Pancreatic Adenocarcinoma

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

- Pancreatic CT scan protocol
- Obtain family history
- Lifestyle risk assessment

Mass in pancreas on imaging?

Metastases?

- Multidisciplinary planning presentation
- Liver function tests, CA 19-9
- CT chest (preferred) or chest x-ray

- Multidisciplinary planning presentation
- Liver function tests, CA 19-9
- EUS with FNA if mass visualized in pancreas
- ERCP with brushings as clinically indicated

Biopsy or brushings positive?

Yes

Surgical consult

No

CT scan or ultrasound-guided biopsy of metastatic disease if accessible. Core needle biopsy is preferred to facilitate next generation sequencing (NGS).

Yes

No

Note: Consider Clinical Trials as treatment options for eligible patients

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Pancreatic Adenocarcinoma

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Note: Consider Clinical Trials as treatment options for eligible patients

**PRESENTATION**

- Pre-operative clinical trial (preferred) or systemic therapy in select patients
- Consider radiation therapy in select patients

**TREATMENT**

- Post-operative clinical trial

**POST-OPERATIVE**

- Evidence of locally advanced and/or metastatic disease?
  - Yes
    - Individualized subsequent therapy
    - Consider best supportive care as indicated
  - No
    - Resection
    - Adequate and uneventful post-operative recovery within 12 weeks:
      - Consider adjuvant chemotherapy based on duration and response to neoadjuvant chemotherapy
      - Consider radiation therapy if not previously given

- Adequate and uneventful post-operative recovery within 12 weeks:
  - Restaging CT, scan
  - CA 19-9
  - Adjuvant gemcitabine or fluorouracil-based chemotherapy
  - Consider radiation therapy following chemotherapy in the setting of an R1 resection

---

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
   - CA 19-9 ≤ 500 units/mL with normal bilirubin
   - Manageable and optimized comorbidities

3. Typically gemcitabine plus paclitaxel or FOLFIRINOX (see Appendix A – Chemotherapy Regimens)

4. Typically FOLFIRINOX or GemCape or single agent gemcitabine (see Appendix A – Chemotherapy Regimens)

5. See Appendix B – Radiation Therapy

6. If post-operative recovery is greater than 12 weeks, adjuvant therapy will be at the discretion of the treating provider

7. If patient exhibits all low-risk features and all other factors are favorable, primary resection can be considered

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

9. Pancreatic CT scan protocol: multiphasic cross sectional imaging and thin slices; consider MRI, PET and/or EUS if CT results are equivocal

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Approved by the Executive Committee of the Medical Staff on 10/19/2021
Pancreatic Adenocarcinoma

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Note: Consider Clinical Trials as treatment options for eligible patients

PRESENTATION

Resectable\(^1\) pancreatic cancer and high-risk\(^2\) clinical features

Comorbidities

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

High-risk features:
- Suspicion of metastatic disease
- CA 19-9 > 500 units/mL, with a normal bilirubin
- Reversible and optimizeable comorbidities

Metastases?

Yes

Follow metastatic section on Page 7

No

Resection

Characterize/optimise comorbidities; diet and exercise recommended

Staging laparoscopy positive for metastatic disease?

Is staging laparoscopy appropriate?

Yes

Pre-operative clinical trial preferred

Systemic chemotherapy\(^3\) with radiation therapy\(^4\) in select patients

Restage after each treatment modality

No

Metastases?

Yes

No

Adequate and uneventful postoperative recovery within 12 weeks\(^5\); Consider adjuvant chemotherapy\(^6\) based on duration and response to neoadjuvant chemotherapy\(^3\)

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 > 500 units/mL, with a normal bilirubin
- Reversible and optimizable comorbidities

3 Typically gemcitabine plus paclitaxel or FOLFIRINOX (see Appendix A – Chemotherapy Regimens)

4 See Appendix B – Radiation Therapy

5 If post-operative recovery is greater than 12 weeks, adjuvant therapy will be at the discretion of the treating provider

6 Typically FOLFIRINOX or GemCape or single agent gemcitabine (see Appendix A – Chemotherapy Regimens)
**Clinical trial** or **Systemic therapy** followed by radiation therapy (in select patients) if no evidence of progression and/or metastatic disease on interval scanning.

### PRESENTATION

**Borderline resectable pancreatic cancer**

- Clinical trial (preferred) or
- Systemic therapy followed by radiation therapy (in select patients) if no evidence of progression and/or metastatic disease on interval scanning

### TREATMENT

- **Clinical trial preferred**
  - Yes: Multidisciplinary planning presentation and consider surgical resection
  - No: For subsequent therapy options for management of progressed/metastatic disease, see Page 7

- **Radiographic, and/or biochemical, and/or clinical evidence of disease progression?**
  - Yes: After resection, consider adjuvant chemotherapy based on duration and response to neoadjuvant therapy
  - No: For subsequent therapy options for management of progressed/metastatic disease, see Page 7

---

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 500 units/mL with a normal bilirubin
     - Reversible and optimizable comorbidities

2. Typically gemcitabine plus paclitaxel or FOLFIRINOX (see Appendix A – Chemotherapy Regimens)
3. See Appendix B – Radiation Therapy
4. Typically FOLFIRINOX or GemCape or single agent gemcitabine (see Appendix A – Chemotherapy Regimens)
**PRESENTATION**

- Locally advanced pancreatic cancer
  - Clinical trial (preferred) or
  - First line systemic therapy

- Serial post-treatment restaging for 4-6 months or as indicated per protocol

**TREATMENT**

- No metastasis and No further local progression
  - Consider:
    - Systemic therapy or
    - Radiation therapy in select patients or
    - Observation

- Local progression only
  - Radiation therapy (if not previously delivered) or
  - Systemic therapy or
  - Best supportive care

- Metastasis
  - Subsequent therapy or
  - Best supportive care

---

1 Locally advanced defined as:
   - Interface between tumor and SMA or celiac greater than 180°
   - Interface with aorta
   - Unresectable venous occlusion

2 Typically gemcitabine plus paclitaxel or FOLFIRINOX (see Appendix A – Chemotherapy Regimens)

3 See Appendix A – Chemotherapy Regimens

4 See Appendix B – Radiation Therapy
Pancreatic Adenocarcinoma

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Note: Consider Clinical Trials as treatment options for eligible patients

**RECURRENT**

Local disease **only** at time of recurrence

- **Yes:** Previous radiation therapy?
  - **Yes:** Systemic chemotherapy
  - **No:** Consider radiation therapy as clinically indicated

- **No:** Symptoms associated to recurrence?
  - **Yes:** Systemic chemotherapy
  - **No:** Individualized surveillance

1 See Appendix A – Chemotherapy Regimens
2 See Appendix B – Radiation Therapy

1 See Appendix A – Chemotherapy Regimens
2 See Appendix B – Radiation Therapy
Presenting disease

**Good performance status (ECOG 0-1)**
- Clinical trial (preferred)
- FOLFIRINOX® if ECOG performance status 0-1
- Gemcitabine plus paclitaxel protein-bound® if ECOG performance status 0-2
- Other gemcitabine doublet® if ECOG performance status 0-1
- Olaparib®

**Poor performance status (ECOG ≥ 2)**
- Best supportive care if ECOG performance status greater than 2
- Gemcitabine alone with or without erlotinib® if ECOG performance status 2

Subsequent therapy:
- Clinical trial (preferred)
- After gemcitabine-based therapy®,
  - Liposomal irinotecan plus fluorouracil®
  - FOLFIRINOX® or
  - mFOLFOX® or XELOX® or
  - Olaparib®
- After FOLFIRINOX®-based therapy®,
  - Gemcitabine plus paclitaxel protein-bound®
  - other gemcitabine doublet® except gemcitabine plus fluorouracil

**Individualized surveillance or additional treatment as clinically indicated**

**Metastatic disease at presentation**

**Metastatic disease after primary treatment**

Note: Consider Clinical Trials as treatment options for eligible patients

ECOG = Eastern Cooperative Oncology Group

1 See Appendix A – Chemotherapy Regimens

2 For patient with ECOG performance status 2, modify dose as appropriate (refer to dosing for average performance status in Appendix A)

3 Olaparib may be used as maintenance treatment in the setting of platinum sensitive tumors with BRCA family mutations and no disease progression during at least 16 weeks of first-line, platinum-based chemotherapy

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### 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>• Surveillance (portal venous phase) CT&lt;sup&gt;1,2&lt;/sup&gt; abdomen</td>
</tr>
<tr>
<td>Perform every 6 months</td>
<td>• Chest x-ray</td>
</tr>
<tr>
<td></td>
<td>• CA 19-9</td>
</tr>
<tr>
<td>Years 4-5:</td>
<td>• Surveillance (portal venous phase) CT&lt;sup&gt;1,2&lt;/sup&gt; abdomen</td>
</tr>
<tr>
<td>Perform every 6 months</td>
<td>• CT chest</td>
</tr>
<tr>
<td></td>
<td>• CA 19-9</td>
</tr>
<tr>
<td>Years 6-10:</td>
<td>• Surveillance (portal venous phase) CT&lt;sup&gt;1,2&lt;/sup&gt; abdomen</td>
</tr>
<tr>
<td>Perform annually</td>
<td>• CA 19-9</td>
</tr>
</tbody>
</table>

<sup>1</sup> Consider dedicated pancreatic CT protocol, MRI, PET and/or EUS if surveillance CT results are equivocal, e.g., suspicion of recurrence within pancreatic remnant, extrapancreatic local recurrence, question of liver metastases, etc.

<sup>2</sup> For patients who cannot undergo contrast enhanced CT (allergy, renal issues, etc.) consider MRI as an alternative
**BILIARY OBSTRUCTION**

Biliary obstruction → Pancreatic CT\(^1\) scan protocol → Biopsy confirmed adenocarcinoma?

- Yes → Metastases?
  - Yes → ERCP with insertion of a biliary stent(s)\(^2\) if biliary system can be drained
  - No or Uncertain → ERCP with insertion of a plastic or metal biliary stent

- No → ERCP with insertion of a plastic or metal biliary stent

\(^1\) Pancreatic CT scan protocol

\(^2\) Biliary stent(s) may be metal or plastic

**MECHANICAL GASTRIC OUTLET OBSTRUCTION**

Mechanical gastric outlet obstruction → Life expectancy > 3 months or non-extensive metastases?

- Yes → Surgical risk
  - High\(^3\) → Duodenal stent with or without radiation therapy
  - Low → Surgical bypass

- No → Duodenal stent with or without radiation therapy
  - Duodenal stent and/or venting gastrostomy tube

\(^3\) Life expectancy > 3 months or non-extensive metastases?

ERCP = endoscopic retrograde cholangiopancreatography

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Note: Consider Clinical Trials as treatment options for eligible patients

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Many MD Anderson GI Oncologists omit Day 1, 8, 15 of gemcitabine plus paclitaxel protein bound (Abraxane®)1,2,3.

Gemcitabine6
- Gemcitabine 600-750 mg/m² IV on Days 1, 8, 15 (fixed dose infusion rate of 10 mg/m²/minute preferred)
- With or without erlotinib 100 mg PO daily
- Repeat every 28 days

GemCis - gemcitabine and cisplatin5
- Gemcitabine 600-750 mg/m² IV on Day 1 (fixed dose infusion rate of 10 mg/m²/minute preferred)
- Cisplatin 30 mg/m² IV over 60 minutes on Day 1
- Repeat every 14 days

GemCape - gemcitabine and capecitabine4
- Gemcitabine 600-750 mg/m² IV on Days 1 and 8 (fixed dose infusion 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 capecitabine4 (dosing from ESPAC 4 in the adjuvant setting)
- Gemcitabine 1,000 mg/m² IV over 30 minutes weekly on Days 1, 8, and 154
- Capecitabine 1,660 mg/m²/day PO in divided doses on Days 1-21
- Repeat every 28 days

GemOx - gemcitabine and oxaliplatin
- Gemcitabine 600-750 mg/m² IV on Day 1 (fixed dose infusion rate of 10 mg/m²/minute preferred)
- Oxaliplatin 85 mg/m² IV over 2 hours on Day 1
- Repeat every 14 days

Gemcitabine-based regimens1,2,3:

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

Gemcitabine plus paclitaxel protein bound (Abraxane®)1,2,3:

- 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 infusion rate of 10 mg/m²/minute 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 infusion rate of 10 mg/m²/minute preferred)
  - Repeat every 14 days

FOLFIRINOX4:
- Gemcitabine 300-400 mg/m² IV on Days 4 and 11 (fixed dose infusion 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

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

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 IV continuous infusion over 46 hours
- Repeat every 14 days

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 IV continuous infusion over 46 hours
- Repeat every 14 days

Liposomal irinotecan (Onivyde®) plus 5-fluorouracil7
- 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, then
- Fluorouracil 2,400 mg/m² IV continuous infusion over 46 hours
- Repeat every 14 days

Fluopyrimidine-based regimens1,2:

- 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 1
- Fluorouracil 400 mg/m² IV bolus on Day 1, then
- Fluorouracil 2,400 mg/m² IV continuous infusion over 46 hours
- Repeat every 14 days

1 For 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 If fixed dose infusion rate not utilized, administer gemcitabine 1,000 mg/m² over 30 minutes.
4 Typical post-operative adjuvant regimens: FOLFIRINOX or GemCape or single-agent gemcitabine (depending on response and recovery).
5 The preferred doublet for tumors with germline BRCA mutations.
6 Many MD Anderson GI Oncologists omit Day 15.
## APPENDIX B: Radiation Therapy

### Chemoradiation Regimens

#### Long course chemoradiation
- Total dose 50 Gy in 25 fractions or 50.4 Gy in 28 fractions
- Concurrent capecitabine $1,650 \text{ mg/m}^2 \text{ PO in two divided doses on each day of radiation or}$
- Concurrent gemcitabine $300-400 \text{ mg/m}^2 \text{ IV given at fixed dose infusion once weekly}$

#### Short course chemoradiation
- Total dose 30 Gy in 10 fractions
- Concurrent capecitabine $1,650 \text{ mg/m}^2 \text{ PO in two divided doses on each day of radiation or}$
- Concurrent gemcitabine $300-400 \text{ mg/m}^2 \text{ IV given at fixed rate dose infusion once weekly}$

#### Hypofractionated chemoradiation
- Total dose 60-67.5 Gy in 15 fractions
- Concurrent capecitabine $1,650 \text{ mg/m}^2 \text{ PO in two divided doses on each day of radiation}$
- Requires image guidance

### Stereotactic Body Radiation Therapy
- Total dose 33-40 Gy in 5 fractions
- Usually requires fiducials
- Requires daily image guidance

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1 Infusional fluorouracil may be used instead
2 If fixed dose infusion rate of 10 mg/m$^2$/minute not utilized, administer gemcitabine over 30 minutes
Pancreatic Adenocarcinoma

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SUGGESTED READINGS


Continued on next page
Pancreatic Adenocarcinoma

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SUGGESTED READINGS - continued


SUGGESTED READINGS - continued


Pancreatic Adenocarcinoma

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