

GASTRIC CANCER TREATMENT REGIMENS (Part 1 of 7)

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.

Principles of Systemic Therapy¹

Chemotherapy regimens should be chosen in the context of performance status, medical comorbidities, toxicity profile, and HER2-neu expression (for adenocarcinoma only). Two-drug cytotoxic regimens are preferred for patients with advanced disease because of lower toxicity. Three-drug cytotoxic regimens should be reserved for medically fit patients with good performance status and access to frequent toxicity evaluation. Doses and schedules for any regimen that is not derived from category 1 evidence is a suggestion, and subject to appropriate modifications depending on the circumstances. Infusional fluorouracil and capecitabine may be used interchangeably (except as indicated). Cisplatin and oxaliplatin may be used interchangeably depending on toxicity profile.

Preoperative Chemoradiation (esophagogastric junction and gastric cardia)¹

Preferred Regimens

REGIMEN	DOSING
Paclitaxel + carboplatin²	Day 1: Paclitaxel 50mg/m ² IV + carboplatin AUC 2mg/mL × min IV. Repeat weekly for 5 weeks.
Cisplatin + 5-fluorouracil (5-FU)^{3,4}	Days 1 and 29: Cisplatin 75–100mg/m ² IV Days 1–4 and 29–32: 5-FU 750–1000mg/m ² IV continuous infusion over 24 hours. OR Days 1–5: Cisplatin 15mg/m ² IV once daily plus 5-FU 800mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days for 2 cycles.
Oxaliplatin + 5-FU^{5,6}	Days 1, 15, and 29: Oxaliplatin 85mg/m ² IV Days 1–33: 5-FU 180mg/m ² IV. OR Day 1: Oxaliplatin 85mg/m ² and leucovorin 400mg/m ² followed by 5-FU 400mg/m ² bolus, then 800mg/m ² 24-hour continuous infusion over days 1 and 2; the first 3 cycles were delivered during radiotherapy (RT), the other 3 after RT; 6 bimonthly (14 days) cycles.
Cisplatin + capecitabine⁷	Day 1: Cisplatin 30mg/m ² IV Days 1–5: Capecitabine 800mg/m ² orally twice daily. Repeat cycle weekly for 5 weeks.
Oxaliplatin + capecitabine⁸	Days 1, 15, and 29: Oxaliplatin 85mg/m ² IV Days 1–5: Capecitabine 625mg/m ² orally twice daily for 5 weeks.

Other Regimens

Irinotecan + cisplatin⁹	Days 1, 8, 22, 29: Irinotecan 65mg/m ² IV plus cisplatin 30mg/m ² IV.
Paclitaxel + 5-FU¹⁰	Day 1: Paclitaxel 45–50mg/m ² IV weekly Days 1–5: 5-FU 300mg/m ² IV continuous infusion. Weekly for 5 weeks.
Paclitaxel + capecitabine¹⁰	Day 1: Paclitaxel 45–50mg/m ² IV Days 1–5: Capecitabine 625–825mg/m ² orally BID. Weekly for 5 weeks.
Epirubicin + cisplatin + 5-FU (ECF)¹¹	Day 1: Epirubicin 50mg/m ² IV bolus + cisplatin 60mg/m ² IV Days 1–21: 5-FU 200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.
ECF modification: epirubicin + oxaliplatin + 5-FU¹²	Day 1: Epirubicin 50mg/m ² IV; oxaliplatin 130mg/m ² IV Days 1–21: 5-FU 200mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.
ECF modification: epirubicin + cisplatin + capecitabine¹²	Day 1: Epirubicin 50mg/m ² IV; cisplatin 60mg/m ² IV Days 1–21: Capecitabine 625mg/m ² orally twice daily. Repeat cycle every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 2 of 7)

Perioperative Chemotherapy (including esophagogastric junction)¹

REGIMEN	DOSING
ECF modification: epirubicin + oxaliplatin + capecitabine¹²	Day 1: Epirubicin 50mg/m ² IV; oxaliplatin 130mg/m ² IV Days 1–21: Capecitabine 625mg/m ² orally twice daily. Repeat cycle every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.
5-FU + cisplatin¹³	Day 1: Cisplatin 75–80mg/m ² IV Days 1–5: 5-FU 800mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 28 days for 2–3 cycles preoperatively and 3–4 cycles postoperatively for a total of 6 cycles.

Postoperative Chemoradiation (including esophagogastric junction)¹

5-FU + leucovorin (category 1)¹⁴	Cycles 1, 3, and 4 (before and after radiation) Days 1–5: Leucovorin 20mg/m ² IVP plus 5-FU 425mg/m ² /day IVP Repeat cycle every 28 days. Cycle 2 (with radiation) Days 1–4 and 31–33: Leucovorin 20mg/m ² IVP Days 1–4: 5-FU 400mg/m ² /day IVP. Repeat cycle every 35 days. The NCCN panel acknowledges that the Intergroup 0116 Trial formed the basis for post-operative adjuvant chemoradiation strategy. However, the panel does not recommend the above specified doses or schedule of cytotoxic agents because of concerns regarding toxicity. The panel recommends one of the following modifications instead.
Capecitabine¹⁵	Days 1–14: Capecitabine 750–1000mg/m ² orally twice daily. Repeat cycle every 28 days; 1 cycle before and 2 cycles after chemoradiation.
5-FU + leucovorin¹⁶	Days 1, 2, 15, and 16: Leucovorin 400mg/m ² IV followed by 5-FU 400mg/m ² IVP and a 24-hour infusion of 5-FU 1200mg/m ² ; 1 cycle before and 2 cycles after chemoradiation. Repeat cycle every 28 days.
5-FU with radiation¹⁷	Days 1–5 OR Days 1–7: 5-FU 200–250mg/m ² IV continuous infusion over 24 hours once daily; weekly for 5 weeks.
Capecitabine with radiation¹⁸	Days 1–5 OR Days 1–7: Capecitabine 625–825mg/m ² orally twice daily; weekly for 5 weeks.

Postoperative Chemotherapy

Capecitabine + oxaliplatin¹⁹	Days 1–14: Capecitabine 1000mg/m ² orally twice daily Day 1: Oxaliplatin 130mg/m ² IV. Repeat cycle every 21 days for 8 cycles.
Capecitabine + cisplatin²⁰	Days 1–14: Capecitabine 1000mg/m ² orally twice daily Day 1: Cisplatin 60mg/m ² IV. Repeat cycle every 21 days for 6 cycles.

Metastatic or Locally Advanced Cancer (where local therapy is not indicated)¹

First-line Therapy

Trastuzumab + chemotherapy (NOTE: for HER2-neu malignancies)²¹	Day 1: Trastuzumab 8mg/kg IV loading dose (Cycle 1 only); followed by trastuzumab 6mg/kg IV every 3 weeks, plus chemotherapy OR Day 1 of Cycle 1: Trastuzumab 6mg/kg IV loading dose, then 4mg/kg IV every 14 days. Chemotherapy: Day 1: Cisplatin 80mg/m ² IV, plus Days 1–14: Capecitabine 1000mg/m ² orally twice daily. OR Days 1–5: 5-FU 800mg/m ² continuous IV infusion. Repeat cycle every 21 days for 6 cycles
Docetaxel + cisplatin + 5-FU (DCF)²²	Day 1: Docetaxel 75mg/m ² IV + cisplatin 75mg/m ² IV Days 1–5: 5-FU 1,000mg/m ² IV continuous infusion over 24 hours, daily. Repeat cycle every 28 days. The panel does not recommend the above specified doses or schedule of cytotoxic agents because of concerns regarding toxicity.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 3 of 7)

Metastatic or Locally Advanced Cancer (where local therapy is not indicated)¹ (continued)

First-line Therapy (continued)

REGIMEN	DOSING
Modified DCF (docetaxel + cisplatin + leucovorin + 5-FU)²³	Day 1: Docetaxel 40mg/m ² IV plus leucovorin 400mg/m ² IV plus 5-FU 400mg/m ² Days 1 and 2: 5-FU 1000mg/m ² IV continuous infusion over 24 hours Day 3: Cisplatin 40mg/m ² IV. Repeat cycle every 14 days.
Modified DCF (docetaxel + oxaliplatin + 5-FU)²⁴	Day 1: Docetaxel 50mg/m ² IV plus oxaliplatin 85mg/m ² Days 1 and 2: 5-FU 1,200mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 14 days.
Modified DCF (docetaxel + carboplatin + 5-FU)²⁵	Day 1: Docetaxel 75mg/m ² Day 2: Carboplatin AUC 6mg/mL × min Days 1-3: 5-FU 1,200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days.
ECF²⁶	Day 1: Epirubicin 50mg/m ² IV bolus + cisplatin 60mg/m ² IV Days 1-21: 5-FU 200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days.
ECF modifications (epirubicin + oxaliplatin + 5-FU)²⁷	Days 1: Epirubicin 50mg/m ² IV plus oxaliplatin 130mg/m ² IV Days 1-21: 5-FU 200mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 21 days.
ECF modifications (epirubicin + cisplatin + capecitabine)²⁷	Day 1: Epirubicin 50mg/m ² IV plus cisplatin 60mg/m ² IV Days 1-21: Capecitabine 625mg/m ² orally twice daily. Repeat cycle every 21 days.
ECF modifications (epirubicin + oxaliplatin + capecitabine)²⁷	Day 1: Epirubicin 50mg/m ² IV plus oxaliplatin 130mg/m ² IV Days 1-21: capecitabine 625mg/m ² IV orally twice daily. Repeat cycle every 21 days.
Fluoropyrimidine and cisplatin (5-FU + cisplatin)³³	Day 1: Cisplatin 75–100mg/m ² IV Days 1-4: 5-FU 1,000mg/m ² IV continuous infusion over 24 hours daily.
Fluoropyrimidine and cisplatin (5-FU + cisplatin + leucovorin)²⁸⁻³¹	Day 1: Cisplatin 50mg/m ² IV plus leucovorin 200mg/m ² IV plus 5-FU 2,000mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 14 days.
Fluoropyrimidine and cisplatin (capecitabine + cisplatin)²⁸⁻³¹	Day 1: Cisplatin 80mg/m ² IV Day 1-14: Capecitabine 1000mg/m ² orally twice daily. Repeat cycle every 3 weeks.
Fluoropyrimidine and oxaliplatin (oxaliplatin + capecitabine)^{29,32,33}	Day 1: Oxaliplatin 130mg/m ² IV Days 1-14: Capecitabine 1000mg/m ² orally twice daily. Repeat cycle every 21 days.
Fluoropyrimidine and oxaliplatin (oxaliplatin + leucovorin + 5-FU)^{29,32,33}	Day 1: Oxaliplatin 85mg/m ² IV plus leucovorin 400mg/m ² IV plus 5-FU 400mg/m ² IVP Days 1 and 2: 5-FU 1200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days. OR Day 1: Oxaliplatin 85mg/m ² IV plus leucovorin 200mg/m ² IV plus 5-FU 2,600mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 14 days.
Fluorouracil and irinotecan (irinotecan + leucovorin + 5-FU)³⁴⁻³⁶	Day 1: Irinotecan 80mg/m ² IV plus leucovorin 500mg/m ² IV plus 5-FU 2000mg/m ² IV continuous infusion over 24 hours. Weekly for 6 weeks followed by 1 week off treatment OR weekly for 6 weeks followed by 2 weeks off treatment. OR Day 1: Irinotecan 150mg/m ² IV plus leucovorin 20mg/m ² IV Days 1-2: 5-FU 1000mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 4 of 7)

Metastatic or Locally Advanced Cancer (where local therapy is not indicated)¹ (continued)

Other Regimens

REGIMEN	DOSING
Paclitaxel + cisplatin or carboplatin ³⁷⁻³⁹	<p>Day 1: Paclitaxel 135–200mg/m² IV Day 2: Cisplatin 75mg/m² IV. Repeat cycle every 21 days.</p> <p>OR</p> <p>Day 1: Paclitaxel 90mg/m² IV plus cisplatin 50mg/m² IV. Repeat cycle every 14 days.</p> <p>OR</p> <p>Day 1: Paclitaxel 200mg/m² IV plus carboplatin AUC 5mg/mL × min Repeat cycle every 21 days.</p>
Docetaxel + cisplatin ^{40,41}	<p>Day 1: Docetaxel 70–85mg/m² IV plus cisplatin 70–75mg/m² IV. Repeat cycle every 21 days.</p>
Docetaxel + irinotecan ⁴²	<p>Days 1 and 8: Docetaxel 35mg/m² IV plus irinotecan 50mg/m² IV. Repeat cycle every 21 days.</p>
Fluoropyridimine ^{32,43,44}	<p>Day 1: Leucovorin 400mg/m² IV plus 5-FU 400mg/m² IVP Days 1 and 2: 5-FU 1200mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days.</p> <p>OR</p> <p>Days 1–5: 5-FU 800mg/m² IV continuous infusion over 24 hours daily. Repeat cycle every 28 days.</p> <p>OR</p> <p>Days 1–14: Capecitabine 1000–1250mg/m² orally twice daily. Repeat cycle every 21 days.</p>
Taxane ⁴⁵⁻⁴⁸	<p>Day 1: Docetaxel 75–100mg/m² IV. Repeat cycle every 21 days.</p> <p>OR</p> <p>Day 1: Paclitaxel 135–250mg/m² IV. Repeat cycle every 21 days.</p> <p>OR</p> <p>Days 1, 8, 15 and 22: Paclitaxel 80mg/m² IV once weekly. Repeat cycle every 28 days.</p>

Second-line Therapy

Trastuzumab + chemotherapy (NOTE: for HER2-neu malignancies) ²³	<p>Day 1: Trastuzumab 8mg/kg IV loading dose (Cycle 1 only); followed by trastuzumab 6mg/kg IV every 3 weeks, plus chemotherapy.</p> <p>OR</p> <p>Day 1 of Cycle 1: Trastuzumab 6mg/kg IV loading dose, then 4mg/kg IV every 14 days.</p> <p>Chemotherapy: Day 1: Cisplatin 80mg/m² IV, plus Days 1–14: Capecitabine 1000mg/m² orally twice daily OR Days 1–5: 5-FU 800mg/m² continuous IV infusion. Repeat cycle every 21 days for 6 cycles.</p>
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Second-line Therapy (preferred regimens)

Ramucirumab for gastric and EGJ adenocarcinoma ⁴⁹	<p>Day 1: Ramucirumab 8mg/kg IV. Repeat cycle every 14 days.</p>
Ramucirumab + paclitaxel for gastric and EGJ adenocarcinoma ⁵⁰	<p>Day 1 and 15: Ramucirumab 8mg/kg IV Day 1, 8, and 15: Paclitaxel 80mg/m². Repeat cycle every 28 days.</p>
Docetaxel ⁴⁹	<p>Day 1: Docetaxel 75–100mg/m² IV. Repeat cycle every 21 days.</p>
Paclitaxel ⁵⁰⁻⁵²	<p>Day 1: Paclitaxel 135–250mg/m² IV. Repeat cycle every 21 days.</p> <p>OR</p> <p>Day 1: Paclitaxel 80mg/m² IV once weekly. Repeat cycle every 28 days.</p> <p>OR</p> <p>Days 1, 8, and 15: Paclitaxel 80mg/m² IV. Repeat cycle every 28 days.</p>

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 5 of 7)

Metastatic or Locally Advanced Cancer (where local therapy is not indicated)¹ (continued)

Second-line Therapy (preferred regimens) (continued)

REGIMEN	DOSING
Irinotecan ^{35,51-53}	<p>Day 1: Irinotecan 250–350mg/m² IV. Repeat cycle every 21 days.</p> <p style="text-align: center;">OR</p> <p>Day 1: Irinotecan 150–180mg/m² IV. Repeat cycle every 14 days.</p> <p style="text-align: center;">OR</p> <p>Days 1 and 8: Irinotecan 125mg/m² IV. Repeat cycle every 21 days.</p>

Other Regimens

Irinotecan + cisplatin ^{32,54}	Days 1 and 8: Irinotecan 65mg/m ² IV plus cisplatin 25–30mg/m ² IV. Repeat cycle every 21 days.
Irinotecan + fluoropyridimine ^{56,57}	Day 1: Irinotecan 250mg/m ² IV Days 1–14: Capecitabine 1000mg/m ² PO BID daily. Repeat cycle every 21 days.
Irinotecan + fluoropyridimine ^{56,57}	Day 1: Irinotecan 180mg/m ² IV plus leucovorin 400mg/m ² IV plus 5-FU 400mg/m ² IVP Days 1 and 2: 5-FU 600–1200mg/m ² /day IV continuous infusion on Days 1 and 2. Repeat cycle every 14 days.
Docetaxel + irinotecan ⁴²	Days 1 and 8: Docetaxel 35mg/m ² IV plus irinotecan 50mg/m ² IV. Repeat cycle every 21 days.

Alternative Regimens for Consideration

Mitomycin + irinotecan ⁵⁷⁻⁵⁹	<p>Day 1: Mitomycin 6mg/m² IV Days 2 and 9: Irinotecan 125mg/m² Repeat cycle every 28 days.</p> <p style="text-align: center;">OR</p> <p>Days 1 and 15: Irinotecan 150mg/m² IV Day 1: Mitomycin 8mg/m² IV. Repeat cycle every 28 days.</p> <p style="text-align: center;">OR</p> <p>Day 1: Irinotecan 125mg/m² IV plus mitomycin 5mg/m² IV. Repeat cycle every 14 days.</p>
Mitomycin + leucovorin + 5-FU ⁶⁰	Days 1 and 22: Mitomycin 10mg/m ² IV Day 1: Leucovorin 500mg/m ² IV plus 5-FU 2600mg/m ² /day IV continuous infusion. Weekly for 6 weeks, followed by 2 weeks off treatment.

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GASTRIC CANCER TREATMENT REGIMENS (Part 7 of 7)

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