PANCREATIC ADENOCARCINOMA TREATMENT REGIMENS (Part 1 of 3)

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 NCCN 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 National Comprehensive Cancer Network 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.

Metastatic Disease[1]

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

Good Performance Status

REGIMEN	DOSING
FOLFIRINOX (oxaliplatin + irinotecan + 5-fluorouracil [5-FU]/leucovorin) (Category 1)[2]	**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-hour continuous 5-FU infusion of 2,400mg/m². Repeat cycle every 2 weeks until disease progression.
Gemcitabine + albumin-bound paclitaxel (Category 1)[3]	**Days 1, 8, and 15:** Nab-paclitaxel 125mg/m² IV + gemcitabine 1,000mg/m² IV. Repeat cycle every 4 weeks until disease progression.
Gemcitabine + erlotinib (Category 1)[4]	**Cycle 1 (8-week cycle):** **Days 1, 8, 15, 22, 29, 36, and 43:** Gemcitabine 1,000mg/m² IV follow by a 1-week rest **Days 1–56:** Erlotinib 100mg PO daily, **followed by:** **Subsequent cycles (4-week cycle):** **Days 1, 8, and 15:** Gemcitabine 1,000mg/m² IV over 30 minutes **Days 1–28:** Erlotinib 100mg PO daily.
Gemcitabine + capecitabine[5]	**Days 1, 8, and 15:** Gemcitabine 1,000mg/m² IV **Days 1–21:** Capecitabine 1,660mg/m² PO daily (830mg/m² twice daily). Repeat cycle every 4 weeks until disease progression.
Gemcitabine + cisplatin[6]	**Days 1 and 15:** Gemcitabine 1,000mg/m² IV + cisplatin 50mg/m² IV. Repeat cycle every 4 weeks until disease progression.
GTX (Fixed-dose rate gemcitabine + docetaxel + capecitabine) (Category 2B)[7]	**Days 1–14:** Capecitabine 750mg/m² PO twice daily **Days 4 and 11:** Gemcitabine 750mg/m² IV + docetaxel 30mg/m² IV. Repeat cycle every 21 days until disease progression.
Fluoropyrimidine (5-FU + leucovorin or capecitabine) + oxaliplatin (Category 2B)[8,9]	**Days 1, 8, 15, and 22:** Leucovorin 200mg/m² IV followed by 5-FU 2g/m² continuous IV infusion over 24 hours **Days 8 and 22:** Oxaliplatin 85mg/m² IV. After a rest of 3 weeks, repeat cycle on day 43. **OR** **Age ≤ 65 years and ECOG performance status 0 to 1:** **Day 1:** Oxaliplatin 130mg/m² IV **Days 1–14:** Capecitabine 1,000mg/m² twice daily. Repeat cycle every 3 weeks. **Age > 65 years and ECOG performance status 2:** **Day 1:** Oxaliplatin 110mg/m² IV **Days 1–14:** Capecitabine 750mg/m² twice daily. Repeat cycle every 3 weeks.

Poor Performance Status

Gemcitabine (Category 1)[1]	**Days 1, 8, and 15:** Gemcitabine 1,000mg/m² IV over 30 minutes. Repeat cycle every 28 days.
Fixed-dose rate gemcitabine (Category 2B)[1]	**Days 1, 8, and 15:** Gemcitabine 10mg/m²/minute IV. Repeat cycle every 28 days.
Capecitabine (Category 2B)[1]	**Days 1–14:** Capecitabine 1,000mg/m² PO twice daily. Repeat cycle every 3 weeks for up to 52 weeks.

continued

PANCREATIC ADENOCARCINOMA TREATMENT REGIMENS (Part 2 of 3)

Second-Line Therapy[1]

Principles of Chemotherapy:

- Second line chemotherapy may consist of gemcitabine-based therapy for those previously treated with fluoropyrimidine-based therapy, and of fluoropyrimidine-based therapy for those previously treated with gemcitabine-based therapy. Results of the CONKO-003 trial demonstrated a significant improvement in overall survival with the addition of oxaliplatin to 5-FU/leucovorin.

Locally Advanced Disease[1]

Principles of Chemotherapy:

- Depending on performance status, mono- or combination systemic chemotherapy may be considered as initial therapy prior to chemoradiation for appropriate patients with locally advanced, unresectable disease.
- Patients should be evaluated for recovery from hematologic and nonhematologic toxicity prior to initiation of chemoradiation.
- Patients who progress with metastatic disease are not candidates for chemoradiation unless required for palliative purposes.

Adjuvant Disease[1]

REGIMEN	DOSING
Gemcitabine (Category 1)[10]	**Days 1, 8, and 15:** Gemcitabine 1,000mg/m² IV over 30 minutes. Repeat cycle every 28 days.
5-FU + leucovorin (Category 1)[11]	**Days 1–5:** Leucovorin 20mg/m² IV bolus, followed by 5-FU 425mg/m² IV bolus. Repeat cycle every 4 weeks.
Gemcitabine + Radiation[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.
Continuous infusion 5-FU + Radiation[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.
Capecitabine (Category 2B)[1]	**Days 1–14:** Capecitabine 1,000mg/m² PO twice daily. Repeat cycle every 3 weeks for up to 52 weeks.

Principles of Chemotherapy:

- The CONKO-001 trial demonstrated significant improvements in disease-free survival and overall survival with use of postoperative gemcitabine as adjuvant chemotherapy versus observation in resectable pancreatic adenocarcinoma.[10]
- ESPAC-3 study results showed no significant difference in overall survival between 5-FU/leucovorin versus gemcitabine following surgery. When the groups receiving adjuvant 5-FU/leucovorin and adjuvant gemcitabine were compared, median survival was 23.0 months and 23.6 months, respectively.[11]
- The use of gemcitabine-based chemotherapy is frequently combined, sequentially, with 5-FU-based chemoradiotherapy.
- No significant differences were observed in the RTOG 97-04 study comparing pre- and post-chemoradiation 5-FU with pre- and post-chemoradiation gemcitabine for postoperative adjuvant treatment.[12]
- For patients who relapse after receiving adjuvant therapy, subsequent therapy may consist of gemcitabine or gemcitabine-based combination therapy for patients previously treated with fluoropyrimidine-based therapy, or fluoropyrimidine-based therapy (e.g., 5-FU/ leucovorin/oxaliplatin21 or CapeOx) for patients previously treated with gemcitabine-based therapy.

Neoadjuvant Therapy[1]

Principles of Chemotherapy:

- There is limited evidence to recommend specific neoadjuvant regimens off-study, and practices vary with regard to the use of chemotherapy and chemoradiation. Acceptable regimens include FOLFIRINOX or gemcitabine + albumin-bound paclitaxel. Subsequent chemoradiation is sometimes included.

continued

References

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