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
    - 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

---

\(^1\) 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
Pancreatic Adenocarcinoma: Potentially Resectable - Low Risk

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

**PRESENTATION**

- 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
    - Adjuvant gemcitabine or fluorouracil-based chemotherapy
    - Consider chemoradiation
    - Restaging CT scan, CA 19-9
    - Adjuvant gemcitabine or fluorouracil-based chemotherapy
    - Consider chemoradiation
- See Surveillance on Page 8

---

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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Pancreatic Adenocarcinoma: Resectable - High Risk

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

### PRESENTATION

1. Elevated CA 19-9 with other clinical indications of metastatic disease
2. Consider staging laparoscopy
3. 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
4. Metastases?
   - Yes
     - Follow metastatic section of this algorithm on Page 6
   - 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

---

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/optimze 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
- No

**Resection?**

- Yes
- No

**TREATMENT**

Multidisciplinary planning presentation and consider surgical resection

Clinical trial preferred

Adjuvant chemotherapy should be administered if patient did not receive neoadjuvant chemotherapy

After resection, consider adjuvant chemotherapy with gemcitabine plus capecitabine based on duration and response to neoadjuvant therapy

Refer to page 6 for management of progressed/metastatic disease for second line options

---

**Borderline resectable pancreatic cancer**

- Clinical trial (preferred)
- Off protocol systemic therapy followed by chemoradiation if no evidence of progression and/or metastatic disease on interval scanning

---

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
Pancreatic Adenocarcinoma: Locally Advanced

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

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

See Appendix A – Chemotherapy Regimens

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Pre-protocol restaging

Post-protocol restaging

Clinical trial (preferred)

Local progression only

Metastasis

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

Second line systemic therapy

Best supportive care

Individualized surveillance

Yes

No

Metastasis?

Chemoradiation (if not previously delivered) or

Continue systemic therapy

Consider surgical consultation

First line systemic therapy

Post-treatment restaging

Second line systemic therapy

Best supportive care

Best supportive care

 Locally advanced pancreatic cancer

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
**PRESENTATION**

- **Good performance status** (Karnofsky greater than or equal to 80%)
  - 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** (Karnofsky less than 80%)
  - Best supportive care
  - Gemcitabine alone with or without erlotinib

**Progression after primary treatment**

- **Good performance status** (Karnofsky greater than or equal to 80%)
  - 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

- **Poor performance status** (Karnofsky less than 80%)
  - Best supportive care

---

1 See Appendix A – Chemotherapy Regimens

---

**Note:** Consider clinical trials as treatment options for eligible patients.
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: Systemic chemotherapy and subsequent chemoradiation as clinically indicated
  - No: Individualized surveillance

Metastatic disease at time of recurrence

- Karnofsky greater performance status greater than 80?
  - Yes: Systemic chemotherapy
  - No: Best supportive care
**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>First 3 years</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>Years 4-5</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>Years 6-10</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: **ERCP with insertion of a biliary stent(s)** if biliary system can be drained
    - No or Uncertain: **ERCP with insertion plastic or metal biliary stent**
      - **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?**
      - High:
        - Duodenal stent and/or radiation therapy
      - Low:
        - Surgical bypass
      - **Duodenal stent and/or radiation therapy**
        - **Duodenal stent and/or venting gastrostomy tube**
    - No: **ERCP = endoscopic retrograde cholangiopancreatography**
      - 1 Biliary Stent(s) may be metal or plastic
      - 2 Presence of comorbidities

---

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### APPENDIX A: Chemotherapy and Chemoradiation Regimens

#### Gemcitabine-based regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Details</th>
</tr>
</thead>
</table>
| 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 (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®)

| Details | 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 |

| Details | 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 |

| Details | 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 |

### Fluoropyrimidine-based regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Details</th>
</tr>
</thead>
</table>
| mFOLFOX 6 | Oxaliplatin 85 mg/m² IV over 2 hours on day 1  
Leucovorin 400 mg/m² IV over 2 hours on day 1  
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 days 1  
Leucovorin 400 mg/m² IV over 2 hours on day 1  
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  
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.

---

**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

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Approved by the Executive Committee of the Medical Staff on 05/30/2017
SUGGESTED READINGS


SUGGESTED READINGS - continued


Pancreatic Adenocarcinoma

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