

GASTRIC CANCER TREATMENT REGIMENS (Part 1 of 6)

Clinical Trials: The National Comprehensive Cancer Network 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 provided only 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 NCCN 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

- Systemic therapy regimens recommended for advanced esophageal and esophagogastric junction (EGJ) adenocarcinoma, squamous cell carcinoma of the esophagus, and gastric adenocarcinoma may be used interchangeably (except as indicated).
- Regimens should be chosen in the context of performance status (PS), medical comorbidities, and toxicity profile.
- Trastuzumab should be added to chemotherapy for HER2 overexpressing metastatic adenocarcinoma.
- 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 PS and access to frequent toxicity evaluation.
- Modifications of category 1 regimen or use of category 2A or 2B regimens may be preferred (as indicated), with evidence supporting a more favorable toxicity profile without compromising efficacy.
- Doses and schedules for any regimen that is not derived from category 1 evidence are a suggestion, and are subject to appropriate modifications depending on the circumstances.
- Alternate combinations and schedules of cytotoxic based on the availability of the agents, practice preferences, and contraindications are permitted.
- Perioperative chemotherapy, or postoperative chemotherapy plus chemoradiation is the preferred approach for localized gastric cancer.
- Postoperative chemotherapy is recommended following primary D2 lymph node dissection.
- In the adjuvant setting, upon completion of chemotherapy or chemoradiation, patients should be monitored for any long-term therapy-related complications.

Preoperative Chemoradiation (esophagogastric junction and gastric cardia)¹

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

Preferred Regimens

REGIMEN	DOSING
Paclitaxel + carboplatin (Category 1)⁶	Day 1: Paclitaxel 50mg/m ² IV + carboplatin AUC 2mg·min/mL IV. Repeat cycle weekly for 5 weeks.
Cisplatin + 5-fluorouracil (5-FU) (Category 1)^{7,8}	Days 1 and 29: Cisplatin 75–100mg/m ² IV Days 1–4 and 29–32: 5-FU 750–1000mg/m ² continuous IV infusion over 24 hours daily. OR Days 1–5: Cisplatin 15mg/m ² IV once daily + 5-FU 800mg/m ² continuous IV infusion over 24 hours daily. Repeat cycle every 21 days for 2 cycles.
Oxaliplatin + 5-FU (Category 1)⁹	Day 1: Oxaliplatin 85mg/m ² + leucovorin 400mg/m ² + 5-FU 400mg/m ² IV push followed by Days 1–2: 5-FU 800mg/m ² 24-hour continuous infusion. Repeat cycle every 14 days for 3 cycles with radiation and 3 cycles after radiation.
Cisplatin + capecitabine⁵⁰	Day 1: Cisplatin 30mg/m ² IV Days 1–5: Capecitabine 800mg/m ² orally twice daily. Repeat cycle weekly for 5 weeks.
Oxaliplatin + capecitabine⁵¹	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

Paclitaxel + 5-FU (Category 2B)¹¹	Day 1: Paclitaxel 45–50mg/m ² IV weekly Days 1–5: 5-FU 300mg/m ² IV continuous infusion. Repeat cycle weekly for 5 weeks.
Paclitaxel + capecitabine (Category 2B)¹¹	Day 1: Paclitaxel 45–50mg/m ² IV Days 1–5: Capecitabine 625–825mg/m ² orally twice daily. Repeat cycle weekly for 5 weeks.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 2 of 6)

Perioperative Chemotherapy (including esophagogastric junction)¹

REGIMEN	DOSING
Epirubicin + cisplatin + 5-FU (ECF) (Category 2B)³	Day 1: Epirubicin 50mg/m ² IV bolus + cisplatin 60mg/m ² IV Days 1–21: 5-FU 200mg/m ² /day 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-FU (Category 2B)⁴	Day 1: Epirubicin 50mg/m ² IV + oxaliplatin 130mg/m ² IV Days 1–21: 5-FU 200mg/m ² /day IV continuous infusion over 24 hours. Repeat cycle every 21 days for 3 cycles preoperatively and 3 cycles postoperatively.
ECF modification: epirubicin + cisplatin + capecitabine (Category 2B)⁴	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.
ECF modification: epirubicin + oxaliplatin + capecitabine (Category 2B)^{4,5}	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 + cisplatin (Category 1)²	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.
5-FU + leucovorin + oxaliplatin^{16,19}	Day 1: Oxaliplatin 85mg/m ² IV + leucovorin 400mg/m ² + 5-FU 400mg/m ² IV push followed by: Days 1–2: 5-FU 1200mg/m ² continuous IV daily over 24 hours. OR Day 1: Oxaliplatin 85mg/m ² + leucovorin 200mg/m ² + 5-FU 2600mg/m ² continuous IV infusion over 24 hours. Repeat cycle every 14 days.
Capecitabine + oxaliplatin²⁰	Day 1: Oxaliplatin 130mg/m ² IV Days 1–14: Capecitabine 1000mg/m ² orally twice daily. Repeat cycle every 21 days.

Postoperative Chemoradiation (including esophagogastric junction)¹

5-FU + leucovorin (Category 1)^{12,52}	Cycles 1, 3, and 4 (before and after radiation) Days 1–5: Leucovorin 20mg/m ² IV push + 5-FU 425mg/m ² /day IV push Repeat cycle every 28 days. Cycle 2 (with radiation) Days 1–4 and 31–33: Leucovorin 20mg/m ² IV push Days 1–4: 5-FU 400mg/m ² /day IV push. Repeat cycle every 35 days. The NCCN panel acknowledges that the Intergroup 0116 Trial formed the basis for postoperative 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.
Capecitabine⁵³	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 + leucovorin⁵⁴	Days 1, 2, 15, and 16: Leucovorin 400mg/m ² IV followed by 5-FU 400mg/m ² IV push 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 radiation⁵⁵	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 radiation⁵⁶	Days 1–5 OR Days 1–7: Capecitabine 625–825mg/m ² orally twice daily; weekly for 5 weeks.
Postoperative Chemotherapy (for patients who have undergone primary D2 lymph node dissection)	
Capecitabine + oxaliplatin (Category 1)¹³	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.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 3 of 6)

Unresectable Locally Advanced, Recurrent or Metastatic Disease (where local therapy is not indicated)¹

First-line Therapy

REGIMEN	DOSING
Trastuzumab + chemotherapy (NOTE: for HER2-neu overexpressing adenocarcinoma) ¹⁴	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. (Category 1) OR Days 1–5: 5-FU 800mg/m ² continuous IV infusion. (Category 2B) Repeat cycle every 21 days for 6 cycles.

Preferred Regimens

Fluoropyrimidine and cisplatin (5-FU + cisplatin) (Category 1)¹⁵	Day 1: Cisplatin 75–100mg/m ² IV Days 1–4: 5-FU 750–1,000mg/m ² IV continuous infusion over 24 hours daily.
Fluoropyrimidine and cisplatin (5-FU + cisplatin + leucovorin) (Category 1)^{16,17}	Day 1: Cisplatin 50mg/m ² IV + leucovorin 200mg/m ² IV + 5-FU 2,000mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 14 days.
Fluoropyrimidine and cisplatin (capecitabine + cisplatin) (Category 1)¹⁸	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)²⁰	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)^{16,19}	Day 1: Oxaliplatin 85mg/m ² IV + leucovorin 400mg/m ² IV + 5-FU 400mg/m ² IVP Days 1–2: 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 + leucovorin 200mg/m ² IV + 5-FU 2,600mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 14 days.

Other Regimens

Modified DCF (docetaxel + cisplatin + leucovorin + 5-FU)³³	Day 1: Docetaxel 40mg/m ² IV + leucovorin 400mg/m ² IV + 5-FU 400mg/m ² IV Days 1–2: 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)³⁴	Day 1: Docetaxel 50mg/m ² IV + oxaliplatin 85mg/m ² IV Days 1–2: 5-FU 1,200mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 14 days.
Modified DCF (docetaxel + carboplatin + 5-FU) (Category 2B)³⁵	Day 1: Docetaxel 75mg/m ² IV Day 2: Carboplatin AUC 6mg·min/mL IV Days 1–3: 5-FU 1,200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 21 days.
ECF (Category 2B)³⁶	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) (Category 2B)^{4,5}	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.
ECF modifications (epirubicin + cisplatin + capecitabine) (Category 2B)^{4,5}	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.
ECF modifications (epirubicin + oxaliplatin + capecitabine) (Category 2B)^{4,5}	Day 1: Epirubicin 50mg/m ² IV + oxaliplatin 130mg/m ² IV Days 1–21: Capecitabine 625mg/m ² IV orally twice daily. Repeat cycle every 21 days.
Fluorouracil and irinotecan (irinotecan + leucovorin + 5-FU)³²	Day 1: Irinotecan 180mg/m ² IV + leucovorin 400mg/m ² IV + 5-FU 400mg/m ² IV push followed by Day 1–2: 5-FU 1200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 4 of 6)

Unresectable Locally Advanced, Recurrent or Metastatic Disease (where local therapy is not indicated)¹ (continued)

First-line Therapy (continued)

Other Regimens (continued)

REGIMEN	DOSING
Paclitaxel + cisplatin or carboplatin ²¹⁻²³	Day 1: Paclitaxel 135–200mg/m ² IV Day 2: Cisplatin 75mg/m ² IV. Repeat cycle every 21 days. OR Day 1: Paclitaxel 90mg/m ² IV + cisplatin 50mg/m ² IV. Repeat cycle every 14 days. OR Day 1: Paclitaxel 200mg/m ² IV + carboplatin AUC 5mg·min/mL IV. Repeat cycle every 21 days.
Docetaxel + cisplatin ^{24,25}	Day 1: Docetaxel 70–85mg/m ² IV + cisplatin 70–75mg/m ² IV. Repeat cycle every 21 days.
Fluoropyridine ^{17,26,27}	Day 1: Leucovorin 400mg/m ² IV + 5-FU 400mg/m ² IV push Days 1–2: 5-FU 1200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days. OR Days 1–5: 5-FU 800mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 28 days. OR Days 1–14: Capecitabine 1000–1250mg/m ² orally twice daily. Repeat cycle every 21 days.
Taxane ²⁸⁻³¹	Day 1: Docetaxel 75–100mg/m ² IV. Repeat cycle every 21 days. OR Day 1: Paclitaxel 135–250mg/m ² IV. Repeat cycle every 21 days. OR Days 1, 8, 15 and 22: Paclitaxel 80mg/m ² IV once weekly. Repeat cycle every 28 days.

Second-line Therapy and Subsequent Therapy

Preferred Regimens

Ramucirumab (Category 1) ⁴²	Day 1: Ramucirumab 8mg/kg IV. Repeat cycle every 14 days.
Ramucirumab + paclitaxel (Category 1) ³⁷	Day 1 and 15: Ramucirumab 8mg/kg IV Day 1, 8, and 15: Paclitaxel 80mg/m ² . Repeat cycle every 28 days.
Docetaxel (Category 1) ^{28,29}	Day 1: Docetaxel 75–100mg/m ² IV. Repeat cycle every 21 days.
Paclitaxel (Category 1) ^{30,31,38}	Day 1: Paclitaxel 135–250mg/m ² IV. Repeat cycle every 21 days. OR Day 1: Paclitaxel 80mg/m ² IV once weekly. Repeat cycle every 28 days. OR Days 1, 8, and 15: Paclitaxel 80mg/m ² IV. Repeat cycle every 28 days.
Irinotecan (Category 1) ³⁸⁻⁴¹	Day 1: Irinotecan 250–350mg/m ² IV. Repeat cycle every 21 days. OR Day 1: Irinotecan 150–180mg/m ² IV. Repeat cycle every 14 days. OR Days 1 and 8: Irinotecan 125mg/m ² IV. Repeat cycle every 21 days.
5-FU + irinotecan (if not previously used in first-line therapy) ³⁹	Day 1: Irinotecan 180mg/m ² IV + leucovorin 400mg/m ² IV + 5-FU 400mg/m ² IV push followed by Day 1 and 2: 5-FU 1200mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 14 days.

continued

GASTRIC CANCER TREATMENT REGIMENS (Part 5 of 6)

Unresectable Locally Advanced, Recurrent or Metastatic Disease (where local therapy is not indicated)¹ (continued)

Second-line Therapy and Subsequent Therapy (continued)

Other Regimens

REGIMEN	DOSING
Irinotecan + cisplatin ^{19,45}	Days 1 and 8: Irinotecan 65mg/m ² IV + cisplatin 25–30mg/m ² IV. Repeat cycle every 21 days.
Docetaxel + irinotecan (Category 2B) ⁴⁹	Days 1 and 8: Docetaxel 35mg/m ² IV + irinotecan 50mg/m ² IV. Repeat cycle every 21 days.
Pembrolizumab (for second-line or subsequent therapy for MSI-H/dMMR tumors; for third-line or subsequent therapy for PD-L1-positive adenocarcinoma) ⁴⁸	Days 1: Pembrolizumab 200 mg IV. Repeat cycle every 21 days.

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