

Gastric Cancer Treatment Regimens

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.

REGIMEN	DOSING
Preferred Regimens	
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 + capecitabine ⁵⁰	Day 1: Cisplatin 30mg/m ² IV Days 1–5: Capecitabine 800mg/m ² orally twice daily. Repeat cycle weekly for 5 weeks.
Oxaliplatin + capecitabine ⁵¹	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

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► 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 + oxaliplatin ²⁰	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.
Capecitabine ⁵³	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 + leucovorin ⁵⁴	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 radiation ⁵⁵	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 radiation ⁵⁶	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

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

REGIMEN	DOSING
First-line Therapy	
Trastuzumab + chemotherapy (NOTE: for HER2-neu overexpressing adenocarcinoma) ¹⁴	<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:</p> <p>Day 1: Cisplatin 80mg/m² IV, plus</p> <p>Days 1–14: Capecitabine 1000mg/m² orally twice daily. (Category 1)</p> <p>OR</p> <p>Days 1–5: 5-FU 800mg/m² continuous IV infusion. (Category 2B)</p> <p>Repeat cycle every 21 days for 6 cycles.</p>
Preferred Regimens	
Fluoropyrimidine and cisplatin (5-FU + cisplatin) (Category 1) ¹⁵	<p>Day 1: Cisplatin 75–100mg/m² IV</p> <p>Days 1–4: 5-FU 750–1,000mg/m² IV continuous infusion over 24 hours daily.</p>
Fluoropyrimidine and cisplatin (5-FU + cisplatin + leucovorin) (Category 1) ^{16,17}	<p>Day 1: Cisplatin 50mg/m² IV + leucovorin 200mg/m² IV + 5-FU 2,000mg/m² IV continuous infusion over 24 hours.</p> <p>Repeat cycle every 14 days.</p>
Fluoropyrimidine and cisplatin (capecitabine + cisplatin) (Category 1) ¹⁸	<p>Day 1: Cisplatin 80mg/m² IV</p> <p>Day 1–14: Capecitabine 1000mg/m² orally twice daily.</p> <p>Repeat cycle every 3 weeks.</p>
Fluoropyrimidine and oxaliplatin (oxaliplatin + capecitabine) ²⁰	<p>Day 1: Oxaliplatin 130mg/m² IV</p> <p>Days 1–14: Capecitabine 1000mg/m² orally twice daily.</p> <p>Repeat cycle every 21 days.</p>
Fluoropyrimidine and oxaliplatin (oxaliplatin + leucovorin + 5-FU) ^{16,19}	<p>Day 1: Oxaliplatin 85mg/m² IV + leucovorin 400mg/m² IV + 5-FU 400mg/m² IVP</p> <p>Days 1–2: 5-FU 1200mg/m² IV continuous infusion over 24 hours daily.</p> <p>Repeat cycle every 14 days.</p> <p>OR</p> <p>Day 1: Oxaliplatin 85mg/m² IV + leucovorin 200mg/m² IV + 5-FU 2,600mg/m² IV continuous infusion over 24 hours.</p> <p>Repeat cycle every 14 days.</p>
Other Regimens	
Modified DCF (docetaxel + cisplatin + leucovorin + 5-FU) ³³	<p>Day 1: Docetaxel 40mg/m² IV + leucovorin 400mg/m² IV + 5-FU 400mg/m² IV</p> <p>Days 1–2: 5-FU 1000mg/m² IV continuous infusion over 24 hours</p> <p>Day 3: Cisplatin 40mg/m² IV.</p> <p>Repeat cycle every 14 days.</p>
Modified DCF (docetaxel + oxaliplatin + 5-FU) ³⁴	<p>Day 1: Docetaxel 50mg/m² IV + oxaliplatin 85mg/m² IV</p> <p>Days 1–2: 5-FU 1,200mg/m² IV continuous infusion over 24 hours.</p> <p>Repeat cycle every 14 days.</p>
Modified DCF (docetaxel + carboplatin + 5-FU) (Category 2B) ³⁵	<p>Day 1: Docetaxel 75mg/m² IV</p> <p>Day 2: Carboplatin AUC 6mg·min/mL IV</p> <p>Days 1–3: 5-FU 1,200mg/m² IV continuous infusion over 24 hours daily.</p> <p>Repeat cycle every 21 days.</p>
ECF (Category 2B) ³⁶	<p>Day 1: Epirubicin 50mg/m² IV bolus + cisplatin 60mg/m² IV</p> <p>Days 1–21: 5-FU 200mg/m² IV continuous infusion over 24 hours daily.</p> <p>Repeat cycle every 21 days.</p>
ECF modifications (epirubicin + oxaliplatin + 5-FU) (Category 2B) ^{4,5}	<p>Day 1: Epirubicin 50mg/m² IV + oxaliplatin 130mg/m² IV</p> <p>Days 1–21: 5-FU 200mg/m² IV continuous infusion over 24 hours.</p> <p>Repeat cycle every 21 days.</p>
ECF modifications (epirubicin + cisplatin + capecitabine) (Category 2B) ^{4,5}	<p>Day 1: Epirubicin 50mg/m² IV + cisplatin 60mg/m² IV</p> <p>Days 1–21: Capecitabine 625mg/m² orally twice daily.</p> <p>Repeat cycle every 21 days.</p>

continued

Gastric Cancer Treatment Regimens

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

REGIMEN	DOSING
First-line Therapy (continued)	
Other Regimens (continued)	
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.
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.
Fluoropyridimine ^{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.

continued

Gastric Cancer Treatment Regimens

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

REGIMEN	DOSING
Second-line Therapy and Subsequent Therapy (continued)	
Preferred Regimens	
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.
Other Regimens	
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.

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology™. Gastric Cancer. V5.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed March 23, 2018.
2. Ychou M, Boige V, Pignon J-P, et al. Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: an FNCLCC and FFCD multicenter phase III trial. *J Clin Oncol*. 2011;29:1715-1721.
3. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006;355:11-20.
4. Sumpter K, Harper-Wynne C, Cunningham D, et al. Report of two protocol planned interim analyses in a randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric cancer receiving ECF. *Br J Cancer*. 2005;92:1976-1983.
5. Cunningham D, Starling N, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. *N Engl J Med*. 2008;358:36-46.
6. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012;366:2074-2084.
7. Tepper J, Krasna MJ, Niedzwiecki D, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. *J Clin Oncol*. 2008;26:1086-1092.
8. Bedenne L, Michel P, Bouche O, et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. *J Clin Oncol*. 2007;25:1160-1168.
9. Conroy T, Galais MP, Raoul JL, et al. Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomised, phase 2/3 trial. *Lancet Oncol*. 2014;15:305-314.
10. Khushalani NI, Leichman CG, Proulx G, et al. Oxaliplatin in combination with protracted-infusion fluorouracil and radiation: report of a clinical trial for patients with esophageal cancer. *J Clin Oncol*. 2002;20:2844-2850.
11. Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. *J Clin Oncol*. 2006;24:3953-3958.
12. Smalley SR, Benedetti JK, Haller DG, et al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. *J Clin Oncol*. 2012;30:2327-2333.
13. Noh SH, Park SR, Yang HK, et al. Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial. *Lancet Oncol*. 2014;15:1389-1396.
14. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet*. 2010;376:687-697.
15. Lorenzen S, Schuster T, Porschen R, et al. Cetuximab plus cisplatin-5-fluorouracil versus cisplatin-5-fluorouracil alone in first-line metastatic squamous cell carcinoma of the esophagus: a randomized phase II study of the Arbeitsgemeinschaft Internistische Onkologie. *Ann Oncol*. 2009;20:1667-1673.
16. Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastro-oesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. *J Clin Oncol*. 2008;26:1435-1442.
17. Bouche O, Raoul JL, Bonnetain F, et al. Randomized multicenter phase II trial of a biweekly regimen of fluorouracil and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study—FFCD 9803. *J Clin Oncol*. 2004;22:4319-4328.

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References (continued)

18. Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. *Ann Oncol*. 2009;20:666-673.
19. Enzinger PC, Burtness BA, Niedzwiecki D, et al. CALGB 80403 (Alliance)/E1206: A Randomized Phase II Study of Three Chemotherapy Regimens Plus Cetuximab in Metastatic Esophageal and Gastroesophageal Junction Cancers. *J Clin Oncol*. 2016;34:2736-2742.
20. Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. *Eur J Cancer*. 2012;48:518-526.
21. Ilson DH, Forastiere A, Arquette M, et al. A phase II trial of paclitaxel and cisplatin in patients with advanced carcinoma of the esophagus. *Cancer*. J 2000;6:316-323.
22. Petrasch S, Welt A, Reinacher A, et al. Chemotherapy with cisplatin and paclitaxel in patients with locally advanced, recurrent or metastatic oesophageal cancer. *Br J Cancer*. 1998;78:511-514.
23. Gadgeel SM, Shields AF, Heilbrun LK, et al. Phase II study of paclitaxel and carboplatin in patients with advanced gastric cancer. *Am J Clin Oncol*. 2003;26:37-41.
24. Ajani JA, Fodor MB, Tjulandin SA, et al. Phase II multi-institutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. *J Clin Oncol*. 2005;23:5660-5667.
25. Kim JY, Do YR, Park KU, et al. A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer. *Cancer Chemother Pharmacol*. 2010;66:31-36.
26. Ohtsu A, Shimada Y, Shirao K, et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: The Japan Clinical Oncology Group Study (JCOG9205). *J Clin Oncol*. 2003;21:54-59.
27. Hong YS, Song SY, Lee SI, et al. A phase II trial of capecitabine in previously untreated patients with advanced and/or metastatic gastric cancer. *Ann Oncol*. 2004;15:1344-1347.
28. Albertsson M, Johansson B, Friesland S, et al. Phase II studies on docetaxel alone every third week, or weekly in combination with gemcitabine in patients with primary locally advanced, metastatic, or recurrent esophageal cancer. *Med Oncol*. 2007;24:407-412.
29. Ford HE, Marshall A, Bridgewater JA, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet Oncol*. 2014;15:78-86.
30. Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. *J Natl Cancer Inst*. 1994;86:1086-1091.
31. Ilson DH, Wadleigh RG, Leichman LP, Kelsen DP. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. *Ann Oncol*. 2007;18:898-902.
32. Guimbaud R, Louvet C, Ries P, et al. Prospective, randomized, multicenter, phase III study of fluorouracil, leucovorin, and irinotecan versus epirubicin, cisplatin, and capecitabine in advanced gastric adenocarcinoma: A French Intergroup (Fédération Francophone de Cancérologie Digestive, Fédération Nationale des Centres de Lutte Contre le Cancer, and Groupe Coopérateur Multidisciplinaire en Oncologie) Study. *J Clin Oncol*. 2014;32:3520-3526.
33. Shah MA, Janjigian YY, Stoller R, et al. Randomized multicenter phase II study of modified docetaxel, cisplatin, and fluorouracil (DCF) versus DCF plus growth factor support in patients with metastatic gastric adenocarcinoma: a study of the US Gastric Cancer Consortium. *J Clin Oncol*. 2015;33:3874-3879.
34. Shankaran V, Mulcahy MF, Hochster HS, et al. Docetaxel, oxaliplatin, and 5-fluorouracil for the treatment of metastatic or unresectable gastric or gastroesophageal junction (GEJ) adenocarcinomas: Preliminary results of a phase II study. *Gastrointestinal Cancers Symposium 2009:Abstract 47*.
35. Elkerkm YM, Elsaid A, AL-Batran S, Pauligk C. Final results of a phase II trial of docetaxel-carboplatin-FU in locally advanced gastric carcinoma [abstract]. Presented at the 2008 Gastrointestinal Cancers Symposium 2008. Abstract 38.
36. Ross P, Nicolson M, Cunningham D, et al. Prospective randomized trial comparing mitomycin, cisplatin, and protracted venous-infusion fluorouracil (PVI 5-FU) with epirubicin, cisplatin, and PVI 5-FU in advanced esophagogastric cancer. *J Clin Oncol*. 2002;20:1996-2004.
37. Wilke H, Muro K, Van Cutsem E, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastroesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol*. 2014;15:1224-1235.
38. Hironaka S, Ueda S, Yasui H, et al. Randomized, open-label, phase III study comparing irinotecan with paclitaxel in patients with advanced gastric cancer without severe peritoneal metastasis after failure of prior combination chemotherapy using fluoropyrimidine plus platinum: WJOG 4007 trial. *J Clin Oncol*. 2013;31:4438-4444.
39. Sym SJ, Hong J, Park J, et al. A randomized phase II study of biweekly irinotecan monotherapy or a combination of irinotecan plus 5-fluorouracil/leucovorin (mFOLFIRI) in patients with metastatic gastric adenocarcinoma refractory to or progressive after first-line chemotherapy. *Cancer Chemother Pharmacol*. 2013;71:481-488.
40. Thuss-Patience PC, Kretzschmar A, Bichev D, et al. Survival advantage for irinotecan versus best supportive care as second-line chemotherapy in gastric cancer—a randomised phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). *Eur J Cancer*. 2011;47:2306-2314.
41. Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. *J Clin Oncol*. 2003;21:807-814.
42. Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet*. 2014;383:31-39.
43. Sym SJ, Ryu MH, Lee JL, et al. Salvage chemotherapy with biweekly irinotecan, plus 5-fluorouracil and leucovorin in patients with advanced gastric cancer previously treated with fluoropyrimidine, platinum, and taxane. *Am J Clin Oncol*. 2008;31:151-156.
44. Assersohn L, Brown G, Cunningham D, et al. Phase II study of irinotecan and 5-fluorouracil/leucovorin in patients with primary refractory or relapsed advanced oesophageal and gastric carcinoma. *Ann Oncol*. 2004;15:64-69.
45. Ilson DH. Phase II trial of weekly irinotecan/cisplatin in advanced esophageal cancer. *Oncology (Williston Park)*. 2004;18:22-25.
46. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science*. 2017;357:409-413.
47. Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med*. 2015;372:2509-2520.
48. Fuchs CS, Doi T, Jang RW-J, et al. KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer [abstract]. *Journal of Clinical Oncology*. 2017;35:4003-4003.
49. Burtness B, Gibson M, Eggleston B, et al. Phase II trial of docetaxel-irinotecan combination in advanced esophageal cancer. *Ann Oncol*. 2009;20:1242-1248.
50. Lee SS, Kim SB, Park SI, et al. Capecitabine and cisplatin chemotherapy (XP) alone or sequentially combined chemoradiotherapy containing XP regimen in patients with three different settings of stage IV esophageal cancer. *Jpn J Clin Oncol*. 2007;37:829-835.
51. Javle MM, Yang G, Nwogu CE, et al. Capecitabine, oxaliplatin and radiotherapy: a phase IB neoadjuvant study for esophageal cancer with gene expression analysis. *Cancer Invest*. 2009;27:193-200.
52. Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med*. 2001;345:725-730.
53. Jansen EP, Boot H, Saunders MP, et al. A phase I-II study of postoperative capecitabine-based chemoradiotherapy in gastric cancer. *Int J Radiat Oncol Biol Phys*. 2007;69:1424-1428.
54. Andre T, Quinaux E, Louvet C, et al. Phase III study comparing a semimonthly with a monthly regimen of fluorouracil and leucovorin as adjuvant treatment for stage II and III colon cancer patients: final results of GERCOR C96.1. *J Clin Oncol*. 2007;25:3732-3738.
55. Leong T, Joon DL, Willis D, et al. Adjuvant chemoradiation for gastric cancer using epirubicin, cisplatin, and 5-fluorouracil before and after three-dimensional conformal radiotherapy with concurrent infusional 5-fluorouracil: a multicenter study of the Trans-Tasman Radiation Oncology Group. *Int J Radiat Oncol Biol Phys*. 2011;79:690-695.
56. Lee HS, Choi Y, Hur WJ, et al. Pilot study of postoperative adjuvant chemoradiation for advanced gastric cancer: adjuvant 5-FU/cisplatin and chemoradiation with capecitabine. *World J Gastroenterol*. 2006;12:603-607.

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