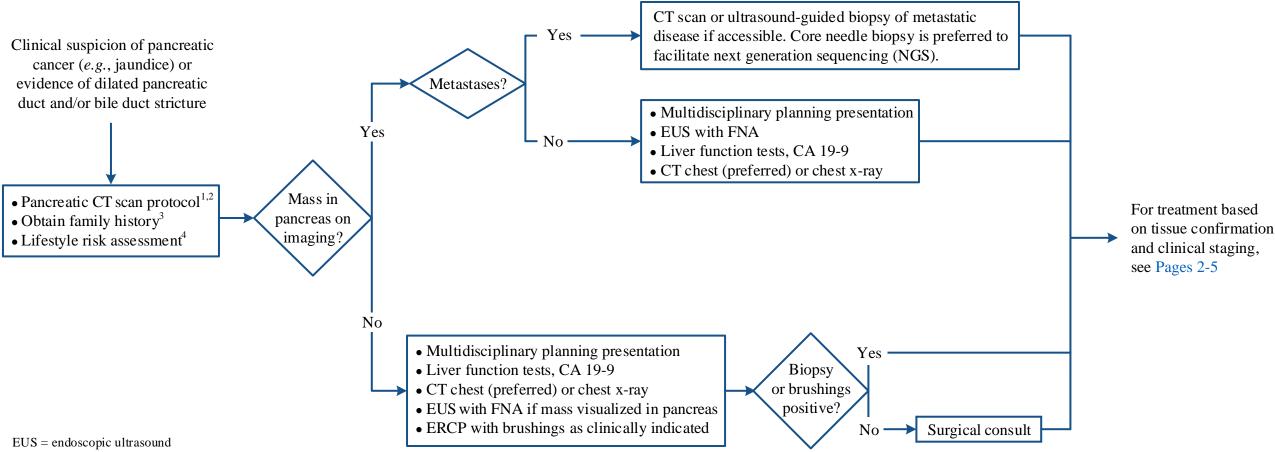


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Note: Consider Clinical Trials as treatment options for eligible patients

CLINICAL PRESENTATION

DIAGNOSTIC WORK-UP AND TISSUE ACQUISITION



FNA = fine needle aspiration

ERCP = endoscopic retrograde cholangiopancreatography

¹Pancreatic 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

³Consider referral for genetic counseling for patients with a family history of cancer. Universal gerrmline testing recommended for eligible patients.

⁴See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

See

Surveillance on Page 8



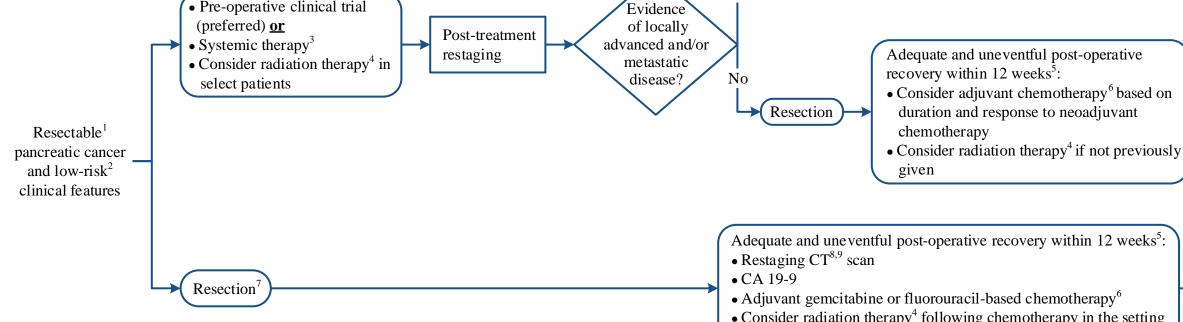
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Pancreatic Adenocarcinoma

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Note: Consider Clinical Trials as treatment options for eligible patients

POST-OPERATIVE PRESENTATION TREATMENT • Individualized subsequent therapy • Consider best supportive care as indicated Yes • Pre-operative clinical trial Evidence



Adequate and uneventful post-operative recovery within 12 weeks⁵:

- Adjuvant gemcitabine or fluorouracil-based chemotherapy⁶
- Consider radiation therapy⁴ following chemotherapy in the setting of an R1 resection

- Patent superior mesenteric vein-portal vein (SMV-PV) confluence
- No interface between tumor and superior mesenteric artery (SMA) or celiac
- No metastases

- No suspicion of metastatic disease
- CA 19-9 \leq 500 units/mL with normal bilirubin
- Manageable and optimized comorbidities

¹Resectable is defined as:

²Low-risk features:

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

⁶Typically FOLFIRINOX or GemCape or single agent gemcitabine (see Appendix A – Chemotherapy Regimens)

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

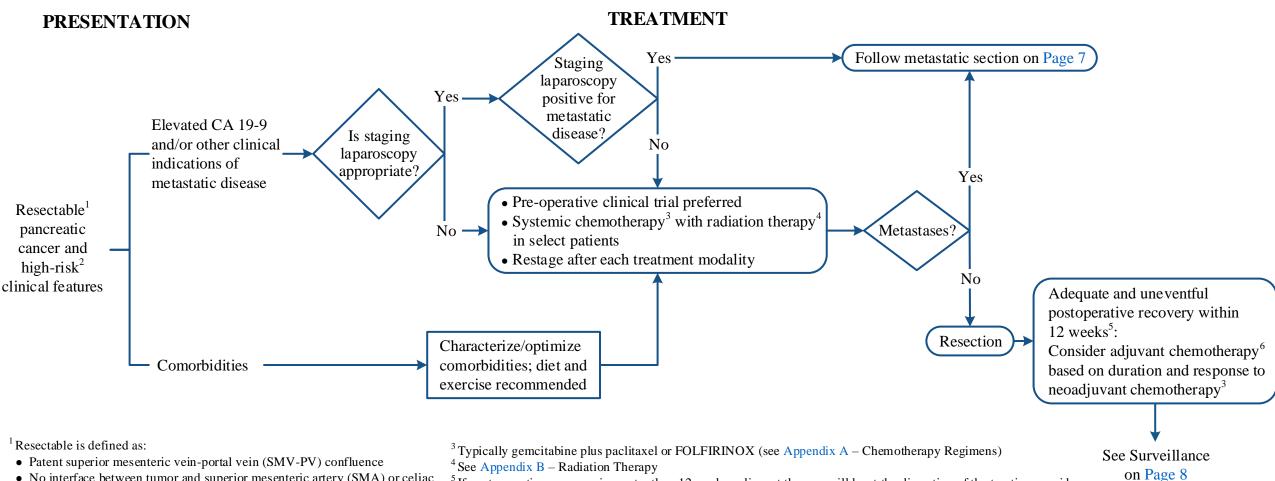
⁸ For patients who cannot undergo contrast enhanced CT (allergy, renal issues, etc.) consider MRI as an alternative

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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[•] 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

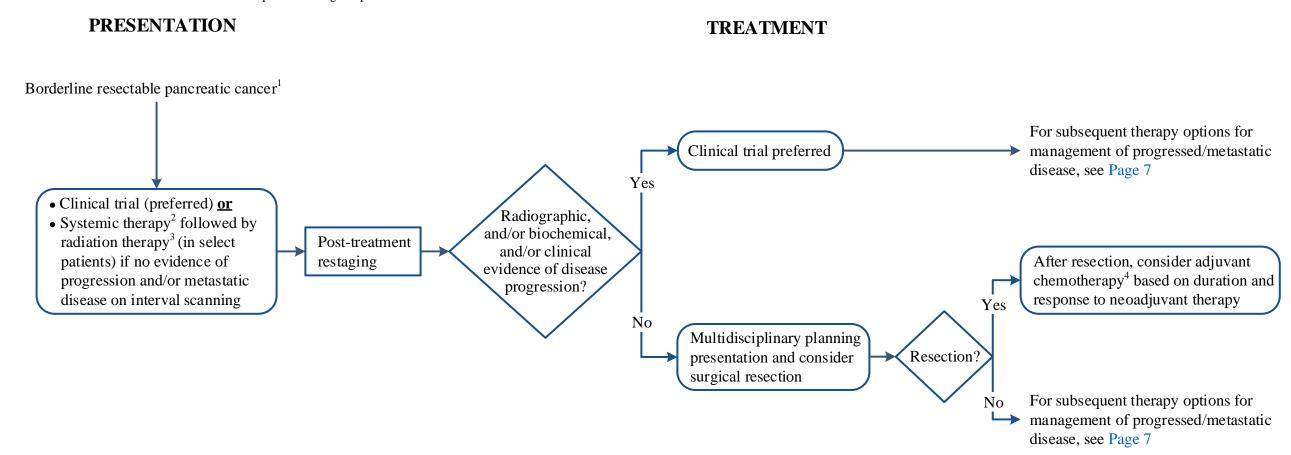
⁵ If post-operative recovery is greater than 12 weeks, adjuvant therapy will be at the discretion of the treating provider

⁶ Typically FOLFIRINOX or GemCape or single agent gemcitabine (see Appendix A – Chemotherapy Regimens)



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Note: Consider Clinical Trials as treatment options for eligible patients



¹MD 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

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

³ See Appendix B – Radiation Therapy

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

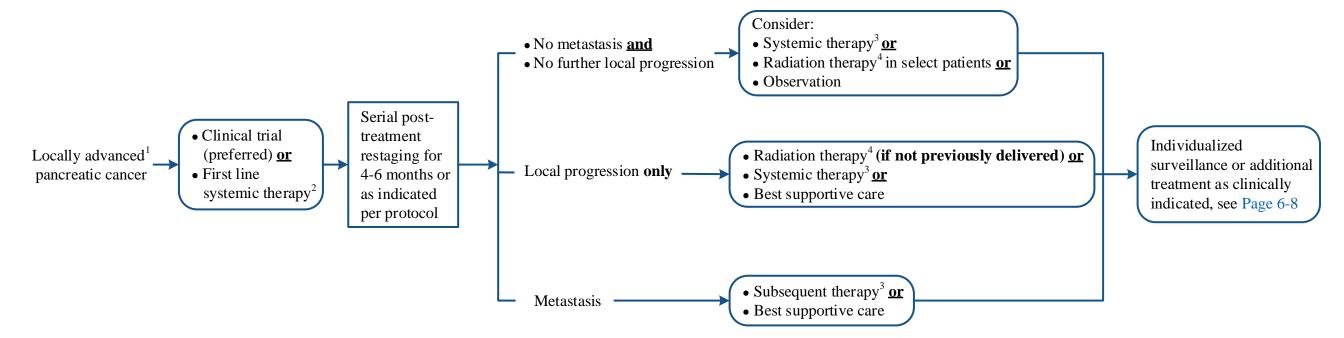


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Note: Consider Clinical Trials as treatment options for eligible patients

PRESENTATION

TREATMENT



¹ Locally advanced defined as:

 $[\]bullet\,$ 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)

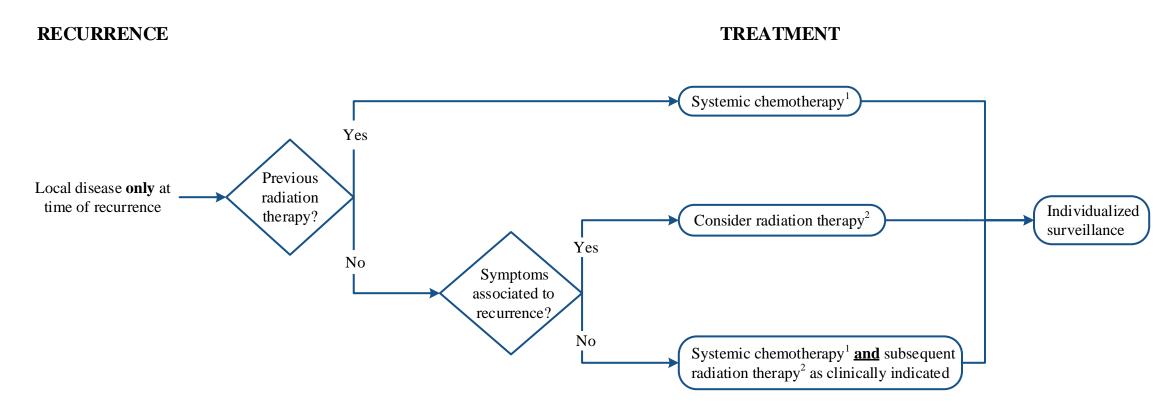
³See Appendix A – Chemotherapy Regimens

⁴ See Appendix B – Radiation Therapy



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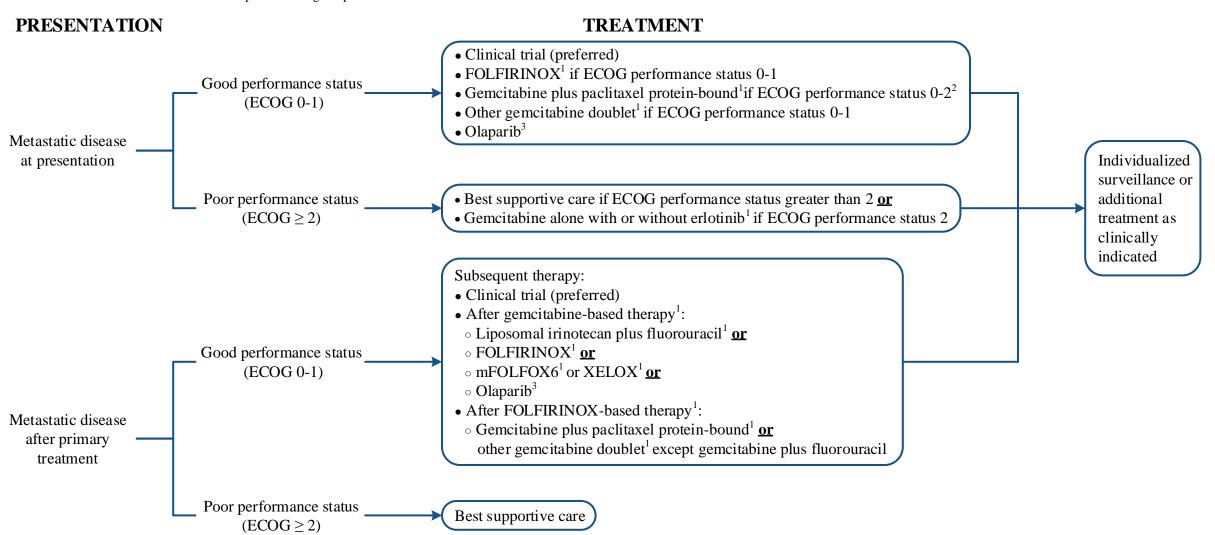
¹See Appendix A – Chemotherapy Regimens

² See Appendix B – Radiation Therapy



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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)

³Olaparib 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)

| Physical Examination | Every 6 months for a total of 5 years, then annually for a total of 5 years |
|---------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| First 3 years: Perform every 6 months | Surveillance (portal venous phase) CT^{1,2} abdomen Chest x-ray CA 19-9 |
| Years 4-5: Perform every 6 months | Surveillance (portal venous phase) CT^{1,2} abdomen CT chest CA 19-9 |
| Years 6-10: Perform annually | Surveillance (portal venous phase) CT^{1,2} abdomen CA 19-9 |

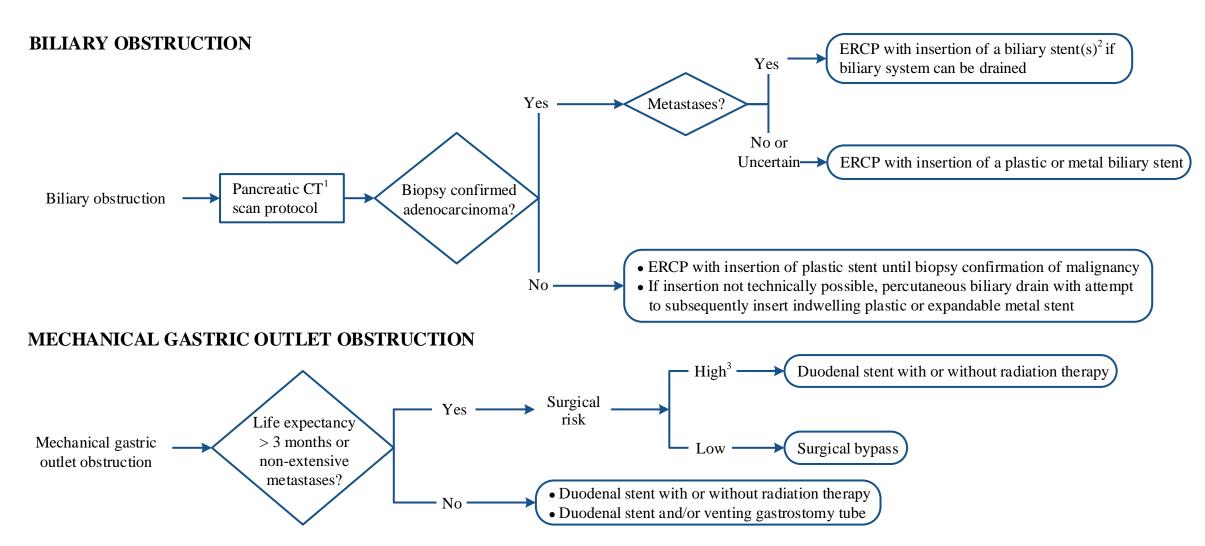
¹ Consider dedicated pancreatic CT protocol, MRI, PET and/or EUS if surveillance CT results are equivocal, *e.g.*, suspicion of recurrence within pancreatic remnant, extrapancreatic local recurrence, question of liver metastases, etc.

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



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Note: Consider Clinical Trials as treatment options for eligible patients



ERCP = endoscopic retrograde cholangiopancreatography

¹ For patients who cannot undergo contrast enhanced CT (allergy, renal issues, etc.) consider MRI as an alternative

²Biliary stent(s) may be metal or plastic

³Presence of comorbidities and malnutrition

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APPENDIX A: Chemotherapy Regimens

Gemcitabine-based regimens^{1,2,3}:

Gemcitabine⁴

- 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/min 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

$\label{eq:GemCape} \textbf{GemCape - gemcitabine} \ \textbf{and capecitabine}^4$

(dosing from ESPAC 4 in the adjuvant setting)

- Gemcitabine 1,000 mg/m² IV over 30 minutes weekly on Days 1, 8, and 15⁶
- Capecitabine 1,660 mg/m²/day PO in divided doses on Days 1-21
- Repeat every 28 days

Gemcitabine plus paclitaxel protein bound (Abraxane®)⁷ 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/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 infusion 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 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

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

Fluoropyrimidine-based regimens^{1,2}:

mFOLFOX 6

- Oxaliplatin 85 mg/m² IV over 2 hours on Day 1
- Leucovorin 400 mg/m² IV over 2 hours on Day 1⁸
- Fluorouracil 400 mg/m² IV bolus on Day 1⁸, then fluorouracil 2,400 mg/m² IV continuous infusion over 46 hours
- Repeat every 14 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

FOLFIRINOX^{4,7}

- 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 1⁷ Fluorouracil 400 mg/m² IV bolus on Day 1⁷, then fluorouracil 2,400 mg/m² IV continuous infusion over 46 hours
- Repeat every 14 days

Liposomal irinotecan (Onivyde®) plus 5-fluorouracil9

- Liposomal irinotecan 70 mg/m² IV over 90 minutes on Day 1¹⁰
- Leucovorin 400 mg/m² IV over 2 hours on Day 1⁷
- Fluorouracil 400 mg/m² IV bolus on Day 1⁷, 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

²Dosing 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

⁴Typical 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

⁶Many MD Anderson GI Oncologists omit Day 15 Copyright 2021 The University of Texas MD Anderson Cancer Center ⁷Typical pre-operative neoadjuvant regimens: gemcitabine plus paclitaxel or FOLFIRINOX

⁸ Many MD Anderson GI Oncologists omit the bolus of fluorouracil/leucovorin

⁹ FDA approved for the treatment of metastatic adenocarcinoma of the pancreas in combination with fluorouracil and leucovorin

¹⁰ For patients with known homozygous *UGT1A1*28* allele reduce the initial starting dose to 50 mg/m²

Department of Clinical Effectiveness V7

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

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APPENDIX B: Radiation Therapy

Chemoradiation Regimens

Long course chemoradiation

- Total dose 50 Gy in 25 fractions or 50.4 Gy in 28 fractions
- Concurrent capecitabine¹ 1,650 mg/m² PO in two divided doses on each day of radiation or
- Concurrent gemcitabine 300-400 mg/m² IV given at fixed dose infusion once weekly²

Short course chemoradiation

- Total dose 30 Gy in 10 fractions
- Concurrent capecitabine¹ 1,650 mg/m² PO in two divided doses on each day of radiation or
- Concurrent gemcitabine 300-400 mg/m² IV given at fixed rate dose infusion once weekly²

Hypofractionated chemoradiation

- Total dose 60-67.5 Gy in 15 fractions
- Concurrent capecitabine¹ 1,650 mg/m² 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

¹ Infusional fluorouracil may be used instead

² If fixed dose infusion rate of 10 mg/m²/minute not utilized, administer gemcitabine over 30 minutes



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Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

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