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Pancreatic Cancer Treatment Protocols

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Treatment Protocols

Treatment protocols for pancreatic cancer are provided below, including the following:

- Surgical resection and chemotherapy/chemoradiation
- Treatment for metastatic disease
- Special considerations

Surgical resection for pancreatic cancer

Considerations include the following:

- Surgical resection is potentially the only curative treatment approach for pancreatic cancer; however, most patients will present with disease that will not be cured with resection.
- Surgical resection depends on the size and location of the tumor and should involve multidisciplinary consultation.
- Pancreatic cancer primary tumor size measurements are often discordant between CT and pathologic specimen after resection. Dimensions of the primary tumor are increasingly relevant in an era of highly conformal radiotherapy. [1]

Treatment recommendations for resectable local disease

Stages I-II

Neoadjuvant therapy [2] :

- There is limited evidence to support specific neoadjuvant regimens; National Comprehensive Cancer Network (NCCN) guidelines advise that treatment at or coordinated through a high-volume center is preferred, when feasible, and participation in a clinical trial is encouraged.

- NCCN-preferred: FOLFIRINOX (oxaliplatin, leucovorin, irinotecan, 5-fluorouracil [5-FU]) with or without subsequent chemoradiation
- Modified FOLFIRINOX (mFOLFIRINOX; oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2, irinotecan 150 mg/m^2, 5-FU 2.4 g/m² over 46 hours) ± subsequent chemoradiation
- NCCN-preferred: Gemcitabine + albumin-bound paclitaxel ± subsequent chemoradiation
- NCCN-preferred regimens in patients with known *BRCA1/2* or *PALB2* mutations: FOLFIRINOX or mFOLFIRINOX ± subsequent chemoradiation or gemcitabine + cisplatin (2–6 cycles) ± subsequent chemoradiation

Adjuvant chemotherapy [3, 4, 5] :

- Gemcitabine monotherapy has been the standard of care since the CONKO-001 trial in 2008 [4]
- Gemcitabine 1000 mg/m ^{2} IV over 30 min weekly for 3 wk; every 4 wk for six cycles
- mFOLFIRINOX , in the Unicancer GI PRODIGE 24/CCTG PA.6 trial, demonstrated superior results compared with gemcitabine monotherapy (median overall survival of 54.5 versus 35 months, respectively) [6]
- mFOLFIRINOX: Every 14 days for 12 cycles

Adjuvant chemotherapy and chemoradiation [7] :

- Gemcitabine 1000 mg/m^2 IV over 30 min weekly for 3 wk [8]
- Concurrent chemoradiation starting 1-2 wk after gemcitabine: 5-FU 250 mg/m^2/day continuous IV infusion via pump during radiation
- Radiotherapy 1.8 Gy/day to a total of 50.4 Gy; **then** 3-5 wk after chemoradiation: gemcitabine 1000 mg/m^2 IV over 30 min weekly; every 28 d for three cycles [7]
- The above regimens may be preceded by capecitabine 800-900 mg/m^2 PO BID plus radiation for 5-6 wk

Treatment recommendations for locally advanced, unresectable disease

Stage III neoadjuvant therapy:

- For patients with stage III unresectable, locally advanced pancreatic cancer, preoperative (neoadjuvant) chemotherapy can be considered, but the benefit in terms of downstaging is modest
- Gemcitabine 1000 mg/m^2 IV over 30 min weekly for 3 wk; every 28 d [4] **or**
- 5-FU 500 mg/m^2/day IV bolus on days 1-3 and 29-31 with concurrent radiotherapy, 40 Gy [9]

Treatment recommendations for metastatic disease

First-line treatment recommendations for advanced metastatic pancreatic cancer (stage IV):

- Paclitaxel protein bound 125 mg/m^2 plus gemcitabine 1000 mg/m^2 IV over 30-40 min on days 1, 8, and 15 of each 28-day cycle [10]
- Gemcitabine 1000 mg/m^2 IV over 30 min weekly for 7 wk, followed by 1 wk off, then weekly for 3 wk; every 28 d [11] **or**
- Gemcitabine 1000 mg/m^2 IV over 30 min on days 1 and 15 **plus** cisplatin 50 mg/m^2 IV over 1 h on days 1 and 15; every 28 d [12] **or**
- Gemcitabine 1000 mg/m^2 IV weekly for 7 wk **plus** erlotinib 100 mg PO daily on days 1-56, followed by 1 wk off; **then** gemcitabine 1000 mg/m^2 IV on days 1, 8, and 15 every 28 d **plus** erlotinib 100 mg PO daily on days 1-28 for up to four cycles [13] **or**
- Gemcitabine 1000 mg/m^2 IV weekly for 3 wk; every 28 d; **plus** capecitabine 1660 mg/m^2/day weekly for 3 wk; every 28 d [14] **or**
- For patients with stage IV disease, median overall survival on gemcitabine-based therapy is from 5.5 to 7 mo; the non–gemcitabine-based regimen FOLFIRINOX (5-FU/leucovorin, irinotecan, and oxaliplatin) showed improved survival of 11.1mo [15] : Oxaliplatin 85 mg/m^2 IV on day 1 **plus** irinotecan 180 mg/m^2 IV on day 1 **plus** leucovorin 400 mg/m^2 IV on day 1, followed by 5-FU 400 mg/m^2 IV bolus on day 1 and then 2400 mg/m^2 IV infusion over 46 h on days 1 and 15

Second-line treatment recommendations for advanced metastatic pancreatic cancer:

- Capecitabine 1250 mg/m^2 PO BID for 14d; every 3 wk [16] **or**
- Capecitabine 1000 mg/m^2 PO BID for 14 d; every 3 wk **plus** erlotinib 150 mg PO daily continuously [17] **or**
- Irinotecan liposomal 70 mg/m^2 IV infused over 90 min, **followed by** leucovorin 400 mg/m^2 IV infused over 30 min, **followed by** 5-FU 2400 mg/m^2 IV infused over 46 h every 3 wk [18] **or**
- 5-FU 2000 mg/m^2 IV over 24 h on days 1, 8, 15, and 22 **plus** leucovorin 200 mg/m^2 IV over 30 min on days 1, 8, 15, and 22 **plus** oxaliplatin 85 mg/m^2 IV on days 8 and 22; every 42 d [19]

Maintenance treatment:

- Olaparib is indicated for maintenance treatment of adults with deleterious or suspected

deleterious germline *BRCA*-mutated metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen

- 300 mg PO BID until disease progression or unacceptable toxicity [20]

Special considerations

For patients whose disease progresses on first-line therapy, few options are available and median survival on therapy ranges between 3 and 7 mo. Because of generally poor outcomes with standard therapy, all patients with pancreatic cancer should be encouraged to participate in clinical trials