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.

▶Neoadjuvant Therapy (Resectable/Borderline Resectable Disease)[1,a,b]

REGIMEN	DOSING
Preferred Regimens	
FOLFIRINOX (Fluorouracil Continuous Infusion/ Leucovorin/ Irinotecan/ Oxaliplatin)[2,3,c-f]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Gemcitabine + Albumin-Bound Paclitaxel[4,c]	**Days 1,8,15:** Albumin-bound paclitaxel 125mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 6 cycles.
Modified FOLFIRINOX[5-7,c-f]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Preferred Regimens Only For Known *BRCA1/2* or *PALB2* Mutations	
FOLFIRINOX[2,3,c-f]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.
Gemcitabine + Cisplatin (≥2-6 cycles)[8-11,c,g]	**Day 1:** Cisplatin 25-30mg/m^2 IV over 1 hour **Day 1:** Gemcitabine 750mg/m^2 IV over 30 minutes **OR** **Day 1:** Gemcitabine IV at a rate of 10mg/m^2/minute. Repeat cycle every 2 weeks for 2-6 cycles.
Modified FOLFIRINOX[5-7,c-f]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-12 cycles.

▶Adjuvant Chemotherapy[1]

Preferred Regimens	
Gemcitabine + Capecitabine (Category 1)[12,13,f]	**Days 1-21:** Capecitabine 830mg/m^2 orally twice daily **Days 1,8,15:** Gemcitabine 1000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 6 cycles.
Modified FOLFIRINOX (Category 1)[5-7,d-f]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶Adjuvant Chemotherapy[1] (continued)

REGIMEN	DOSING
Other Recommended Regimens	
Capecitabine (Category 2B)[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks for 8 cycles.
Fluorouracil Continuous Infusion[16,17,f]	**Days 1-28:** Fluorouracil 250mg/m^2 IV continuous infusion over 24 hours daily. Repeat every 6 weeks for 1-4 cycles.
Fluorouracil Continuous Infusion Followed by Chemoradiation[16,17,f,h]	**Days 1-21:** Fluorouracil 250mg/m^2 IV continuous infusion over 24 hours daily. Administer for one 3-week cycle, **followed by:** Concurrent chemotherapy and radiation therapy (See Chemoradiation).
Fluorouracil Continuous Infusion Followed by Chemoradiation Followed by Fluorouracil Continuous Infusion[16,17,f,h]	**Days 1-21:** Fluorouracil 250mg/m^2 IV continuous infusion over 24 hours daily. Administer for one 3-week cycle, **followed by:** Concurrent chemotherapy and radiation therapy (See Chemoradiation), **followed by:** **Days 1-28:** Fluorouracil 250mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 6 weeks for 2 cycles.
Fluorouracil + Leucovorin (Category 1)[18,f]	**Days 1-5:** Leucovorin 20mg/m^2 IV push daily, **followed by:** **Days 1-5:** Fluorouracil 425mg/m^2 IV push daily. Repeat cycle every 4 weeks for 2-6 cycles.
Fluorouracil + Leucovorin Followed by Chemoradiation[18,f,h]	**Days 1-5:** Leucovorin 20mg/m^2 IV push daily, **followed by:** **Days 1-5:** Fluorouracil 425mg/m^2 IV push daily. Repeat cycle every 4 weeks for 2-6 cycles, **followed by:** concurrent chemotherapy and radiation therapy (See Chemoradiation).
Fluorouracil + Leucovorin Followed by Chemoradiation Followed by Fluorouracil + Leucovorin[1,f,h]	See NCCN Pancreatic Adenocarcinoma Guidelines[1]
Gemcitabine (Category 1)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 2-6 cycles.
Gemcitabine Followed by Chemoradiation[9,17,19-21,h]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 2-6 cycles, **followed by:** Concurrent chemotherapy and radiation therapy (See Chemoradiation).
Gemcitabine Followed by Chemoradiation Followed by Gemcitabine[1,h]	See NCCN Pancreatic Adenocarcinoma Guidelines[1]

▶First-Line Chemotherapy for Locally Advanced Disease and Good Performance Status[1]

Preferred Regimens	
FOLFIRINOX[2,3,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-6 cycles (as induction) or every 2 weeks.
Gemcitabine + Albumin-Bound Paclitaxel[4,j]	**Days 1,8,15:** Albumin-bound Paclitaxel 125mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 4-6 cycles (as induction) or every 4 weeks.
Modified FOLFIRINOX[5-7,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-6 cycles (as induction) or every 2 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶First-Line Chemotherapy for Locally Advanced Disease and Good Performance Status[1] (continued)

REGIMEN	DOSING
Preferred Regimens Only For Known *BRCA1/2* or *PALB2* Mutations	
FOLFIRINOX[2,3,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-6 cycles (as induction) or every 2 weeks.
Gemcitabine + Cisplatin[8-11,g]	**Days 1,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes **Days 1,15:** Cisplatin 50mg/m^2 IV over 1 hour. Repeat cycle every 4 weeks for 4-6 cycles (as induction).
Modified FOLFIRINOX[5-7,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks for 4-6 cycles (as induction) or every 2 weeks.
Other Recommended Regimens	
Capecitabine (Category 2B)[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks for 4-6 cycles (as induction) or every 3 weeks.
CapeOX (Capecitabinef + Oxaliplatin) (Category 2B)[22,f]	**Days 1-14:** Capecitabine 750-1,000mg/m^2 orally twice daily **Day 1:** Oxaliplatin 110-130mg/m^2 IV over 2 hours. Repeat cycle every 3 weeks for 4-6 cycles (as induction) or every 3 weeks.
Fluorouracil, Continuous Infusion (Category 2B)[16,17,f]	**Days 1-4:** Fluorouracil 1000mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 3 weeks for 4-6 cycles (as induction) or every 3 weeks.
OFF (Fluorouracil + Leucovorin + Oxaliplatin) (Category 2B)[23,24,f]	**Days 1,8,15,22:** Leucovorin 200mg/m^2 IV over 2 hours (leucovorin infusion time should match the infusion time of oxaliplatin when these agents are given concurrently) **Days 8,22:** Oxaliplatin 85mg/m^2 IV over 2 hours, **followed by:** **Days 1,8,15,22:** Fluorouracil 2,000mg/m^2 IV continuous infusion over 24 hours. Repeat cycle every 6 weeks for 4-6 cycles (induction) or every 6 weeks.
Gemcitabine[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 4-6 cycles (as induction) or every 4 weeks.
Gemcitabine + Albumin-Bound Paclitaxel + Cisplatin (Category 2B)[25,26,g]	**Days 1,8:** Albumin-bound Paclitaxel 100mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8:** Cisplatin 25mg/m^2 IV over 1 hour, **followed by:** **Days 1,8:** Gemcitabine 800mg/m^2 IV over 30 minutes. Repeat cycle every 3 weeks for 4-6 cycles (induction) or every 3 weeks, **OR** **Days 1,8:** Albumin-bound Paclitaxel 125mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8:** Cisplatin 25mg/m^2 IV over 1 hour, **followed by:** **Days 1,8:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 3 weeks for 4-6 cycles (induction) or every 3 weeks.
Gemcitabine + Capecitabine[12,13,f]	**Days 1-21:** Capecitabine 830mg/m^2 orally twice daily **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 4-6 cycles (as induction) or every 4 weeks.
Gemcitabine + Erlotinib[27-29]	**Days 1-28:** Erlotinib 100mg orally daily **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 4-6 cycles (as induction).
GTX (Gemcitabine [fixed-dose rate] + Docetaxel + Capecitabine[f]) (Category 2B)[30,k] *Docetaxel requires premedication.*	**Days 4,11:** Gemcitabine 750mg/m^2 IV at a rate of 10mg/m^2/minute, **followed by:** **Days 4,11:** Docetaxel 30mg/m^2 IV over 1 hour **Days 1-14:** Capecitabine 750mg/m^2 orally twice daily. Repeat cycle every 3 weeks for 4-6 cycles (as induction) or every 3 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶First-Line Chemotherapy for Locally Advanced Disease and Good Performance Status[1] (continued)

REGIMEN	DOSING
Useful in Certain Circumstances	
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)[a]	See NCCN Pancreatic Adenocarcinoma Guidelines[1]
Chemoradiation or SBRT (in select patients who are not candidates for combination therapy)[a,l]	See NCCN Pancreatic Adenocarcinoma Guidelines[1]

▶First-Line Chemotherapy for Locally Advanced Disease and Poor Performance Status[1]

Preferred Regimens	
Capecitabine (Category 2B)[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat every 3 weeks for 4-6 cycles (as induction).
Fluorouracil, Continuous Infusion (Category 2B)[16,17,f]	**Days 1-4:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 3 weeks for 4-6 cycles (induction) or every 3 weeks.
Gemcitabine (Category 1)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks for 4-6 cycles (as induction) or every 4 weeks.
Gemcitabine (fixed-dose rate) (Category 2B)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV at a rate of 10mg/m^2/minute. Repeat cycle every 4 weeks.

▶First-Line Chemotherapy for Metastatic Disease and Good Performance Status[1]

Preferred Regimens	
FOLFIRINOX (Category 1)[2,3,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
Gemcitabine + Albumin-Bound Paclitaxel (Category 1)[4,j]	**Days 1,8,15:** Albumin-bound Paclitaxel 125mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Modified FOLFIRINOX[5-7,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
Preferred Regimens Only For Known *BRCA1/2* or *PALB2* Mutations	
FOLFIRINOX (Category 1)[2,3,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m2 IV over 46 hours). Repeat cycle every 2 weeks.
Gemcitabine + Cisplatin[8-11,g]	**Days 1,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes **Days 1,15:** Cisplatin 50mg/m^2 IV over 1 hour. Repeat cycle every 4 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶First-Line Chemotherapy for Metastatic Disease and Good Performance Status[1] (continued)

REGIMEN	DOSING
Preferred Regimens Only For Known *BRCA1/2* or *PALB2* Mutations (continued)	
Modified FOLFIRINOX[5-7,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
Other Recommended Regimens	
CapeOx (Capecitabinef + Oxaliplatin) (Category 2B)[22,f]	**Days 1-14:** Capecitabine 750-1,000mg/m^2 orally twice daily **Day 1:** Oxaliplatin 110-130mg/m^2 IV over 2 hours. Repeat cycle every 3 weeks.
OFF (Fluorouracil + Leucovorin + Oxaliplatin) (Category 2B)[23,24,f]	**Days 1,8,15,22:** Leucovorin 200mg/m^2 IV over 2 hours (leucovorin infusion time should match the infusion time of oxaliplatin when these agents are given concurrently) **Days 8,22:** Oxaliplatin 85mg/m^2 IV over 2 hours, **followed by:** **Days 1,8,15,22:** Fluorouracil 2,000mg/m^2 IV continuous infusion over 24 hours. Repeat cycle every 6 weeks.
Gemcitabine (Category 1)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine + Albumin-Bound Paclitaxel + Cisplatin[25,26,g]	**Days 1,8:** Albumin-bound Paclitaxel 100mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8:** Cisplatin 25mg/m^2 IV over 1 hour, **followed by:** **Days 1,8:** Gemcitabine 800mg/m^2 IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Days 1,8:** Albumin-bound Paclitaxel 125mg/m2 IV over 30 minutes, **followed by:** **Days 1,8:** Cisplatin 25mg/m^2 IV over 1 hour, **followed by:** **Days 1,8:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 3 weeks.
Gemcitabine + Capecitabine[12,13,f]	**Days 1-21: C**apecitabine 830mg/m^2 orally twice daily **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes Repeat cycle every 4 weeks.
Gemcitabine + Erlotinib (Category 1)[27-29]	**Days 1-28:** Erlotinib 100mg orally daily **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
GTX (Gemcitabine [Fixed-Dose Rate] + Docetaxel + Capecitabine[f]) (Category 2B)[30,k] *Docetaxel requires premedication.*	**Days 4,11:** Gemcitabine 750mg/m^2 IV at a rate of 10mg/m^2/minute, **followed by:** **Days 4,11:** Docetaxel 30mg/m^2 IV over 1 hour **Days 1-14:** Capecitabine 750mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
Useful in Certain Circumstances	
Pembrolizumab (for patients with MSI-H, dMMR, or TMB-H [≥10mut/Mb])[31-35,a,m]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for a maximum of 24 months of therapy. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for a maximum of 24 months of therapy.

▶First-Line Chemotherapy for Metastatic Disease and Poor Performance Status[1]

Preferred Regimens	
Capecitabine (Category 2B)[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat every 3 weeks.
Fluorouracil, Continuous Infusion (Category 2B)[16,17,f]	**Days 1-4:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 3 weeks.
Gemcitabine (Category 1)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine (Fixed-Dose Rate) (Category 2B)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV at a rate of 10mg/m^2/minute. Repeat cycle every 4 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶First-Line Chemotherapy for Metastatic Disease and Poor Performance Status[1] (continued)

REGIMEN	DOSING
Useful in Certain Circumstances	
Entrectinib (if *NTRK* gene fusion positive) (Category 2B)[36-38]	**Days 1-28:** Entrectinib 600mg orally once daily. Repeat cycle every 4 weeks.
Larotrectinib (if NTRK gene fusion positive)[38-40]	**Days 1-28:** Larotrectinib 100mg orally twice daily. Repeat cycle every 4 weeks.
Pembrolizumab (for patients with MSI-H, dMMR, or TMB-H [≥10mut/Mb])[31-35,a,m]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for a maximum of 24 months of therapy. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for a maximum of 24 months of therapy.

▶Maintenance Therapy for Patients with Metastatic Disease and Good Performance Status[1,n]

Preferred Regimens	
Olaparib (for patients with germline *BRCA1/2* mutations if previous platinum-based chemotherapy)[42-44]	**Days 1-28:** Olaparib 300mg orally twice daily. Repeat cycle every 4 weeks.
Other Recommended Regimens	
Capecitabine (if previous first-line FOLFIRINOX)[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
Gemcitabine (if previous first-line Gemcitabine + Albumin-Bound Paclitaxel) (Category 2B)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 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)[45]	**Days 1,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes **Days 1,15:** Albumin-Bound Paclitaxel 125mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Useful in Certain Circumstances	
Fluorouracil + Leucovorin (Simplified) (if previous first-line FOLFIRINOX)[46,47,f,o]	**Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
Fluorouracil + Leucovirin + Irinotecan (if previous first-line FOLFIRINOX)[46,47,e,f,o]	**Day 1:** Irinotecan 90mg/m^2 IV over 1 hour, **concurrent with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 1,000mg/m^2 IV continuous infusion (2,000mg/m2 IV over 46 hours), **followed by:** **Day 3:** Irinotecan 90mg/m^2 IV over 1 hour. Repeat cycle every 2 weeks.
FOLFOX (if previous first-line FOLFIRINOX) (Category 2B)[48-50,f,p]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **concurrent with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours (leucovorin infusion time should match the infusion time of oxaliplatin when these agents are given concurrently), **followed by:** **Days 1-2:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily (2,000mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks. **OR** **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **concurrent with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours (leucovorin infusion time should match the infusion time of oxaliplatin when these agents are given concurrently), **followed by:** **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
Rucaparib (for patients with germline or somatic *BRCA1/2* or *PALB2* mutations, if previous platinum-based chemotherapy)[51,52,q]	**Days 1-28:** Rucaparib 600mg orally twice daily. Repeat cycle every 4 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶Subsequent Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Good Performance Status[1]

REGIMEN	DOSING
Preferred Regimens	
Entrectinib (if *NTRK* gene fusion positive)[36-38]	**Days 1-28:** Entrectinib 600mg orally once daily. Repeat cycle every 4 weeks.
Larotrectinib (if *NTRK* gene fusion positive)[38-40]	**Days 1-28:** Larotrectinib 100mg orally twice daily. Repeat cycle every 4 weeks.
Pembrolizumab (for patients with MSI-H, dMMR, or TMB-H [≥10mut/Mb])[31-35,a,m]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for a maximum of 24 months of therapy. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for a maximum of 24 months of therapy.
Other Recommended Regimens (if prior gemcitabine-based therapy)	
Capecitabine[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
CapeOx (Capecitabine[f] + Oxaliplatin)[22]	**Days 1-14:** Capecitabine 750-1,000mg/m^2 orally twice daily **Day 1:** Oxaliplatin 110-130mg/m^2 IV over 2 hours. Repeat cycle every 3 weeks.
Fluorouracil, Continuous Infusion[16,17,f]	**Days 1-4:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 3 weeks.
Fluorouracil + Leucovorin + Liposomal Irinotecan (Category 1 for metastatic disease)[53,e,f,r]	**Day 1:** Liposomal Irinotecan 70mg/m^2 IV over 90 minutes, **followed by:** **Day 1:** Leucovorin 400mg/m^2 IV over 30 minutes, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 over 46 hours). Repeat cycle every 2 weeks.
FOLFIRI[50,54-56,e,f]	**Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes, **concurrent with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks. **OR** **Day 1:** Irinotecan 70mg/m^2 IV over 1 hour, **concurrent with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours, **followed by:** **Days 1-2:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily (2,000mg/m^2 IV over 46 hours), **followed by:** **Day 3:** Irinotecan 70mg/m^2 IV over 1 hour. Repeat cycle every 2 weeks. **OR** **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes **Days 1-2:** Leucovorin 200mg/m^2 IV over 2 hours daily, **followed by:** **Days 1-2:** Fluorouracil 400mg/m^2 IV push daily, **followed by:** **Days 1-2:** Fluorouracil 600mg/m^2 IV continuous infusion over 24 hours daily (1,200mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
FOLFIRINOX[2,3,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 180mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
FOLFOX[48-50,f]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours (leucovorin infusion time should match the infusion time of oxaliplatin when these agents are given concurrently), **followed by:** **Days 1-2:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily (2,000mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks. **OR** **Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours, **with:** **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours (leucovorin infusion time should match the infusion time of oxaliplatin when these agents are given concurrently), **followed by:** **Day 1:** Fluorouracil 400mg/m^2 IV push, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶Subsequent Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Good Performance Status[1] (continued)

REGIMEN	DOSING
Other Recommended Regimens (if prior gemcitabine-based therapy) (continued)	
Modified FOLFIRINOX[5-7,d-f,i]	**Day 1:** Oxaliplatin 85mg/m^2 IV over 2 hours **Day 1:** Leucovorin 400mg/m^2 IV over 2 hours **Day 1:** Irinotecan 150mg/m^2 IV over 90 minutes (begin 30 minutes after start of leucovorin infusion) **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m^2 IV over 46 hours). Repeat cycle every 2 weeks.
OFF (Fluorouracil + Leucovorin + Oxaliplatin)[23,24,f]	**Days 1,8,15,22:** Leucovorin 200mg/m^2 IV over 2 hours **Days 8,22:** Oxaliplatin 85mg/m^2 IV over 2 hours, **followed by:** **Days 1,8,15,22:** Fluorouracil 2,000mg/m^2 IV continuous infusion over 24 hours. Repeat cycle every 6 weeks.
Other Recommended Regimens (if prior fluoropyrimidine-based therapy)	
Fluorouracil + Leucovorin + Liposomal Irinotecan (If no prior Irinotecan)[53,e,f,r]	**Day 1:** Liposomal Irinotecan 70mg/m^2 IV over 90 minutes, **followed by:** **Day 1:** Leucovorin 400mg/m^2 IV over 30 minutes, **followed by:** **Days 1-2:** Fluorouracil 1,200mg/m^2 IV continuous infusion over 24 hours daily (2,400mg/m2 over 46 hours). Repeat cycle every 2 weeks.
Gemcitabine[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine + Albumin-Bound Paclitaxel[4,j]	**Days 1,8,15:** Albumin-bound Paclitaxel 125mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine + Albumin-Bound Paclitaxel + Cisplatin (Category 2B)[25,26,g]	**Days 1,8:** Albumin-bound Paclitaxel 100mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8:** Cisplatin 25mg/m^2 IV over 1 hour, **followed by:** **Days 1,8:** Gemcitabine 800mg/m^2 IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Days 1,8:** Albumin-bound Paclitaxel 125mg/m^2 IV over 30 minutes, **followed by:** **Days 1,8:** Cisplatin 25mg/m^2 IV over 1 hour, **followed by:** **Days 1,8:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 3 weeks.
Gemcitabine + Cisplatin (for patients with known *BRCA1/2* or *PALB2* mutations)[8-11,g]	**Days 1,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes **Days 1,15:** Cisplatin 50mg/m^2 IV over 1 hour. Repeat cycle every 4 weeks.
Gemcitabine + Erlotinib[27-29]	**Days 1-28:** Erlotinib 100mg orally daily **Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Useful in Certain Circumstances	
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[1]

▶Subsequent Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Poor Performance Status[1]

Preferred Regimens	
Entrectinib (if *NTRK* gene fusion positive)[36-38]	**Days 1-28:** Entrectinib 600mg orally once daily. Repeat cycle every 4 weeks.
Larotrectinib (if *NTRK* gene fusion positive)[38-40]	**Days 1-28:** Larotrectinib 100mg orally twice daily. Repeat cycle every 4 weeks.

continued

Pancreatic Adenocarcinoma Treatment Regimens

▶Subsequent Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease: Poor Performance Status[1] (continued)

REGIMEN	DOSING
Preferred Regimens (continued)	
Pembrolizumab (for patients with MSI-H, dMMR, or TMB-H [≥10mut/Mb])[31-35,a,m]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for a maximum of 24 months of therapy. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for a maximum of 24 months of therapy.
Other Recommended Regimens	
Capecitabine (Category 2B)[14,15,f]	**Days 1-14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 3 weeks.
Fluorouracil, Continuous Infusion (Category 2B)[16,17,f]	**Days 1-4:** Fluorouracil 1,000mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle every 3 weeks.
Gemcitabine (Category 1)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Gemcitabine (fixed-dose rate) (Category 2B)[9,17,19-21]	**Days 1,8,15:** Gemcitabine 1,000mg/m^2 IV at a rate of 10mg/m^2/minute. Repeat cycle every 4 weeks.

▶Chemoradiation[1]

Preferred Regimens	
Capecitabine + Concurrent RT[9,57,58,a,f]	**Days 1-5 or Days 1-7:** Capecitabine 800-900mg/m^2 orally twice daily. Repeat cycle weekly for 5-6 cycles with concurrent radiation.
Fluorouracil, Continuous Infusion + Concurrent RT[17,a,f]	**Days 1-5 or Days 1-7:** Fluorouracil 250mg/m^2 IV continuous infusion over 24 hours daily. Repeat cycle weekly for 6 cycles with concurrent radiation.
Other Recommended Regimens	
Gemcitabine + Concurrent RT[59-63,a]	**Day 1:** Gemcitabine 300-600mg/m^2 IV over 30 minutes. Repeat weekly for 6-7 cycles with concurrent radiation.

[a] MSI-H, microsatellite instability-high; dMMR, mismatch repair deficient; TMB-H, tumor mutational burden-high; RT, radiation therapy; SBRT, stereotactic body radiation therapy.

[b] 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 considered or recommended, treatment at or coordinated through a high-volume center is preferred, when feasible. Participation in a clinical trial is encouraged.

[c] Can be administered with or without subsequent chemoradiation.

[d] FOLFIRINOX or modified FOLFIRINOX should be limited to those with ECOG 0-1.

[e] Patients who are homozygous for the UGT1A1*28 allele or who have a clinical diagnosis of Gilbert's Syndrome have an increased risk of neutropenia when started on irinotecan. This agent may cause severe diarrhea.
— Early diarrhea may be prevented and treated with atropine: atropine 0.25mg IV or subcutaneously at the onset of diarrhea. May repeat 0.25mg IV or subcutaneously in 15 minutes if no response.
— Late diarrhea should be treated with loperamide: loperamide 4 mg orally at the onset of diarrhea, then 2mg every 2 hours until the patient is diarrhea-free for 12 hours (maximum 16mg/day).

[f] Patients with dihydropyridine dehydrogenase (DPD) deficiency are unable to metabolize fluorouracil normally and may have severe unexpected toxicity.

[g] Hydration is required with supplemental electrolytes pre- and post-administration of Cisplatin.

[h] If considering chemoradiation due to positive margins, chemotherapy should be given prior to the administration of chemotherapy.

[i] Due to the high toxicity of this regimen, bolus Fluorouracil is often omitted.

[j] Gemcitabine + Albumin-Bound Paclitaxel is reasonable for patients with ECOG 0-2.

[k] For Docetaxel: Premedication with Dexamethasone for fluid retention is required. One recommended dosing strategy is: Dexamethasone 8mg orally the night before, the morning of, and the night of Docetaxel administration.

[l] If patients present with poorly controlled pain or local obstructive symptoms, it may be preferable to start with upfront chemoradiation or SBRT.

[m] Early- and late-onset immune-related adverse events affecting multiple organ systems can occur in patients receiving immune checkpoint inhibitors. Patients with neurologic or life-threatening autoimmune disorders as well as receiving high levels of immunosuppression for their underlying disease should be approached with caution when considering immunotherapy. All patients will require extensive resources including ongoing intensive monitoring and supportive care.

[n] 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.

[o] Fluorouracil +/- Irinotecan may be considered for maintenance therapy in the case of oxaliplatin-related progressive neuropathy or allergy to oxaliplatin.

[p] While FOLFOX is not commonly used in the maintenance setting, it may be considered as an alternative to irinotecan-based therapy when GI toxicity is a concern.

[q] For patients who did not have disease progression following their most recent platinum-based chemotherapy.

[r] Fluorouracil + Leucovorin + Liposomal Irinotecan is a reasonable second-line option for patients with ECOG 0-2.

continued

Pancreatic Adenocarcinoma Treatment Regimens

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