactively discuss quality of life issues. In people with pancreatic cancer, dietary concerns, pain and fatigue are major concerns.

- Referral to palliative care services can facilitate addressing many of the non-treatment-related issues patients face and should be offered for all people with pancreatic cancer, regardless of stage of disease or expected prognosis. Patients should understand that referral to consult palliative care services is not synonymous with a referral to hospice care.

- Providing realistic hope to people diagnosed with pancreatic cancer, while the prognosis may be very short, is very important. Patients deserve to know that their medical team is working to help them reach their goals.

- Providing patients with resources to help them communicate better with their healthcare team is also advisable.

# Health Disparities

- Although ASCO clinical practice guidelines represent expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many people have limited access to medical care.

- People with cancer who are members of racial/ethnic minorities suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving care of poor quality than other Americans.

- Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.

# Multiple Chronic Conditions

- People with metastatic pancreatic cancer with MCCs are a complex and heterogeneous population, making it difficult to account for all of the possible permutations to develop specific recommendations for care.

- In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials whose study selection criteria may exclude people in order to avoid potential interaction effects or confounding of results associated with MCCs.

- As many people with pancreatic cancer for whom guideline recommendations apply present with MCCs, any treatment plan needs to take into account the complexity and uncertainty created by the presence of MCCs and highlight the importance of shared decision making regarding guideline use and implementation.

# Cost Implications

- There are limited cost-effectiveness analyses regarding the various treatment modalities employed in the multidisciplinary management of metastatic pancreatic cancer.

- The available data appear to support the recommendations in this guideline.

- Given the favorable cost per QALY, the improvement in clinical efficacy, and the limited available treatment options, FOLFIRINOX represents an attractive cost-effective treatment.

# Limitation of the Research & Future Directions

- Research groups are collaborating to find treatments, improve screening and diagnosis with biomarkers of pancreatic cancer, which could help physicians diagnose the disease earlier and provide better treatments to people with pancreatic cancer.

- Other strategies, which would de-emphasize treating all cases of metastatic pancreatic cancer with the same intervention, should also be explored.

- It would be more effective to investigate the molecular genetics and biology of pancreatic cancers to identify subsets which would respond to single agents or combinations of targeted agents or a cytotoxic backbone.

- Each of these options recognizes the individual variation between patients with metastatic pancreatic cancer and allows for individualized treatments.

# Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/guidelines/MetPC

Patient information is available at www.cancer.net and www.pancan.org

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