

# Pancreatic Adenocarcinoma Treatment Regimens

**Clinical Trials:** The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The National Comprehensive Cancer Network Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

**Note:** All recommendations are category 2A unless otherwise indicated.

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup>

REGIMEN	DOSING
<b>Noadjuvant Chemotherapy (Resectable/Borderline Resectable Disease)<sup>a</sup></b>	
<b>Preferred Regimens</b>	
FOLFIRINOX <sup>2,b,c</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Modified FOLFIRINOX <sup>3,b,c</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b> <b>Day 1:</b> Irinotecan 135mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 300mg/m <sup>2</sup> IV bolus, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Gemcitabine + Albumin-Bound Paclitaxel <sup>4,b,d</sup>	<b>Days 1,8,15:</b> Albumin-bound Paclitaxel 125mg/m <sup>2</sup> IV over 30 minutes <b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks for 2-6 cycles.
<b>Preferred Regimens Only For Known BRCA1/2 or PALB2 Mutations</b>	
FOLFIRINOX <sup>2,b,c</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Modified FOLFIRINOX <sup>3,b,c</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b> <b>Day 1:</b> Irinotecan 135mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 300mg/m <sup>2</sup> IV bolus, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Gemcitabine + Cisplatin (≥2-6 cycles) <sup>5,6,b,e</sup>	<b>Day 1:</b> Gemcitabine 750mg/m <sup>2</sup> IV over 30 minutes <b>Day 1:</b> Cisplatin 25-50mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 2 weeks for 2-6 cycles. <b>OR</b> <b>Day 1:</b> Gemcitabine 750mg/m <sup>2</sup> IV at a rate of 10mg/m <sup>2</sup> /minute <b>Day 1:</b> Cisplatin 25-50mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 2 weeks for 2-6 cycles.
<b>Adjuvant Chemotherapy</b>	
<b>Preferred Regimens</b>	
Modified FOLFIRINOX (Category 1) <sup>3,c</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b> <b>Day 1:</b> Irinotecan 135mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 300mg/m <sup>2</sup> IV bolus, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Gemcitabine + Capecitabine (Category 1) <sup>7</sup>	<b>Days 1,8,15:</b> Gemcitabine 1000mg/m <sup>2</sup> IV <b>Days 1-21:</b> Capecitabine 830mg/m <sup>2</sup> orally twice daily Repeat cycle every 4 weeks for 6 cycles.

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>Adjuvant Chemotherapy</b> (continued)	
<b>Other Recommended Regimens</b>	
Capecitabine (Category 2B) <sup>8</sup>	<b>Days 1-14:</b> Capecitabine 825-1,000mg/m <sup>2</sup> orally twice daily. Repeat cycle every 3 weeks for 8 cycles.
Fluorouracil, Continuous Infusion <sup>9</sup>	<b>Days 1-28:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Repeat every 42 days for 4 cycles.
Fluorouracil, Continuous Infusion (followed by chemoradiation) <sup>9,f</sup>	<b>Days 1-21:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Administer for one 21-day cycle, <b>followed by:</b> concurrent chemotherapy and radiation therapy (See Chemoradiation).
Fluorouracil, Continuous Infusion (followed by chemoradiation) followed by Fluorouracil + Leucovorin <sup>9,f</sup>	<b>Days 1-21:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Administer for one 21-day cycle, <b>followed by:</b> concurrent chemotherapy and radiation therapy (See Chemoradiation), <b>followed by:</b> <b>Days 1-28:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Repeat cycle every 42 days for 2 cycles.
Fluorouracil + Leucovorin (Category 1) <sup>10</sup>	<b>Days 1-5:</b> Leucovorin 20mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-5:</b> Fluorouracil 425mg/m <sup>2</sup> IV push. Repeat cycle every 4 weeks for 6 cycles.
Fluorouracil + Leucovorin (followed by chemoradiation) <sup>10,f</sup>	<b>Days 1-5:</b> Leucovorin 20mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-5:</b> Fluorouracil 425mg/m <sup>2</sup> IV push. Repeat cycle every 4 weeks for 2-6 cycles <b>followed by:</b> concurrent chemotherapy and radiation therapy (See Chemoradiation).
Fluorouracil + Leucovorin (followed by chemoradiation followed by Fluorouracil + Leucovorin) <sup>f</sup>	See NCCN Pancreatic Adenocarcinoma Guidelines.
Gemcitabine (Category 1) <sup>9,11,12</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks for 6 cycles.
Gemcitabine (followed by chemoradiation) <sup>9,11,12,f</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks for 2-6 cycles, <b>followed by:</b> concurrent chemotherapy and radiation therapy (See Chemoradiation).
Gemcitabine (followed by chemoradiation followed by Gemcitabine) <sup>9,11,12,f</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Administer for one 28-day cycle, <b>followed by:</b> concurrent chemotherapy and radiation therapy (See Chemoradiation), <b>followed by:</b> <b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks for 3 cycles.
<b>First-Line Chemotherapy for Locally Advanced Disease and Good Performance Status</b>	
<b>Preferred Regimens</b>	
FOLFIRINOX <sup>2,c,g,h</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Modified FOLFIRINOX <sup>3,c,g,h</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b> <b>Day 1:</b> Irinotecan 135mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 300mg/m <sup>2</sup> IV bolus, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Gemcitabine + Albumin-Bound Paclitaxel <sup>4,d,h</sup>	<b>Days 1,8,15:</b> Albumin-bound Paclitaxel 125mg/m <sup>2</sup> IV over 30 minutes <b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks for 2-6 cycles.

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>First-Line Chemotherapy for Locally Advanced Disease and Good Performance Status</b> (continued)	
<b>Preferred Regimens for Known <i>BRCA1/2</i> or <i>PALB2</i> Mutations</b>	
FOLFIRINOX <sup>2,c,g,h</sup>	<p><b>Day 1:</b> Oxaliplatin 85mg/m<sup>2</sup> IV over 2 hours</p> <p><b>Day 1:</b> Irinotecan 180mg/m<sup>2</sup> IV over 90 minutes</p> <p><b>Day 1:</b> Leucovorin 400mg/m<sup>2</sup> IV over 90 minutes, <b>followed by:</b></p> <p><b>Day 1:</b> Fluorouracil 400mg/m<sup>2</sup> IV push, <b>followed by:</b></p> <p><b>Days 1-2:</b> Fluorouracil 1,200mg/m<sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m<sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.</p>
Modified FOLFIRINOX <sup>3,c,g,h</sup>	<p><b>Day 1:</b> Oxaliplatin 85mg/m<sup>2</sup> IV over 2 hours, <b>followed by:</b></p> <p><b>Day 1:</b> Leucovorin 400mg/m<sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b></p> <p><b>Day 1:</b> Irinotecan 135mg/m<sup>2</sup> IV over 90 minutes, <b>followed by:</b></p> <p><b>Day 1:</b> Fluorouracil 300mg/m<sup>2</sup> IV bolus, <b>followed by:</b></p> <p><b>Days 1-2:</b> Fluorouracil 1,200mg/m<sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m<sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.</p>
Gemcitabine + Cisplatin <sup>13,14,e</sup>	<p><b>Days 1,15:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes</p> <p><b>Days 1,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks for 2-6 cycles.</p> <p><b>OR</b></p> <p><b>Days 1,8,15,29,36,43:</b> Cisplatin 25mg/m<sup>2</sup> IV over 60 minutes</p> <p><b>Days 1,8,15,29,36,43:</b> Gemcitabine 1000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Administer for one 56-day cycle, <b>followed by:</b></p> <p><b>Days 1,8,15:</b> Cisplatin 25mg/m<sup>2</sup> over 60 minutes</p> <p><b>Days 1,8,15:</b> Gemcitabine 1000mg/m<sup>2</sup> over 30 minutes.</p> <p>Repeat cycle every 4 weeks for a maximum of 4 cycles.</p>
<b>Other Recommended Regimens</b>	
Capecitabine (Category 2B) <sup>15</sup>	<p><b>Days 1-14:</b> Capecitabine 1,000mg/m<sup>2</sup> orally twice daily.</p> <p>Repeat cycle every 3 weeks for 2-6 cycles.</p>
CapeOX (Category 2B) <sup>16</sup>	<p><b>Day 1:</b> Oxaliplatin 110-130mg/m<sup>2</sup> IV over 2 hours</p> <p><b>Days 1-14:</b> Capecitabine 750-1,000mg/m<sup>2</sup> orally twice daily.</p> <p>Repeat cycle every 3 weeks for 2-6 cycles.</p>
Fluorouracil, Continuous Infusion (Category 2B) <sup>9</sup>	<p><b>Days 1-28:</b> Fluorouracil 250mg/m<sup>2</sup> IV continuous infusion over 24 hours.</p> <p>Repeat cycle every 42 days for 2-6 cycles.</p>
Fluorouracil + Leucovorin + Oxaliplatin [OFF] (Category 2B) <sup>17</sup>	<p><b>Days 1,8,15,22:</b> Leucovorin 200mg/m<sup>2</sup> IV over 2 hours</p> <p><b>Days 8,22:</b> Oxaliplatin 85mg/m<sup>2</sup> IV over 2 hours, <b>followed by:</b></p> <p><b>Days 1,8,15,22:</b> Fluorouracil 2,000mg/m<sup>2</sup> IV continuous infusion over 24 hours.</p> <p>Repeat cycle every 42 days for 2-6 cycles.</p>
Gemcitabine <sup>18,19</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks for 2-6 cycles.</p>
Gemcitabine + Capecitabine <sup>20</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1-21:</b> Capecitabine 830mg/m<sup>2</sup> orally twice daily.</p> <p>Repeat cycle every 4 weeks for 2-6 cycles.</p>
Gemcitabine + Erlotinib <sup>21</sup>	<p><b>Days 1,8,15,22,29,36,43:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1-56:</b> Erlotinib 100mg orally daily.</p> <p>Administer for one 56-day cycle, <b>followed by:</b></p> <p><b>Days 1,8,15 (subsequent cycles):</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1-28:</b> Erlotinib 100mg orally daily.</p> <p>Repeat cycle every 4 weeks for a maximum of 4 cycles.</p>
Gemcitabine (fixed-dose rate) + Docetaxel + Capecitabine [GTX] (Category 2B) <sup>22</sup>	<p><b>Days 1-14:</b> Capecitabine 750mg/m<sup>2</sup> orally twice daily.</p> <p><b>Days 4,11:</b> Gemcitabine 750mg/m<sup>2</sup> IV at a rate of 10mg/m<sup>2</sup>/minute</p> <p><b>Days 4,11:</b> Docetaxel 30mg/m<sup>2</sup> IV over 60 minutes.</p> <p>Repeat cycle every 3 weeks for 2-6 cycles.</p>

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>First-Line Chemotherapy for Locally Advanced Disease and Good Performance Status</b> (continued)	
<b>Useful in Certain Circumstances</b>	
Induction chemotherapy with any of the preferred/other regimens (≥4-6 cycles) followed by chemoradiation or SBRT (in selected patients, locally advanced disease without systemic metastases)	See NCCN Pancreatic Adenocarcinoma Guidelines
Chemoradiation <sup>1</sup> or SBRT <sup>1</sup> (in select patients who are not candidates for combination therapy)	See NCCN Pancreatic Adenocarcinoma Guidelines
<b>First-Line Chemotherapy for Locally Advanced Disease and Poor Performance Status</b>	
<b>Preferred Regimens</b>	
Capecitabine (Category 2B) <sup>15</sup>	<b>Days 1-14:</b> Capecitabine 1,000mg/m <sup>2</sup> orally twice daily. Repeat every 3 weeks for 2-6 cycles.
Fluorouracil, Continuous Infusion (Category 2B) <sup>9</sup>	<b>Days 1-28:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Repeat cycle every 42 days for 2-6 cycles.
Gemcitabine (Category 1) <sup>18,19</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks for 2-6 cycles.
Gemcitabine (fixed-dose rate) (Category 2B) <sup>23</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000-1,500mg/m <sup>2</sup> IV at a rate of 10mg/m <sup>2</sup> /infusion. Repeat cycle every 4 weeks for 2-6 cycles.
<b>First-Line Chemotherapy for Metastatic Disease and Good Performance Status</b>	
<b>Preferred Regimens</b>	
FOLFIRINOX (Category 1) <sup>2,c,g</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks.
Modified FOLFIRINOX <sup>3,c,g</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b> <b>Day 1:</b> Irinotecan 135mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Days 1:</b> Fluorouracil 300mg/m <sup>2</sup> IV bolus, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks.
Gemcitabine + Albumin-Bound Paclitaxel (Category 1) <sup>4,d</sup>	<b>Days 1,8,15:</b> Albumin-bound Paclitaxel 125mg/m <sup>2</sup> IV over 30 minutes <b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks.
<b>Preferred Regimens Only for Known BRCA1/2 or PALB2 Mutations</b>	
FOLFIRINOX (Category 1) <sup>2,c,g</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks.
Modified FOLFIRINOX <sup>3,c,g</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b> <b>Day 1:</b> Irinotecan 135mg/m <sup>2</sup> IV over 90 minutes, <b>followed by:</b> <b>Days 1:</b> Fluorouracil 300mg/m <sup>2</sup> IV bolus, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks.

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>First-Line Chemotherapy for Metastatic Disease and Good Performance Status</b> (continued)	
<b>Preferred Regimens Only for Known <i>BRCA1/2</i> or <i>PALB2</i> Mutations</b> (continued)	
Gemcitabine + Cisplatin <sup>13,14,e</sup>	<p><b>Days 1,15:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes  <b>Days 1,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.            Repeat cycle every 3 weeks.</p> <p><b>OR</b></p> <p><b>Days 1,8,15,29,36,43:</b> Cisplatin 25mg/m<sup>2</sup> IV over 60 minutes  <b>Days 1,8,15,29,36,43:</b> Gemcitabine 1000mg/m<sup>2</sup> IV over 30 minutes.            Administer for one 56-day cycle, <b>followed by:</b>  <b>Days 1,8,15:</b> Cisplatin 25mg/m<sup>2</sup> over 60 minutes  <b>Days 1,8,15:</b> Gemcitabine 1000mg/m<sup>2</sup> over 30 minutes.            Repeat cycle every 4 weeks.</p>
<b>Other Recommended Regimens</b>	
CapeOX (Category 2B) <sup>16</sup>	<p><b>Day 1:</b> Oxaliplatin 110-130mg/m<sup>2</sup> IV over 2 hours  <b>Days 1-14:</b> Capecitabine 750-1,000mg/m<sup>2</sup> orally twice daily.            Repeat cycle every 3 weeks.</p>
Fluorouracil + Leucovorin + Oxaliplatin [OFF] (Category 2B) <sup>17</sup>	<p><b>Days 1,8,15,22:</b> Leucovorin 200mg/m<sup>2</sup> IV over 2 hours  <b>Days 8,22:</b> Oxaliplatin 85mg/m<sup>2</sup> IV over 2 hours, <b>followed by:</b>  <b>Days 1,8,15,22:</b> Fluorouracil 2,000mg/m<sup>2</sup> IV continuous infusion over 24 hours.            Repeat cycle every 42 days.</p>
Gemcitabine (Category 1) <sup>18,19</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.            Repeat cycle every 4 weeks.</p>
Gemcitabine + Capecitabine <sup>20</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes  <b>Days 1-21:</b> Capecitabine 830mg/m<sup>2</sup> orally twice daily.            Repeat cycle every 4 weeks.</p>
Gemcitabine + Erlotinib (Category 1) <sup>21</sup>	<p><b>Days 1,8,15,22,29,36,43:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes  <b>Days 1-56:</b> Erlotinib 100mg orally daily.            Administer for one 56-day cycle, <b>followed by:</b>  <b>Days 1,8,15 (subsequent cycles):</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes  <b>Days 1-28:</b> Erlotinib 100mg orally daily.            Repeat cycle every 4 weeks.</p>
Gemcitabine (fixed-dose rate) + Docetaxel + Capecitabine [GTx] (Category 2B) <sup>22</sup>	<p><b>Days 1-14:</b> Capecitabine 750mg/m<sup>2</sup> orally twice daily.  <b>Days 4,11:</b> Gemcitabine 750mg/m<sup>2</sup> IV at a rate of 10mg/m<sup>2</sup>/minute  <b>Days 4,11:</b> Docetaxel 30mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks.</p>
<b>First-Line Chemotherapy for Metastatic Disease and Poor Performance Status</b>	
<b>Preferred Regimens</b>	
Capecitabine (Category 2B) <sup>15</sup>	<p><b>Days 1-14:</b> Capecitabine 1,000mg/m<sup>2</sup> orally twice daily.            Repeat cycle every 3 weeks.</p>
Fluorouracil, Continuous Infusion (Category 2B) <sup>9</sup>	<p><b>Days 1-28:</b> Fluorouracil 250mg/m<sup>2</sup> IV continuous infusion over 24 hours.            Repeat cycle every 42 days.</p>
Gemcitabine (Category 1) <sup>18,19</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.            Repeat cycle every 4 weeks.</p>
Gemcitabine (fixed-dose rate) (Category 2B) <sup>23</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000-1,500mg/m<sup>2</sup> IV at a rate of 10mg/m<sup>2</sup>/minute.            Repeat cycle every 4 weeks.</p>
<b>Useful in Certain Circumstances</b>	
Entrectinib (if <i>NTRK</i> gene fusion positive) (Category 2B) <sup>24,25</sup>	<p><b>Days 1-28:</b> Entrectinib 600mg orally once daily.            Repeat cycle every 4 weeks.</p>
Larotrectinib (if <i>NTRK</i> gene fusion positive) (Category 2B) <sup>26,27</sup>	<p><b>Days 1-28:</b> Larotrectinib 100mg orally twice daily.            Repeat cycle every 4 weeks.</p>

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>First-Line Chemotherapy for Metastatic Disease and Poor Performance Status</b> (continued)	
Useful in Certain Circumstances (continued)	
Pembrolizumab (only for MSI-H or dMMR tumors) <sup>28,29</sup>	<b>Day 1:</b> Pembrolizumab 200mg IV. Repeat cycle every 3 weeks.
<b>Maintenance Therapy for Patients With Metastatic Disease and Good Performance Status<sup>1</sup></b>	
Preferred Regimens	
FOLFIRI (if previous first-line FOLFIRINOX) <sup>30,31</sup>	<b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes, <b>with:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV every 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks.
Other Recommended Regimens	
FOLFOX (if previous first-line FOLFIRINOX) (Category 2B) <sup>32</sup>	<b>Day 1:</b> Oxaliplatin 100mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,500mg/m <sup>2</sup> IV continuous infusion over 24 hours (3,000mg/m <sup>2</sup> IV over 46 hours) Repeat cycle every 2 weeks.
Useful in Certain Circumstances	
Capecitabine (if previous first-line FOLFIRINOX) <sup>15</sup>	<b>Days 1-14:</b> Capecitabine 1,000mg/m <sup>2</sup> orally twice daily. Repeat cycle every 3 weeks.
Gemcitabine (if previous first-line Gemcitabine + Albumin-Bound Paclitaxel) (Category 2B) <sup>18,19</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine + Albumin-Bound Paclitaxel, Modified Schedule (if previous first-line Gemcitabine + Albumin-Bound Paclitaxel) (Category 2B) <sup>33</sup>	<b>Days 1,15:</b> Albumin-Bound Paclitaxel 125mg/m <sup>2</sup> IV over 30 minutes <b>Days 1,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks.
Olaparib (only for germline BRCA1/2 mutations, if previous platinum-based chemotherapy) <sup>34,35</sup>	<b>Days 1-28:</b> Olaparib 300mg orally twice daily. Repeat cycle every 4 weeks.
<b>Second-Line Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Good Performance Status</b>	
Other Recommended Regimens (if prior gemcitabine-based therapy)	
Capecitabine <sup>15</sup>	<b>Days 1-14:</b> Capecitabine 1,000mg/m <sup>2</sup> orally twice daily. Repeat cycle every 3 weeks.
CapeOX <sup>16,36</sup>	<b>Day 1:</b> Oxaliplatin 110-130mg/m <sup>2</sup> IV over 2 hours <b>Days 1-14:</b> Capecitabine 750-1,000mg/m <sup>2</sup> orally twice daily. Repeat cycle every 3 weeks.
Fluorouracil, Continuous Infusion <sup>9</sup>	<b>Days 1-28:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Repeat cycle every 42 days.
Fluorouracil + Leucovorin + Liposomal Irinotecan (Category 1 for metastatic disease) <sup>37,38,k</sup>	<b>Day 1:</b> Liposomal Irinotecan 80mg/m <sup>2</sup> IV (equivalent to 70mg/m <sup>2</sup> IV Irinotecan in free base), <b>followed by:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV continuous infusion (2,400mg/m <sup>2</sup> over 46 hours). Repeat cycle every 2 weeks.
Fluorouracil + Leucovorin + Oxaliplatin [OFF] <sup>17</sup>	<b>Days 1,8,15,22:</b> Leucovorin 200mg/m <sup>2</sup> IV over 2 hours <b>Days 8,22:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Days 1,8,15,22:</b> Fluorouracil 2,000mg/m <sup>2</sup> IV continuous infusion over 24 hours. Repeat cycle every 42 days.
FOLFIRI <sup>30,31</sup>	<b>Day 1:</b> Irinotecan 180mg/m <sup>2</sup> IV over 90 minutes, <b>with:</b> <b>Day 1:</b> Leucovorin 400mg/m <sup>2</sup> IV over 2 hours, <b>followed by:</b> <b>Day 1:</b> Fluorouracil 400mg/m <sup>2</sup> IV push, <b>followed by:</b> <b>Days 1-2:</b> Fluorouracil 1,200mg/m <sup>2</sup> IV every 24 hours (2,400mg/m <sup>2</sup> IV over 46 hours). Repeat cycle every 2 weeks.

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>Second-Line Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Good Performance Status</b> (continued)	
<b>Other Recommended Regimens (if prior gemcitabine-based therapy)</b> (continued)	
FOLFOX <sup>32</sup>	<p><b>Day 1:</b> Oxaliplatin 100mg/m<sup>2</sup> IV over 2 hours</p> <p><b>Day 1:</b> Leucovorin 400mg/m<sup>2</sup> IV over 2 hours, <b>followed by:</b></p> <p><b>Day 1:</b> Fluorouracil 400mg/m<sup>2</sup> IV push, <b>followed by:</b></p> <p><b>Days 1-2:</b> Fluorouracil 1,500mg/m<sup>2</sup> IV continuous infusion over 24 hours (3,000mg/m<sup>2</sup> IV over 46 hours)</p> <p>Repeat cycle every 2 weeks.</p>
FOLFIRINOX <sup>2,c</sup>	<p><b>Day 1:</b> Oxaliplatin 85mg/m<sup>2</sup> IV over 2 hours</p> <p><b>Day 1:</b> Irinotecan 180mg/m<sup>2</sup> IV over 90 minutes</p> <p><b>Day 1:</b> Leucovorin 400mg/m<sup>2</sup> IV over 90 minutes, <b>followed by:</b></p> <p><b>Day 1:</b> Fluorouracil 400mg/m<sup>2</sup> IV push, <b>followed by:</b></p> <p><b>Days 1-2:</b> Fluorouracil 1,200mg/m<sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m<sup>2</sup> IV over 46 hours).</p> <p>Repeat cycle every 2 weeks.</p>
Modified FOLFIRINOX <sup>3,c</sup>	<p><b>Day 1:</b> Oxaliplatin 85mg/m<sup>2</sup> IV over 2 hours, <b>followed by:</b></p> <p><b>Day 1:</b> Leucovorin 400mg/m<sup>2</sup> IV over 2 hours, <b>followed (after 30 minutes) by:</b></p> <p><b>Day 1:</b> Irinotecan 135mg/m<sup>2</sup> IV over 90 minutes, <b>followed by:</b></p> <p><b>Day 1:</b> Fluorouracil 300mg/m<sup>2</sup> IV bolus, <b>followed by:</b></p> <p><b>Days 1-2:</b> Fluorouracil 1,200mg/m<sup>2</sup> IV continuous infusion over 24 hours (2,400mg/m<sup>2</sup> IV over 46 hours).</p> <p>Repeat cycle every 2 weeks.</p>
<b>Other Recommended Regimens (if prior fluoropyrimidine-based therapy)</b>	
Fluorouracil + Leucovorin + Liposomal Irinotecan (if no prior Irinotecan) <sup>37,38,k</sup>	<p><b>Day 1:</b> Liposomal Irinotecan 80mg/m<sup>2</sup> IV (equivalent to 70mg/m<sup>2</sup> IV Irinotecan in free base), <b>followed by:</b></p> <p><b>Day 1:</b> Leucovorin 400mg/m<sup>2</sup> IV, <b>followed by:</b></p> <p><b>Days 1-2:</b> Fluorouracil 1,200mg/m<sup>2</sup> IV continuous infusion (2,400mg/m<sup>2</sup> over 46 hours).</p> <p>Repeat cycle every 2 weeks.</p>
Gemcitabine <sup>18,19</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks.</p>
Gemcitabine + Albumin-Bound Paclitaxel <sup>4,d</sup>	<p><b>Days 1,8,15:</b> Albumin-bound Paclitaxel 125mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1,8,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks.</p>
Gemcitabine + Cisplatin (only for known <i>BRCA1/2</i> or <i>PALB2</i> mutations) <sup>13,14,e</sup>	<p><b>Days 1,15:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes</p> <p><b>Days 1,15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks.</p> <p><b>OR</b></p> <p><b>Days 1,8,15,29,36,43:</b> Cisplatin 25mg/m<sup>2</sup> IV over 60 minutes</p> <p><b>Days 1,8,15,29,36,43:</b> Gemcitabine 1000mg/m<sup>2</sup> IV over 30 minutes.</p> <p>Administer for one 56-day cycle, <b>followed by:</b></p> <p><b>Days 1,8,15:</b> Cisplatin 25mg/m<sup>2</sup> over 60 minutes</p> <p><b>Days 1,8,15:</b> Gemcitabine 1000mg/m<sup>2</sup> over 30 minutes.</p> <p>Repeat cycle every 4 weeks.</p>
Gemcitabine + Erlotinib <sup>21</sup>	<p><b>Days 1,8,15,22,29,36,43:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1-56:</b> Erlotinib 100mg orally daily.</p> <p>Administer for one 56-day cycle, <b>followed by:</b></p> <p><b>Days 1,8,15 (subsequent cycles):</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Days 1-28:</b> Erlotinib 100mg orally daily.</p> <p>Repeat cycle every 4 weeks.</p>
<b>Useful in Certain Circumstances</b>	
Entrectinib (if <i>NTRK</i> gene fusion positive) <sup>24,25</sup>	<p><b>Days 1-28:</b> Entrectinib 600mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>
Larotrectinib (if <i>NTRK</i> gene fusion positive) <sup>26,27</sup>	<p><b>Days 1-28:</b> Larotrectinib 100mg orally twice daily.</p> <p>Repeat cycle every 4 weeks.</p>
Pembrolizumab (only for MSI-H or dMMR tumors) <sup>28,29</sup>	<p><b>Day 1:</b> Pembrolizumab 200mg IV.</p> <p>Repeat cycle every 3 weeks.</p>

continued

# Pancreatic Adenocarcinoma Treatment Regimens

## ► Systemic Therapy for Pancreatic Adenocarcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>Second-Line Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Good Performance Status</b> (continued)	
<b>Useful in Certain Circumstances</b> (continued)	
Chemoradiation, if not previously given (only for locally advanced disease if primary site is the sole site of progression or select patients with recurrent disease in combination with systemic therapy)	See NCCN Pancreatic Adenocarcinoma Guidelines.
<b>Second-Line Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Poor Performance Status</b>	
<b>Other Recommended Regimens</b>	
Capecitabine (Category 2B) <sup>15</sup>	<b>Days 1-14:</b> Capecitabine 1,000mg/m <sup>2</sup> orally twice daily. Repeat cycle every 3 weeks.
Fluorouracil, Continuous Infusion (Category 2B) <sup>9</sup>	<b>Days 1-28:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours. Repeat cycle every 42 days.
Gemcitabine (Category 1) <sup>18,19</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine (fixed-dose rate) (Category 2B) <sup>23</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000-1,500mg/m <sup>2</sup> IV at a rate of 10mg/m <sup>2</sup> /minute. Repeat cycle every 4 weeks.
<b>Useful in Certain Circumstances</b>	
Entrectinib (if <i>NTRK</i> gene fusion positive) (Category 2B) <sup>24,25</sup>	<b>Days 1-28:</b> Entrectinib 600mg orally once daily. Repeat cycle every 4 weeks.
Larotrectinib (if <i>NTRK</i> gene fusion positive) <sup>26,27</sup>	<b>Days 1-28:</b> Larotrectinib 100mg orally twice daily. Repeat cycle every 4 weeks.
Pembrolizumab (only for MSI-H or dMMR tumors) <sup>28,29</sup>	<b>Day 1:</b> Pembrolizumab 200mg IV. Repeat cycle every 3 weeks.
<b>Chemoradiation</b>	
<b>Preferred Regimens</b>	
Capecitabine + Concurrent RT <sup>6,39</sup>	<b>Days 1-5:</b> Capecitabine 850mg/m <sup>2</sup> orally twice daily. <sup>l</sup> Administer weekly cycle for 5-6 weeks with concurrent RT.
Fluorouracil, Continuous Infusion + Concurrent RT <sup>9</sup>	<b>Days 1-5 or Days 1-7:</b> Fluorouracil 250mg/m <sup>2</sup> IV continuous infusion over 24 hours daily. Repeat cycle weekly for 6 weeks with concurrent radiation.
<b>Other Recommended Regimens</b>	
Gemcitabine + Concurrent RT <sup>40-42</sup>	<b>Day 1:</b> Gemcitabine 300-600mg/m <sup>2</sup> IV over 30 minutes. <sup>m</sup> Repeat weekly for 6-7 cycles with concurrent radiation therapy.

- a. There is limited evidence to recommend specific neoadjuvant regimens off-study, and practices vary with regard to the use of chemotherapy and radiation. Subsequent chemoradiation is sometimes included. When considering neoadjuvant therapy, consultation at a high-volume center is preferred. If neoadjuvant therapy is recommended, treatment at or coordinated through a high-volume center is preferred, when feasible. Participation in a clinical trial is encouraged.
- b. Can be administered with or without subsequent chemoradiation. See section on Chemoradiation for chemoradiation regimens.
- c. FOLFIRINOX or modified FOLFIRINOX should be limited to those with ECOG 0-1.
- d. Gemcitabine + Albumin-Bound Paclitaxel is reasonable for patients with ECOG 0-2.
- e. Hydration is required with supplemental electrolytes pre- and post-administration of Cisplatin.
- f. If considering chemoradiation due to positive margins, chemotherapy should be given prior to the administration of chemotherapy.
- g. Due to the high toxicity of this regimen, bolus Fluorouracil is often omitted.
- h. The recommendations for FOLFIRINOX and Gemcitabine + Albumin-Bound Paclitaxel in patients with locally advanced disease are based on extrapolations from randomized trials in patients with metastatic disease.
- i. If patients present with poorly controlled pain or local obstructive symptoms, it may be preferable to start with upfront chemoradiation or SBRT.
- j. Patients who have response or stable disease after 4-6 months of chemotherapy may undergo maintenance therapy. ECOG 0-2 for combination regimens; ECOG 0-3 for single agent options.
- k. Fluorouracil + Leucovorin + Liposomal Irinotecan is a reasonable second-line option for patients with ECOG 0-2.
- l. Capecitabine 800-900mg/m<sup>2</sup> orally twice daily on days 1-5 is recommended in the adjuvant setting.
- m. Gemcitabine 400-600mg/m<sup>2</sup> IV on day 1 is recommended in the adjuvant setting.

continued

# Pancreatic Adenocarcinoma Treatment Regimens

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