

# CHEMOTHERAPY REGIMENS

## Pancreatic, Thyroid, and Other Endocrine Cancers

### Pancreatic Adenocarcinoma

The selection, dosing, and administration of anticancer 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 anticancer 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.

NOTE: Grey shaded boxes contain updated regimens.

## Pancreatic, Thyroid, and Other Endocrine Cancers

PANCREATIC ADENOCARCINOMA (Part 1 of 2)	
<b>General treatment notes:</b>	
<ul style="list-style-type: none"> <li>Systemic chemotherapy is used in the neoadjuvant or adjuvant setting and in the management of locally advanced, unresectable, and metastatic disease.<sup>1</sup></li> <li>Enrollment in a clinical trial strongly recommended.<sup>1</sup></li> <li>In adjuvant therapy, the use of gemcitabine-based chemotherapy is frequently combined, sequentially, with 5-FU-based chemoradiotherapy.<sup>1</sup></li> </ul>	
REGIMEN	DOSING
Metastatic Disease	
<b>Gemcitabine</b> (Gemzar) <sup>1,2</sup>	<p><b>Cycle 1 ( 8 week cycle)</b>  <b>Days 1, 8, 15, 22, 29, 36 and 43:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV administered over 30 min, <b>followed by</b> a 1-week rest.</p> <p><b>Subsequent cycles (4 week cycle)</b>  <b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV administered over 30 min, <b>followed by</b> a 1-week rest.</p> <p>Fixed-dose gemcitabine (10mg/m<sup>2</sup>/min IV) can be substituted for standard infusion of gemcitabine over 30 min.</p>
<b>Gemcitabine + erlotinib</b> (Tarceva) <sup>1,3</sup>	<p><b>Cycle 1 (8 week cycle)</b>  <b>Days 1, 8, 15, 22, 29, 36 and 43:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV <b>followed by</b> a 1-week rest, <b>plus</b></p> <p><b>All days:</b> Erlotinib 100mg/day or 150mg/day orally, <b>followed by</b></p> <p><b>Subsequent cycles (4 week cycle)</b>  <b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 min.  <b>All days:</b> Erlotinib 100mg/day or 150mg/day orally.</p>
<b>Gemcitabine + cisplatin</b> (Platinol; CDDP) <sup>1,4</sup>	<p><b>Days 1 and 15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV + cisplatin 50mg/m<sup>2</sup> IV. Repeat cycle every 4 weeks.</p>
<b>GEMOX</b> (fixed-dose rate gemcitabine + oxaliplatin [Eloxatin]) <sup>1,5,6</sup>	<p><b>Day 1:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV, <b>plus</b>  <b>Day 2:</b> Oxaliplatin 100mg/m<sup>2</sup> IV.  Repeat cycle every 2 weeks until disease progression.</p>
<b>Gemcitabine + fluoropyrimidine</b> (capecitabine, Xeloda) <sup>1,7</sup>	<p><b>Days 1-21:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV once weekly + capecitabine 1,660mg/m<sup>2</sup> orally (830mg/m<sup>2</sup> twice daily). Repeat cycle every 4 weeks until disease progression.</p>
<b>FOLFIRINOX</b> (oxaliplatin + irinotecan + 5-fluorouracil/leucovorin) <sup>8</sup>	<p><b>Day 1:</b> Oxaliplatin 85mg/m<sup>2</sup> IV + irinotecan 180mg/m<sup>2</sup> IV + leucovorin 400mg/m<sup>2</sup> IV, <b>followed by</b> a 5-FU bolus of 400mg/m<sup>2</sup> and a 46-hr continuous 5-FU infusion of 2,400mg/m<sup>2</sup>. Repeat cycle every 2 weeks.</p>
Second-Line Therapy	
<b>Gemcitabine</b> (in gemcitabine-naïve patients)	<p><b>Cycle 1 ( 8 week cycle)</b>  <b>Days 1, 8, 15, 22, 29, 36 and 43:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV administered over 30 min, <b>followed by</b> a 1-week rest.</p> <p><b>Subsequent cycles (4 week cycle)</b>  <b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV administered over 30 min, <b>followed by</b> a 1-week rest.</p> <p>Fixed-dose gemcitabine (10mg/m<sup>2</sup>/min IV) can be substituted for standard infusion of gemcitabine over 30 min.</p>
<b>Capecitabine</b> <sup>1,9</sup>	<p><b>Days 1-14:</b> 1,250mg/m<sup>2</sup> orally twice daily. Repeat cycle every 3 weeks for up to 52 weeks.</p>
<b>5-fluorouracil (5-FU) + leucovorin + oxaliplatin</b> <sup>1,10</sup>	<p><b>Days 1, 8, 15 and 22:</b> 5-FU 2g/m<sup>2</sup> IV + leucovorin 200mg/m<sup>2</sup> IV, <b>plus</b>  <b>Days 8 and 22:</b> Oxaliplatin 85mg/m<sup>2</sup> IV.</p>
<b>CapeOx</b> (capecitabine + oxaliplatin) <sup>1,11</sup>	<p><b>Age &lt;65yrs and ECOG PS &lt;2</b>  <b>Days 1-14:</b> Oxaliplatin 130mg/m<sup>2</sup> + capecitabine 1,000mg/m<sup>2</sup> twice daily. Repeat cycle every 3 weeks.</p> <p><b>Age &gt;65yrs and ECOG PS=2</b>  <b>Days 1-14:</b> Oxaliplatin 110mg/m<sup>2</sup> + capecitabine 750mg/m<sup>2</sup> twice daily. Repeat cycle every 3 weeks.</p>

*continued*

## PANCREATIC ADENOCARCINOMA (Part 2 of 2)

REGIMEN	DOSING
<b>Locally Advanced Disease</b>	
<b>Gemcitabine or gemcitabine-based combination therapy<sup>1</sup></b>	May be considered as initial therapy prior to 5-FU-based chemoradiation for patients with locally advanced, unresectable disease.
<b>Adjuvant Therapy</b>	
<b>Treatment notes:</b> 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 (eg, 5-FU/leucovorin/oxaliplatin or CapeOx) for patients previously treated with gemcitabine-therapy. <sup>1, 10, 11</sup>	
<b>5-FU<sup>1, 12</sup></b>	<p><b>Prior to chemoradiation</b>  <b>Days 1–21:</b> 5-FU 250mg/m<sup>2</sup>/day continuous IV infusion; initiate 1–2 weeks prior to chemoradiation (50.4Gy + 5-FU 250mg/m<sup>2</sup>/day).</p> <p><b>After chemoradiation</b>  <b>Days 1–28:</b> 5-FU 250mg/m<sup>2</sup>/day continuous IV infusion; initiate 3–5 weeks following chemoradiation.                      Repeat cycle every 6 weeks for 3 months.</p>
<b>Gemcitabine<sup>1, 12</sup></b>	<p><b>Prior to chemoradiation</b>  <b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV; initiate 1–2 weeks prior to chemoradiation (50.4Gy + 5-FU 250mg/m<sup>2</sup>/day).</p> <p><b>After chemoradiation</b>  <b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV; initiate 3–5 weeks following chemoradiation.                      Repeat cycle every 4 weeks for 3 months.</p>
<b>Post-operative gemcitabine<sup>1, 13</sup></b>	<b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV. Repeat cycle every 4 weeks for 6 months.
<b>Leucovorin + 5-FU<sup>14</sup></b>	<b>Days 1–5:</b> Leucovorin 20mg/m <sup>2</sup> IV bolus, <b>followed by</b> 5-FU 425mg/m <sup>2</sup> IV bolus. Repeat cycle every 4 weeks.
<b>References</b>	
<ol style="list-style-type: none"> <li>1. NCCN Clinical Practice Guidelines in Oncology™. Pancreatic Adenocarcinoma. v 1.2012. Available at: <a href="http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf">http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf</a>. Accessed October 16, 2011.</li> <li>2. Gemzar [prescribing information]. Indianapolis, IN: Eli Lilly; 2011.</li> <li>3. Moore MJ, Goldstein D, Hamm J, et al. Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: a phase III trial of the National Cancer Institute of Canada Clinical Trials Group. <i>J Clin Oncol</i>. 2007;25:1960–1966.</li> <li>4. Heinemann V, Quietzsch D, Gieseler F, Gonnermann M. Randomized phase III trial of gemcitabine plus cisplatin compared with gemcitabine alone in advanced pancreatic cancer. <i>J Clin Oncol</i>. 2006 20;24(24):3946–3952.</li> <li>5. Heinemann V, Labianca R, Hinke A, Louvet C. Increased survival using platinum analog combined with gemcitabine as compared to single-agent gemcitabine in advanced pancreatic cancer: pooled analysis of two randomized trials, the GERCOR/GISCAD intergroup study and a German multicenter study. <i>Ann Oncol</i>. 2007;18:1652–1659.</li> <li>6. Demols A, Peeters M, Polus M, et al. Gemcitabine and oxaliplatin (GEMOX) in gemcitabine refractory advanced pancreatic adenocarcinoma: a phase II study. <i>Br J Cancer</i>. 2006;94:481–485.</li> <li>7. Cunningham D, Chau I, Stocken DD, et al. Phase III randomized comparison of gemcitabine versus gemcitabine plus capecitabine in patients with advanced pancreatic cancer. <i>J Clin Oncol</i>. 2009;27:5513–5518.</li> <li>8. Conroy T, Desseigne F, Ychou M, et al. Randomized phase III trial comparing FOLFIRINOX (F: 5FU/leucovorin [LV], irinotecan [I], and oxaliplatin [O]) versus gemcitabine (G) as first-line</li> </ol>	<p>treatment for metastatic pancreatic adenocarcinoma (MPA): Preplanned interim analysis results of the PRODIGE 4/ACCORD 11 trial. <i>J Clin Oncol</i>. 2010;28 (suppl; abstr 4010):15s.</p> <ol style="list-style-type: none"> <li>9. Cartwright TH, Cohn A, Varkey JA, et al. Phase II study of oral capecitabine in patients with advanced or metastatic pancreatic cancer. <i>J Clin Oncol</i>. 2002;20:160–164.</li> <li>10. Pelzer U, Kubica K, Stieler I, et al. A randomized trial in patients with gemcitabine refractory pancreatic cancer. Final results of the CONKO 003 study. <i>J Clin Oncol</i>. 26:2008 (May 20 suppl;abstr 4508).</li> <li>11. Xiong HQ, Varadhachary GR, Blais JC, Hess KR, Abbruzzese JL, Wolff RA. Phase 2 trial of oxaliplatin plus capecitabine (XELOX) as second-line therapy for patients with advanced pancreatic cancer. <i>Cancer</i>. 2008;113:2046–2052.</li> <li>12. Regine WF, Winter KW, Abrams R, et al. Fluorouracil vs gemcitabine chemotherapy before and after fluorouracil-based chemoradiation following resection of pancreatic adenocarcinoma: a randomized controlled trial. <i>JAMA</i>. 2008;299 9:1019–1026.</li> <li>13. Neuhaus P, Riess H, Post S, et al. CONKO-001: final results of the randomized, prospective, multicenter phase III trial of adjuvant chemotherapy with gemcitabine versus observation in patients with resected pancreatic cancer (PC). <i>J Clin Oncol</i>. 26: 2008 (May 20 suppl; abstr 4504).</li> <li>14. Neoptolemos J, Büchler M, Stocken DD, et al. ESPAC-3(v2): A multicenter, international, open-label, randomized, controlled phase III trial of adjuvant 5-fluorouracil/folinic acid (5-FU/FA) versus gemcitabine (GEM) in patients with resected pancreatic ductal adenocarcinoma. <i>J Clin Oncol</i>. 27:18s, 2009 (suppl; abstr LBA4505).</li> </ol>
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