Pancreatic Adenocarcinoma

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Note: Consider clinical trials as treatment options for eligible patients.

**CLINICAL PRESENTATION**

Clinical suspicion of pancreatic cancer (e.g. jaundice) or evidence of dilated pancreatic duct and/or bile duct stricture

- Pancreatic CT\(^1,2\) scan protocol
- Obtain family history\(^3\)

**DIAGNOSTIC WORK-UP AND TISSUE ACQUISITION**

Metastases?

- Yes
  - CT scan or ultrasound guided biopsy of metastatic disease if accessible

- No
  - Yes
    - Multidisciplinary planning presentation
    - EUS with FNA
    - Liver function test, CA 19-9
    - Chest CT (preferred) or x-ray
  - No
    - Multidisciplinary planning presentation
    - Liver function tests, CA 19-9
    - Chest CT preferred or chest x-ray
    - EUS with FNA if mass visualized in pancreas
    - ERCP with brushings as clinically indicated
    - Biopsy or brushings positive?
      - Yes
        - Individualize treatment plan based on tissue confirmation and clinical staging, see Pages 2-5 for treatment options
      - No
        - Surgical consult

---

EUS = endoscopic ultrasound  
FNA = fine needle aspiration  
ERCP = endoscopic retrograde cholangiopancreatography

\(^1\) Pancreatic CT scan protocol: multiphasic cross sectional imaging and thin slices; consider MRI, PET and/or EUS if CT results are equivocal

\(^2\) For patients who cannot undergo contrast enhanced CT (allergy, renal issues, etc) consider MRI as an alternative

\(^3\) Consider referral for genetic counseling for patients with a family history of cancer

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**Preoperative clinical trial (preferred) or Off protocol systemic therapy**

**Post-treatment restaging**

**Evidence of locally advanced and/or metastatic disease?**

- Yes
  - Individualized second line systemic therapy
  - Consider best supportive care as indicated

- No
  - Resection

**Adequate and uneventful postoperative recovery within 12 weeks:**

- Consider adjuvant chemotherapy based on duration and response to neoadjuvant chemotherapy
- Consider chemoradiation

**Resectable\(^1\) pancreatic cancer and low risk\(^2\) clinical features**

- Yes
  - Restaging CT scan, CA 19-9
  - Adjuvant gemcitabine or fluorouracil-based chemotherapy
  - Consider chemoradiation

---

\(^1\) Resectable is defined as:
- Patent superior mesenteric vein-portal vein (SMV-PV) confluence
- No interface between tumor and superior mesenteric artery (SMA) or celiac
- No metastases

\(^2\) Low risk features:
- No suspicion of metastatic disease
- CA19-9 less than 1,000 units/mL with normal bilirubin
- No comorbidities

\(^3\) See Appendix A – Chemotherapy Regimens

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Note: Consider clinical trials as treatment options for eligible patients.
**Resectable** pancreatic cancer and high-risk clinical features

1. Elevated CA 19-9 with other clinical indications of metastatic disease
2. Comorbidities

**Consider staging laparoscopy**

- Staging laparoscopy positive for metastatic disease?
  - Yes
    - Pre-operative clinical trial preferred
    - Off protocol systemic chemotherapy **with or without** chemoradiation
    - Restage after each treatment modality
  - No
  - Follow metastatic section of this algorithm on Page 6

- Metastases?
  - Yes
  - No
  - Resection

- Adequate and uneventful postoperative recovery within 12 weeks:
  - Consider adjuvant chemotherapy based on duration and response to neoadjuvant chemotherapy

See surveillance on Page 8

**Note:** Consider clinical trials as treatment options for eligible patients.

---

1. Resectable is defined as:
   - Patent superior mesenteric vein-portal vein (SMV-PV) confluence
   - No interface between tumor and superior mesenteric artery (SMA) or celiac
   - No metastases

2. High Risk Features:
   - Suspicion of metastatic disease
   - CA 19-9 greater than 1,000 u/mL with a normal bilirubin
   - Comorbidities suggesting high operative risk

3. See Appendix A – Chemotherapy Regimens

4. Characterize/optimize comorbidities, diet and exercise recommended
**Clinical trial (preferred)**
Off protocol systemic therapy followed by chemoradiation if no evidence of progression and/or metastatic disease on interval scanning.

**PRESENTATION**
Radiographic, and/or biochemical, and/or clinical evidence of disease progression?
- **Yes**
  - Multidisciplinary planning presentation and consider surgical resection
- **No**
  - Post-treatment restaging

**TREATMENT**
Clinical trial preferred
- **Yes**
  - Refer to page 6 for management of progressed/metastatic disease for second line options
- **No**
  - Radiographic, and/or biochemical, and/or clinical evidence of disease progression?
    - **Yes**
      - Multidisciplinary planning presentation and consider surgical resection
    - **No**
      - Clinical trial preferred

---

1 MD Anderson Cancer Center’s Definition for **borderline resectable pancreatic cancer with or without high risk features:**
Based on anatomic considerations; a tumor abutment of less than or equal to 180° of circumference of superior mesenteric artery (SMA); short-segment encasement abutment of the common hepatic artery or gastroduodenal artery; short-segment occlusion of superior mesenteric vein (SMV) or superior mesenteric vein-portal vein (SMV-PV) and patent vessel above and below.

High Risk Features:
- Suspicion of metastatic disease
- CA 19-9 greater than 1,000 u/mL with a normal bilirubin
- Comorbidities suggesting high operative risk

2 See Appendix A – Chemotherapy Regimens

---

**Note:** Consider clinical trials as treatment options for eligible patients.
PRESENTATION

Locally advanced pancreatic cancer

- First line systemic therapy
  - Post-treatment restaging
  - No metastasis and no local progression

  - Consider continuing on clinical trial if permitted per protocol
  - Consider observation
  - Consider continuing systemic therapy
  - Consider surgical consultation
  - Consider chemoradiation

  - Chemoradiation (if not previously delivered)
  - Systemic therapy
  - Multidisciplinary planning presentation
  - Best supportive care

- Metastasis
  - Yes
    - Chemoradiation (if not previously delivered) or
    - Continue systemic therapy
    - Consider surgical consultation
  - No
    - Second line systemic therapy
    - Best supportive care

- Individualized surveillance

1 Locally advanced defined as:
  - No interface between tumor and SMA or celiac greater than 180°
  - Interface with aorta
  - Unresectable venous occlusion

2 See Appendix A – Chemotherapy Regimens

Note: Consider clinical trials as treatment options for eligible patients.
**Pancreatic Adenocarcinoma: Progression/Metastatic Disease**

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**PRESENTATION**

- **Metastatic disease at presentation**
  - Good performance status (Karnofsky greater than or equal to 80%)
  - Poor performance status (Karnofsky less than 80%)

- **Progression after primary treatment**
  - Good performance status (Karnofsky greater than or equal to 80%)
  - Poor performance status (Karnofsky less than 80%)

---

**TREATMENT**

- **Good performance status**
  - Clinical trial (preferred)
  - FOLFIRINOX for Karnofsky 90 or greater
  - Gemcitabine plus paclitaxel protein-bound for Karnofsky 70 or greater
  - Other gemcitabine doublet
  - Gemcitabine alone with or without erlotinib

- **Poor performance status**
  - Best supportive care or Gemcitabine alone with or without erlotinib

- **Second line therapy:**
  - Clinical trial (preferred)
  - After gemcitabine-based therapy:
    - Liposomal irinotecan (non-formulary) plus fluorouracil
    - Consider FOLFIRINOX if performance status improved
    - mFOLFOX6 or XELOX
  - After FOLFIRINOX-based therapy:
    - Gemcitabine plus paclitaxel protein-bound or other gemcitabine doublet except gemcitabine plus fluorouracil

- **Best supportive care**

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**Note:** Consider clinical trials as treatment options for eligible patients.

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1 See Appendix A – Chemotherapy Regimens

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Pancreatic Adenocarcinoma: Local Disease

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Note: Consider clinical trials as treatment options for eligible patients.

**RECURRENT**

Local disease only at time of recurrence

- Previous radiation therapy?
  - Yes: Systemic chemotherapy
  - No: Consider chemoradiation

Symptoms associated to recurrence?

- Yes: Consider chemoradiation
- No: Systemic chemotherapy and subsequent chemoradiation as clinically indicated

Metastatic disease at time of recurrence

- Karnofsky greater performance status greater than 80?
  - Yes: Systemic chemotherapy
  - No: Best supportive care

Individualized surveillance
### SURVEILLANCE

(for patients who had surgery as primary treatment)

<table>
<thead>
<tr>
<th>Physical Examination</th>
<th>Every 6 months for a total of 5 years then annually for a total of 5 years.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First 3 years</strong></td>
<td>Perform every 6 months</td>
</tr>
<tr>
<td></td>
<td>• Standard CT abdomen</td>
</tr>
<tr>
<td></td>
<td>• Chest x-ray</td>
</tr>
<tr>
<td></td>
<td>• CA19-9</td>
</tr>
<tr>
<td><strong>Years 4-5</strong></td>
<td>Perform every 6 months</td>
</tr>
<tr>
<td></td>
<td>• Standard CT abdomen</td>
</tr>
<tr>
<td></td>
<td>• CT chest</td>
</tr>
<tr>
<td></td>
<td>• CA 19-9</td>
</tr>
<tr>
<td><strong>Years 6-10</strong></td>
<td>Perform annually</td>
</tr>
<tr>
<td></td>
<td>• Standard CT abdomen</td>
</tr>
<tr>
<td></td>
<td>• CA 19-9</td>
</tr>
</tbody>
</table>

**Note:** Consider clinical trials as treatment options for eligible patients.
**Pancreatic Adenocarcinoma**

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**Note:** Consider clinical trials as treatment options for eligible patients.

**MANAGEMENT OF CLINICAL SITUATIONS ASSOCIATED WITH PANCREATIC ADENOCARCINOMA**

## BILIARY OBSTRUCTION

- **Biliary obstruction**
  - Pancreatic CT scan protocol
  - Biopsy confirmed adenocarcinoma?
    - Yes → Metastases?
      - Yes → ERCP with insertion of a biliary stent(s)¹ if biliary system can be drained
      - No or Uncertain → ERCP with insertion plastic or metal biliary stent
    - No → ERCP with insertion of plastic stent until biopsy confirmation of malignancy
    - If insertion not technically possible percutaneous biliary drain with attempt to subsequently insert indwelling plastic or expandable metal stent

## MECHANICAL GASTRIC OUTLET OBSTRUCTION

- **Mechanical gastric outlet obstruction**
  - Life expectancy greater than 3 months?
    - Yes → Surgical risk?
      - High² → Duodenal stent and/or radiation therapy
      - Low → Surgical bypass
    - No → Duodenal stent and/or radiation therapy
      - Duodenal stent and/or venting gastrostomy tube

**Notes:**

- ERCP = endoscopic retrograde cholangiopancreatography
- ¹ Biliary Stent(s) may be metal or plastic
- ² Presence of comorbidities
APPENDIX A: Chemotherapy and Chemoradiation Regimens

**Gemcitabine**
- Gemcitabine 600-750 mg/m² IV on days 1, 8, 15 (fixed dose rate of 10 mg/m²/minute preferred)
- With or without erlotinib 100 mg PO daily
- Repeat every 28 days

**GemCis - gemcitabine and cisplatin**
- Gemcitabine 600-750 mg/m² IV on day 1 (fixed dose rate of 10 mg/m²/min preferred)
- Cisplatin 30 mg/m² IV over 60 minutes on day 1
- Repeat every 14 days

**GemCape - gemcitabine and capecitabine**
- Gemcitabine 600-750 mg/m² IV on days 1 and 8 (fixed dose rate of 10 mg/m²/minute preferred)
- Capecitabine 1,500-1,800 mg/m²/day PO divided twice daily on days 1-14
- Repeat every 21 days

**GemCape - gemcitabine and capecitabine**
(dosing from ESPAC 4 in the adjuvant setting)
- Gemcitabine 1,000 mg/m² IV over 30 minutes weekly on days 1, 8, and 15
- Capecitabine 1,660 mg/m²/day PO in divided doses on days 1-21
- Repeat every 28 days

**Gemcitabine plus paclitaxel protein bound (Abraxane®)**
- Good performance status:
  - Paclitaxel protein-bound 100-125 mg/m² IV on days 1, 8, 15
  - Gemcitabine 600-750 mg/m² IV on days 1, 8, 15 (fixed dose rate of 10 mg/m²/min preferred)
  - Repeat every 28 days
- Average performance status:
  - Paclitaxel protein-bound 125-175 mg/m² IV on day 1
  - Gemcitabine 600-750 mg/m² IV on day 1 (fixed dose rate of 10 mg/m²/min preferred)
  - Repeat every 14 days

**GTX**
- Gemcitabine 300-400 mg/m² IV on days 4 and 11 (fixed dose rate of 10 mg/m²/minute preferred)
- Docetaxel 30-40 mg/m² IV on days 4 and 11
- Capecitabine 1,000 mg/m²/day PO divided twice daily on days 1-14
- Repeat every 21 days

**Chemoradiation Regimens**

**Gemcitabine-based chemoradiation**
- Gemcitabine 300-400 mg/m² given at fixed dose rate once weekly combined with radiation to total dose 50.4 Gy

**Capecitabine-based chemoradiation**
- Capecitabine 1650 mg/m²/day in two divided doses Monday - Friday, only on EACH DAY OF RADIATION (weekends/holidays off). Radiation to a total dose of 50.4 Gy

**mFOLFOX 6**
- Oxaliplatin 85 mg/m² IV over 2 hours on day 1
- Leucovorin 400 mg/m² IV over 2 hours on day 1³
- Fluorouracil 400 mg/m² IV bolus on day 1, then Fluorouracil 2,400 mg/m² over 46 hours IV continuous infusion
- Repeat every 14 days

**XELOX or CapeOx**
- Capecitabine 1,500-1,800 mg/m² divided twice daily on days 1-14, then Oxaliplatin 85-100 mg/m² IV over 2 hours on day 1
- Repeat every 21 days

**FOLFIRINOX**
- Oxaliplatin 75-85 mg/m² IV over 2 hours on day 1
- Irinotecan 125-180 mg/m² IV over 90 minutes on day 1
- Leucovorin 400 mg/m² IV over 2 hours on day 1³
- Fluorouracil 400 mg/m² IV bolus on day 1, then Fluorouracil 2,400 mg/m² over 46 hours IV continuous infusion
- Repeat every 14 days

**Liposomal irinotecan (Onivyde®) plus 5-fluorouracil†**
- Liposomal irinotecan 70 mg/m² IV over 90 minutes on day 1 (*non-formulary)
- Leucovorin 400 mg/m² IV over 2 hours on day 1
- Fluorouracil 400 mg/m² IV bolus on day 1
- Fluorouracil 2,400 mg/m² over 46 hours IV continuous infusion
- Repeat every 14 days

1 Gemcitabine-based and fluorouracil-based regimen, combination chemotherapy is preferred over monotherapy in the preoperative setting
2 Dosing should be started at the lower level and modified as patient tolerates
3 Many MDACC GI Oncologists skip the bolus of fluorouracil/leucovorin
4 FDA approved for the treatment of metastatic adenocarcinoma of the pancreas in combination with fluorouracil and leucovorin
Pancreatic Adenocarcinoma

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SUGGESTED READINGS


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SUGGESTED READINGS - continued


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