PANCREATIC ADENOCARCINOMA CHEMOTHERAPY REGIMENS (Part 1 of 2)

The selection, dosing, and administration of anti-cancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anti-cancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The chemotherapy regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

General treatment notes:

- Systemic chemotherapy is used in the neoadjuvant or adjuvant setting and in the management of locally advanced, unresectable, and metastatic disease.[1]
- Enrollment in a clinical trial strongly recommended.[1]
- In adjuvant therapy, the use of gemcitabine-based chemotherapy is frequently combined, sequentially, with 5-FU-based chemoradiotherapy.[1]

REGIMEN	DOSING
Metastatic Disease	
Gemcitabine (Gemzar)[1, 2]	Cycle 1 (8 week cycle) **Days 1, 8, 15, 22, 29, 36 and 43:** Gemcitabine 1,000mg/m² IV administered over 30 min, followed by a 1-week rest. Subsequent cycles (4 week cycle) **Days 1, 8 and 15:** Gemcitabine 1,000mg/m² IV administered over 30 min, followed by a 1-week rest. Fixed-dose gemcitabine (10mg/m²/min IV) can be substituted for standard infusion of gemcitabine over 30 min.
Gemcitabine + erlotinib (Tarceva)[1, 3]	Cycle 1 (8 week cycle) **Days 1, 8, 15, 22, 29, 36 and 43:** Gemcitabine 1,000mg/m² IV followed by a 1-week rest, plus **All days:** Erlotinib 100mg/day or 150mg/day orally, followed by Subsequent cycles (4 week cycle) **Days 1, 8 and 15:** Gemcitabine 1,000mg/m² IV over 30 min. **All days:** Erlotinib 100mg/day or 150mg/day orally.
Gemcitabine + cisplatin (Platinol; CDDP)[1, 4]	**Days 1 and 15:** Gemcitabine 1,000mg/m² IV + cisplatin 50mg/m² IV. Repeat cycle every 4 weeks.
GEMOX (fixed-dose rate gemcitabine + oxaliplatin [Eloxatin])[1, 5, 6]	**Day 1:** Gemcitabine 1,000mg/m² IV, plus **Day 2:** Oxaliplatin 100mg/m² IV. Repeat cycle every 2 weeks until disease progression.
Gemcitabine + fluoropyrimidine (capecitabine, Xeloda)[1, 7]	**Days 1–21:** Gemcitabine 1,000mg/m² IV once weekly + capecitabine 1,660mg/m² orally (830mg/m² twice daily). Repeat cycle every 4 weeks until disease progression.
FOLFIRINOX (oxaliplatin + irinotecan + 5-fluorouracil/ leucovorin)[8]	**Day 1:** Oxaliplatin 85mg/m² IV + irinotecan 180mg/m² IV + leucovorin 400mg/m² IV, followed by a 5-FU bolus of 400mg/m² and a 46-hr continuous 5-FU infusion of 2,400mg/m². Repeat cycle every 2 weeks.
Second-Line Therapy	
Gemcitabine (in gemcitabine-naïve patients)	Cycle 1 (8 week cycle) **Days 1, 8, 15, 22, 29, 36 and 43:** Gemcitabine 1,000mg/m² IV administered over 30 min, followed by a 1-week rest. Subsequent cycles (4 week cycle) **Days 1, 8 and 15:** Gemcitabine 1,000mg/m² IV administered over 30 min, followed by a 1-week rest. Fixed-dose gemcitabine (10mg/m²/min IV) can be substituted for standard infusion of gemcitabine over 30 min.
Capecitabine[1, 9]	**Days 1–14:** 1,250mg/m² orally twice daily. Repeat cycle every 3 weeks for up to 52 weeks.
5-fluorouracil (5-FU) + **leucovorin + oxaliplatin**[1, 10]	**Days 1, 8, 15 and 22:** 5-FU 2g/m² IV + leucovorin 200mg/m² IV, plus **Days 8 and 22:** Oxaliplatin 85mg/m² IV.

continued

PANCREATIC ADENOCARCINOMA CHEMOTHERAPY REGIMENS (Part 2 of 2)

REGIMEN	DOSING
Second-Line Therapy (continued)	
CapeOx (capecitabine + oxaliplatin)[1, 11]	Age <65yrs and ECOG PS <2 **Days 1–14:** Oxaliplatin 130mg/m² + capecitabine 1,000mg/m² twice daily. Repeat cycle every 3 weeks. Age >65yrs and ECOG PS=2 **Days 1–14:** Oxaliplatin 110mg/m² + capecitabine 750mg/m² twice daily. Repeat cycle every 3 weeks.
Locally Advanced Disease	
Gemcitabine or gemcitabine-based combination therapy[1]	May be considered as initial therapy prior to 5-FU-based chemoradiation for patients with locally advanced, unresectable disease.
Adjuvant Therapy	
5-FU[1, 12]	Prior to chemoradiation **Days 1–21:** 5-FU 250mg/m²/day continuous IV infusion; initiate 1–2 weeks prior to chemoradiation (50.4Gy + 5-FU 250mg/m²/day). After chemoradiation **Days 1–28:** 5-FU 250mg/m²/day continuous IV infusion; initiate 3–5 weeks following chemoradiation. Repeat cycle every 6 weeks for 3 months.
Gemcitabine[1, 12]	Prior to chemoradiation **Days 1, 8 and 15:** Gemcitabine 1,000mg/m² IV; initiate 1–2 weeks prior to chemoradiation (50.4Gy + 5-FU 250mg/m²/day). After chemoradiation **Days 1, 8 and 15:** Gemcitabine 1,000mg/m² IV; initiate 3–5 weeks following chemoradiation. Repeat cycle every 4 weeks for 3 months.
Post-operative gemcitabine[1, 13]	**Days 1, 8 and 15:** Gemcitabine 1,000mg/m² IV. Repeat cycle every 4 weeks for 6 months.
Leucovorin + 5-FU[14]	**Days 1–5:** Leucovorin 20mg/m² IV bolus, followed by 5-FU 425mg/m² IV bolus. Repeat cycle every 4 weeks.

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