JAMA | Review

Gastric Cancer
A Review

Anuj Kishor Patel, MD; Nilay S. Sethi, MD, PhD; Haeseong Park, MD, MPH

IMPORTANCE Globally, 968 350 new cases and 659 853 deaths from gastric cancer were reported in 2022. In the US, 30 300 new cases and 10 780 deaths were estimated in 2025.

OBSERVATIONS Gastric cancer is more common in men, and the median age at diagnosis is 68 years. Most gastric cancers (>90%) are adenocarcinomas. Worldwide, 85% of cases arise from the stomach body or antrum and 15% from the cardia. In the US, more than 90% of patients diagnosed with gastric cancer present with symptoms such as weight loss and abdominal pain. At presentation, approximately 13% have localized disease (limited to the stomach), 15% to 25% have locally advanced disease, defined as a tumor that has spread to regional lymph nodes, and 35% to 65% have metastatic disease. *Helicobacter pylori* infection is a treatable risk factor associated with 90% of gastric body and antrum cancers globally. Additional modifiable risk factors include smoking, alcohol, obesity, and salt intake. In countries with high incidence such as Japan and Korea, routine endoscopic screening beginning at age 40 years is associated with improved survival. Diagnosis is made by endoscopic biopsy. Patients with localized gastric cancer are treated with surgical resection and have a 5-year relative survival rate of 75% with treatment. Patients with more advanced-stage disease should receive gastrectomy, perioperative chemotherapy with 5-fluorouracil, oxaliplatin, and docetaxel and immunotherapy (durvalumab). Metastatic or unresectable disease may be treated with chemotherapy, immunotherapy, and/or targeted therapy depending on biomarkers, including programmed cell death ligand 1 (PD-L1), human epidermal growth factor receptor 2 (*ERBB2*; formerly *HER2* or *HER2/neu*), and claudin-18, isoform 2 (CLDN18.2). For PD-L1–expressing gastric cancer, adding immune checkpoint inhibitors, such as nivolumab and pembrolizumab, is associated with an additional 3 months of survival when compared with chemotherapy alone. For gastric cancers overexpressing the ERBB2 or CLDN18.2 proteins, the addition of trastuzumab or zolbetuximab, respectively, is associated with an additional 3 to 4 months' survival. Early supportive care focusing on symptom management and on nutritional and psychosocial support is associated with 3 months of survival benefit. Less than 10% of patients with metastatic gastric cancer survive more than 5 years.

CONCLUSIONS AND RELEVANCE Approximately 30 300 new cases of gastric cancer are diagnosed annually in the US. Localized gastric cancer is treated with gastrectomy, and locally advanced disease is treated with surgery and chemoimmunotherapy. For patients with unresectable or metastatic gastric cancer, chemotherapy with immune checkpoint inhibitors and targeted therapies such as trastuzumab or zolbetuximab improves survival by several months.

JAMA. doi:10.1001/jama.2025.20034
Published online January 7, 2026.

Multimedia

Supplemental content

CME at jamacmelookup.com

Author Affiliations: Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts.

Corresponding Author: Haeseong Park, MD, MPH, Dana-Farber Cancer Institute, Harvard Medical School, 450 Brookline Ave, Boston, MA 02215 (haeseong_park@dfci.harvard.edu).

Gastric cancer is the fifth most diagnosed cancer and the fifth leading cause of cancer-related deaths worldwide. Globally, 968 350 new cases and 659 853 deaths from gastric cancer were reported in 2022.[1] Incidence is higher in East Asia, Eastern Europe, and South America than in North America.[2] In the US, 30 300 new cases and 10 780 deaths are estimated for 2025.[2] Gastric adenocarcinoma comprises more than 90% of gastric cancers[3]; less common histological subtypes include neuroendocrine tumors, gastrointestinal stromal tumors, and lymphoid malignancies.[3] In countries with high incidence rates, endoscopic screening is associated with diagnosis at earlier stages of disease. Endoscopic resection can be curative in 90% of early-stage gastric cancers that only involve the mucosa; if evidence of more advanced disease is found, additional surgical resection may be required.[4] More than 50% of patients with gastric cancer in the US are diagnosed at advanced stages, for which systemic therapy is the predominant treatment modality. Recent advances, including immune checkpoint inhibitors for programmed cell death ligand 1 (PD-L1)–expressing tumors and targeted therapies against human epidermal growth factor receptor 2 (*ERBB2*; formerly *HER2* or *HER2/neu*) have improved survival outcomes by 3 to 4 months.

This review summarizes current evidence regarding the epidemiology, pathophysiology, diagnosis, and management of gastric cancer.

Methods

We performed a PubMed search for articles on epidemiology, risk factors, prevention, symptoms, and molecular subtypes in gastric or stomach cancer published between January 1, 2011, and June 5, 2025. An additional PubMed search was performed for clinical trials studying gastric cancer. Recent clinical guidelines from major organizations, including the American Gastroenterological Association (AGA), National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology, and the European Society for Medical Oncology (ESMO), were also reviewed. Additional articles, including publications prior to 2011, were identified from the references in the guidelines or review articles. We selected articles based on relevance to current practice and generalizability of the results, prioritizing recent randomized trials of higher quality, and included a total of 106 articles, comprising 49 observational studies, 31 randomized clinical trials, 17 systematic reviews or meta-analyses, and 9 guideline recommendations.

Discussion

Epidemiology and Risk Factors

In the US, gastric cancer is diagnosed at a median age of 68 years and is more common in men (8.4 cases per 100 000 per year) than in women (4.8 cases per 100 000 per year).[2] Over the past 4 decades, gastric cancer incidence rates in the US have decreased, and relative survival (weighted average of all disease stages) has increased (5-year relative survival rate for all stages, 15% in 1977 vs 36% in 2020).[2] However, the incidence of gastric cancer in patients younger than 50 years is rising in the US, with age-adjusted incidence rates in females increasing from 1.2 per 100 000 in 2013 to 1.8 in 2022 (average annual percent change [AAPC], 4.0%; 95% CI, 3.5%-4.7%) and in males increasing from 1.5 to 1.6 per 100 000 (AAPC, 1.7%; 95% CI, 0.3%-2.8%).[5] Globally, 85% of gastric cancer cases arise from the body or antrum. In contrast, in North America and Western Europe, gastric cancers located in the cardia or at the gastroesophageal junction comprise 30% to 40% of all gastric cancers. (For frequently asked questions, see the **Box**.)[6]

The most common risk factor for gastric cancer globally is *Helicobacter pylori* infection, which is associated with nearly 90% of cases of noncardia gastric cancer.[7] *H pylori* may cause nonatrophic gastritis, which can progress to atrophic gastritis, intestinal metaplasia, dysplasia, and invasive cancer.[8] *H pylori* infection affects 43.9% of adults and 35.1% of children and adolescents worldwide and is more prevalent in Asian countries.[9] In the US, the prevalence of *H pylori* is lower, affecting 17.6% of adults and 14.2% of children and adolescents.[9] Epstein-Barr virus infection is a less common infectious risk factor, associated with approximately 7.5% of gastric cancers.[10]

A global pooled analysis of 13 331 gastric cancer cases and 31 381 controls from 34 case-control and nested case-control studies identified additional risk factors, including family history of gastric

BOX. Three Questions Commonly Asked About Gastric Cancer

What are common risk factors for gastric cancer?

Approximately 90% of gastric cancers involving the gastric body and antrum are associated with *Helicobacter pylori* infection; treatment of infected individuals reduces the risk of developing gastric cancer. Other modifiable risk factors include tobacco use, heavy alcohol use (4 or more alcoholic drinks daily), high salt diet, and obesity. Approximately 1% to 3% of patients with metastatic gastric cancer have an inherited predisposition due to a germline gene variant.

What is the prognosis of gastric cancer?

Patients with early-stage gastric cancer treated with endoscopic or surgical resection have 5-year relative survival rates of 75%. For patients with locally advanced disease, perioperative chemotherapy improves overall survival by approximately 15 months, with a median survival of 50 months. For patients with unresectable or metastatic gastric cancer, systemic treatment and supportive care is associated with a median survival of 14 to 20 months. Less than 10% of patients with metastatic gastric cancer survive more than 5 years.

Which biomarker tests guide treatment in gastric cancer?

At diagnosis, all patients with gastric cancer should undergo mismatch repair or microsatellite instability testing. Patients with mismatch repair-deficient locally advanced disease should receive neoadjuvant immunotherapy (eg, ipilimumab and nivolumab) instead of chemotherapy before surgery. Patients with locally advanced or unresectable or metastatic gastric cancer should undergo additional biomarker testing, including human epidermal growth factor receptor 2, programmed cell death ligand 1 (PD-L1), and claudin-18 isoform 2 (CLDN18.2). Patients with PD-L1–positive tumors should receive an immune checkpoint inhibitor (eg, nivolumab, pembrolizumab, or tislelizumab) with chemotherapy. Patients with ERBB2-positive tumors benefit from the addition of trastuzumab to first-line chemotherapy with expected median survival of about 20 months. Patients with CLDN18.2-positive but negative ERBB2 tumors should be treated with the monoclonal antibody zolbetuximab in addition to first-line chemotherapy.

cancer, tobacco smoking, reported salty taste preference, obesity, and gastroesophageal reflux disease. In this analysis, 15.8% (942 of 5946) of patients with gastric cancer had a family history compared with 7.7% (979 of 12 776) of controls (odds ratio [OR], 1.84; 95% CI, 1.64-2.04).[11] Patients with gastric cancer were more likely to currently smoke (27.7%, 2783 of 10 290) compared with 24.1% (6178 of 26 145) of controls (pooled OR, 1.25; 95% CI, 1.11-1.40).[12] Heavy alcohol use was associated with an increased risk of gastric cancer; 32.8% to 42.4% of patients with gastric cancer reported 4 or more alcoholic drinks daily, compared with 28.3% to 36.3% of controls (pooled OR, 1.37; 95% CI, 1.19-1.58 compared with those who never drink alcohol).[13,14] Among patients with gastric cancer, 34.6% (1581 of 10 283) reported a salty taste preference compared with 25.5% (1845 of 24 643) of controls (OR, 1.59; 95% CI, 1.25-2.03).[15] This study reported a strong association between a history of gastric ulcer and gastric cancer: 12.6% (487 of 3868) of patients with gastric cancer had a history of gastric ulcer compared with 5% (276 of 6662) of controls (OR, 3.04; 95% CI, 2.07-4.49).[14,16] In a case-control study, 38.5% (75 of 195) of patients with gastric cardia cancer had body mass index (BMI) of 25 or higher (calculated as weight in kilograms divided by height in meters squared) compared with 33.2% (3316 of 10 000) of controls (OR, 1.46; 95% CI, 0.98-2.18).[17] This association was confirmed in a meta-analysis of 24 prospective studies reporting that a BMI greater than 30 was associated with cancers of the cardia or gastroesophageal junction compared with a BMI between 18.5 and 24.9 (OR, 1.82; 95% CI, 1.32-2.49), but not with noncardia cancers.[18]

Approximately 1% to 3% of gastric cancers are associated with an identified genetic predisposition.[19] Germline variants in genes such as *CDH1*, *CTNNA1*, or *PALB2* are associated with an increased risk of hereditary diffuse gastric cancer.[20,21] Other hereditary syndromes, including Lynch syndrome (*MLH1, MSH2, MSH6*, and *PMS2*), juvenile polyposis syndrome (*SMAD4* and *BMPR1A*), Peutz Jeghers syndrome (*STK11*), and familial adenomatous polyposis (*APC*), and hereditary breast and ovarian cancer syndrome (*BRCA1* and *BRCA2*) are also associated with a higher risk of gastric cancer.[22-26]

Prevention

Identification and treatment of *H pylori* reduces the risk of developing gastric cancer.[27-31] A meta-analysis of 10 randomized clinical trials, with 8323 healthy individuals and 1841 patients with gastric cancer, reported that the incidence of gastric cancer was 1.6% in patients infected with *H pylori* who received eradication therapy compared with 3.0% who did not (relative risk [RR], 0.54; 95% CI, 0.40- 0.72).[31] In a 2024 update from a population-based, cluster-randomized trial in China, 102 330 participants with *H pylori* infection were randomized to quadruple anti–*H pylori* treatment (omeprazole, tetracycline, metronidazole, and bismuth citrate) or to symptom alleviation treatment (daily omeprazole and bismuth citrate) and were followed up for 11.8 years. The annual incidence of gastric cancer was 54 cases per 100 000 in participants who had successful eradication of *H pylori* compared with 68 per 100 000 in those treated for symptoms only (hazard ratio [HR], 0.81; 95% CI, 0.69-0.96).[29] Additional gastric cancer prevention strategies may include reducing salt intake, maintaining healthful weight, smoking cessation, decreasing alcohol use, and exercising regularly; however, prospective evidence to support these strategies is lacking.

Screening

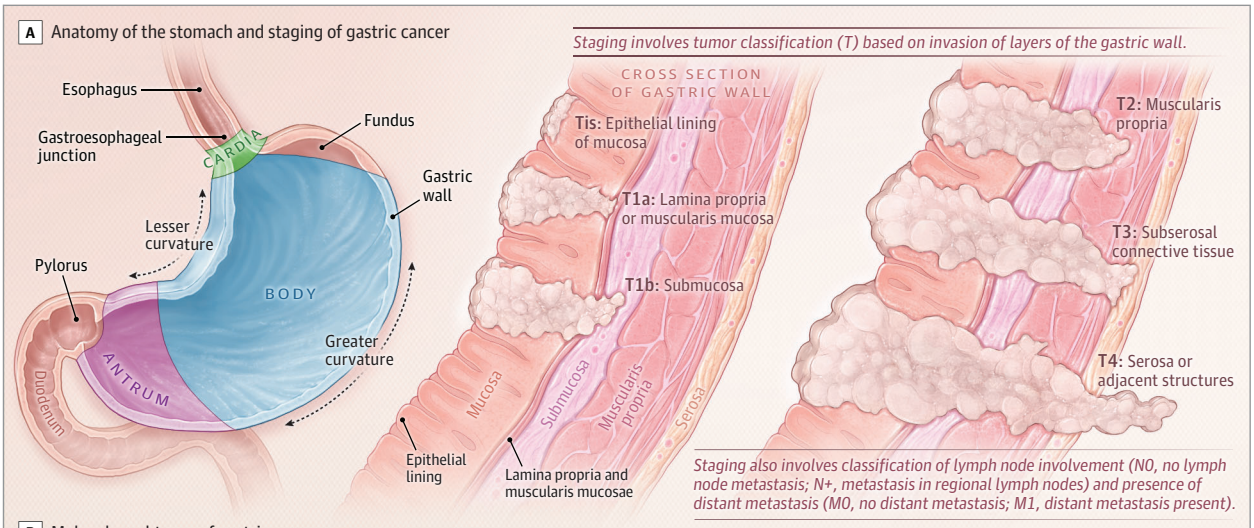
In some countries with high incidence rates of gastric cancer, routine upper endoscopy screenings are performed every 2 years for the general population starting at age 40 years (South Korea) or age 50 years (Japan), with no upper age limit for screening.[32,33] In South Korea, the proportion of eligible adults receiving endoscopic screening increased from 39.4% in 2005 to 77.5% in 2023, and the percentage with localized stage gastric cancer increased from 51.7% in 2005 to 69.8% in 2022.[34] Compared with the years 2001 through 2005, the expected 5-year relative survival rate for gastric cancer in South Korea increased from 58% to 78.4% in the years 2018 through 2022.[34] In a Japanese prospective cohort study of 80 272 participants, annual gastric cancer mortality rates at 13 years of median follow-up were 99 per 100 000 in the unscreened population compared with 45 per 100 000 in the endoscopically screened population (HR for death, 0.39; 95% CI, 0.30-0.51).[35] In the US, given the relatively low incidence of gastric cancer, guidelines do not recommend screening endoscopy for the general population. However, the 2025 AGA expert review recommended screening endoscopy in high-risk populations, such as foreign-born individuals from moderate- to high-incidence regions, including Eastern Europe, Andean Latin America, and East Asia.[36]

Anatomy, Pathophysiology, and Therapeutic Biomarkers

Gastric cancer includes cancers arising from the gastric cardia, body, or antrum. For tumors involving the gastroesophageal junction, the American Joint Committee on Cancer (AJCC) staging system classifies those with a tumor epicenter, defined as the midpoint of the upper and lower tumor borders, located more than 2 cm into the proximal stomach as gastric cancer. Molecularly, gastroesophageal junction adenocarcinomas are similar to gastric cardia cancers.[4]

Gastric cancer has traditionally been classified into major histological subtypes: intestinal (≈ 50%), diffuse (30%), and mixed (20%).[37] Intestinal type indicates tumors with a gland-like structure; diffuse-type cancer, also classified as poorly cohesive carcinoma, tends to have a more cellular appearance with intracellular mucin. However, molecular subtypes derived from genomic profiling may better reflect the molecular pathophysiological features of tumors than histological appearance or anatomical location (**Figure 1**).[38] Four molecular subtypes have been defined: chromosomal instability, microsatellite instability, Epstein-Barr virus positive, and genome stable.[39] The chromosomal instability subtype, comprising 50% of all gastric cancer and 80% of gastroesophageal junction and cardia tumors, is characterized by the tumor suppressor *TP53* gene variation and extensive copy number alterations including amplification of oncogenes such as epidermal growth factor receptor (*EGFR*), *ERBB2*, fibroblast growth factor receptor 2 (*FGFR2*), and Kirsten rat sarcoma virus (*KRAS*).[39-41] The microsatellite instability subtype (20%) involves defects in DNA mismatch repair, resulting in a high tumor mutational burden phenotype.[39,40] Gastric cancer positive for Epstein-Barr virus, the least common subtype (≤10%), harbors more frequent genetic variants in phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (*PIK3CA*) and has prominent immune cell infiltration on histology.[39,40] Microsatellite instability and Epstein-Barr virus–positive subtypes are associated with better responses to immune checkpoint inhibitor therapy.[42] Genome-stable subtype tumors (4%-20%) are typically associated with diffuse-type histology.

Figure 1. Clinical and Pathophysiologic Features of Gastric Cancer



B Molecular subtypes of gastric cancer

	Chromosomal instability	Microsatellite instability	Epstein-Barr virus positive	Genome stable
Genomic features and biomarkers	• Genetic variants of tumor suppressor *TP53* • Focal amplifications of oncogenes (eg, *EGFR*, *ERBB2*, *FGFR2*)	• Defects in DNA mismatch repair genes • Loss of *MLH1*, *MSH2*, *MSH6*, *PMS2*; high TMB	• Genetic variants of *PIK3CA* • High CLDN18.2 expression	• Genetic variants of *CDH1* and *RHOA* • High CLDN18.2 expression
Percentage of gastric cancer cases (by all cases and by cases in each anatomical region)	All gastric cancer: **≈50%**	**≈20%**	**≤10%**	**≈20%**
	Cardia: **≈80%**	**≈10%**	**≈5%**	**<5%**
	Body: **≈50%**	**≈25%,**	**≈15%**	**≈10%**
	Antrum: **≈50%**	**≈25%**	**<5%**	**≈20%**
Characteristic findings	• Intestinal-type adenocarcinoma histology • Median age at diagnosis, ≈65 y • Slight male predominance • Liver metastasis most common; peritoneal spread less frequent	• Intestinal or medullary variant histology; dense lymphocytic infiltration • Median age at diagnosis, ≈65 y • No predominance based on sex • Lower likelihood of distant metastasis	• Lymphoepithelioma-like histology, prominent immune cell infiltration • Median age at diagnosis, ≈65 y • Strong male predominance • Lower likelihood of distant metastasis	• Diffuse-type histology; signet-ring cells are common • Median age at diagnosis, ≈53 y • Female predominance • Early lymphatic metastasis; frequent peritoneal carcinomatosis
Clinical implications	• Targeted therapies available if actionable genetic alterations present (eg, *ERBB2*) • Prognosis depends on actionable amplifications	• Better response to immune checkpoint inhibitor therapy • Better prognosis after resection	• Better response to immune checkpoint inhibitor therapy • Better prognosis after resection	• Poor prognosis due to signet-ring cell histology and peritoneal spread

CDH1 indicates cadherin 1; CLDN18.2, claudin-18 isoform 2; *EGFR*, epidermal growth factor receptor; *ERBB2*, human epidermal growth factor receptor 2 (formerly *HER2* or *HER2/neu*); *FGFR2*, fibroblast growth factor receptor 2; *PIK3CA*, phosphati-dylinosito-4.5, bisphosphate 3-kinase catalytic subunit alpha; *RHOA*, Ras homolog family member A.

The Epstein-Barr virus–positive and genome-stable subtypes are both associated with high levels of claudin-18 isoform 2 (CLDN18.2) protein expression, another therapeutic target.[39,40]

Based on gastric cancer molecular subtypes, biomarkers used to guide treatment decisions include microsatellite instability or mismatch repair deficiency, PD-L1, ERBB2, and CLDN18.2. PD-L1, a protein that regulates the immune system, is reported as a combined positive score indicating the proportion of PD-L1–expressing tumor cells and immune cells. ERBB2 is a protein on the surface of cells that plays a role in gastric cancer cell growth and division. CLDN18.2 is a protein in the tight junctions of normal gastric mucosa that becomes more exposed to the mucosal surface during malignant transformation.

Clinical Presentation and Diagnosis

In the US, most patients with gastric cancer are symptomatic at diagnosis. In a single-center, retrospective study of 263 patients diagnosed with gastric cancer, only 3% were asymptomatic.[43] A retrospective review of 18 365 cases reported that the most common symptoms were weight loss (62%), abdominal pain (52%), nausea (34%), anorexia (32%), and dysphagia (26%).[44] In a single-site, retrospective study of 126 Canadian patients with gastric cancer, 40% had iron deficiency anemia at diagnosis.[45]

The diagnosis of gastric cancer is made with upper endoscopy and biopsy of gastric tissue. For patients with new-onset dyspepsia, the American Society for Gastrointestinal Endoscopy recommends upper endoscopy at age 50 years or older, and the AGA

Table 1. Overview of Treatment and Prognosis by Stage of Gastric Cancer in the US

Clinical stage	Localized	Locally advanced	Metastatic
Proportion of new cases in the US, %[50]	13-29	15-25	36-65
American Joint Committee on Cancer tumor, node, and metastasis staging	Stage I T1a (tumor invades the lamina propria or muscularis mucosae) T1b (tumor invades the submucosa) T2 (tumor invades the muscularis propria) and N0 (no regional lymph nodes), M0 (no distant metastasis)	Stage II and III T1 or 2 and N+ (metastasis in regional lymph nodes) T3 (tumor penetrates the subserosal connective tissue) T4 (tumor invades the serosa or adjacent structures) and any N M0	Stage IV Any T, any N M1 (distant metastasis)
Treatment intent	Curative	Curative	Palliative, prolonged survival
Treatment	Endoscopic procedures or surgery	Perioperative systemic therapy with surgery if resectable[a]	Systemic therapy
5-y relative survival, %[b]	75	35	<10

[a] Patients with unresectable disease are treated similarly with those with metastatic disease.

[b] Weighted average of all disease stages.

recommendation is at age 55 years or older.[46,47] These guidelines, based on expert opinion, also recommend endoscopy for individuals of any age with dyspepsia who present with concurrent alarm signs or symptoms such as dysphagia, unexplained weight loss, melena, hematochezia, or unexplained iron-deficiency anemia.[48] For patients with metastatic lesions identified at presentation, biopsy of a metastatic site confirms disease stage and provides additional tissue for testing. The NCCN recommends evaluation of either mismatch repair deficiency (assessed by immunohistochemistry) or microsatellite instability status (assessed by genomic sequencing) from the tissue obtained for all patients with newly diagnosed gastric cancer. Patients with known or suspected advanced disease should also have tumor testing for PD-L1, ERBB2, and CLDN18.2.

Staging and Prognosis

The AJCC TNM staging system is the most commonly used classification for gastric cancer to determine prognosis and treatment[49] (**Table 1**).[50] Stage I gastric cancer is localized to the stomach and has a 5-year relative survival of 75% with treatment. Locally advanced stages (stages II or III) include cancer that is localized but invading deeper layers of the stomach wall or involving regional lymph nodes. Median 5-year overall survival with perioperative treatment and surgery is 45%.[51] Metastatic stage IV gastric cancer most commonly involves the liver (26%-48%), peritoneum (32%-46%), and distant lymph nodes (11%-20%)[52,53] and has a 5-year survival rate of less than 10%.

To determine stage, all patients with gastric cancer should undergo computed tomography (CT) of the chest, abdomen, and pelvis. If metastatic disease is not detected on CT, additional studies should be obtained to determine eligibility for potentially curative resection. Endoscopic ultrasound is used to assess T and N stages and is recommended by both the NCCN and ESMO prior to surgical evaluation.[54,55] In a network meta-analysis of 12 observational studies reporting the accuracy of endoscopic ultrasound and CT in 2047 patients with gastric cancer, endoscopic ultrasound had higher sensitivity for detecting T1 tumors than CT (71% vs 52%, $P = .04$), although with similar specificity (93% vs 94%, $P = .52$); endoscopic ultrasound was more sensitive for distinguishing node-negative from node-positive disease (79% vs 73%, $P = .02$) but less specific than CT (64% vs 68%, $P = .02$).[56]

In addition to endoscopic ultrasound, positron emission tomography (PET)/CT should be obtained for patients without evidence of distant metastasis on CT to confirm eligibility for surgery. Fluorodeoxyglucose (FDG)-PET/CT is more sensitive (≤74%) than CT (47%-59%) for detecting distant metastases.[57] In a prospective study of 113 patients, PET/CT identified metastases in an additional 10% of patients staged as locally advanced by CT and endoscopic ultrasound.[58]

Sensitivity for detecting peritoneal metastases is limited with both CT (25%-50%) and FDG-PET (7%) compared with laparoscopy (>80%).[59-61] Patients being evaluated for curative surgery should undergo diagnostic laparoscopy prior to surgery; laparoscopic evaluation should include peritoneal lavage because positive cytology from lavage indicates distant metastasis even in the absence of visible peritoneal lesions.[57] A multicenter prospective cohort study of 394 patients with potentially resectable disease, as determined by CT, reported that 18% had metastatic disease detected by laparoscopy.[60]

Treatment

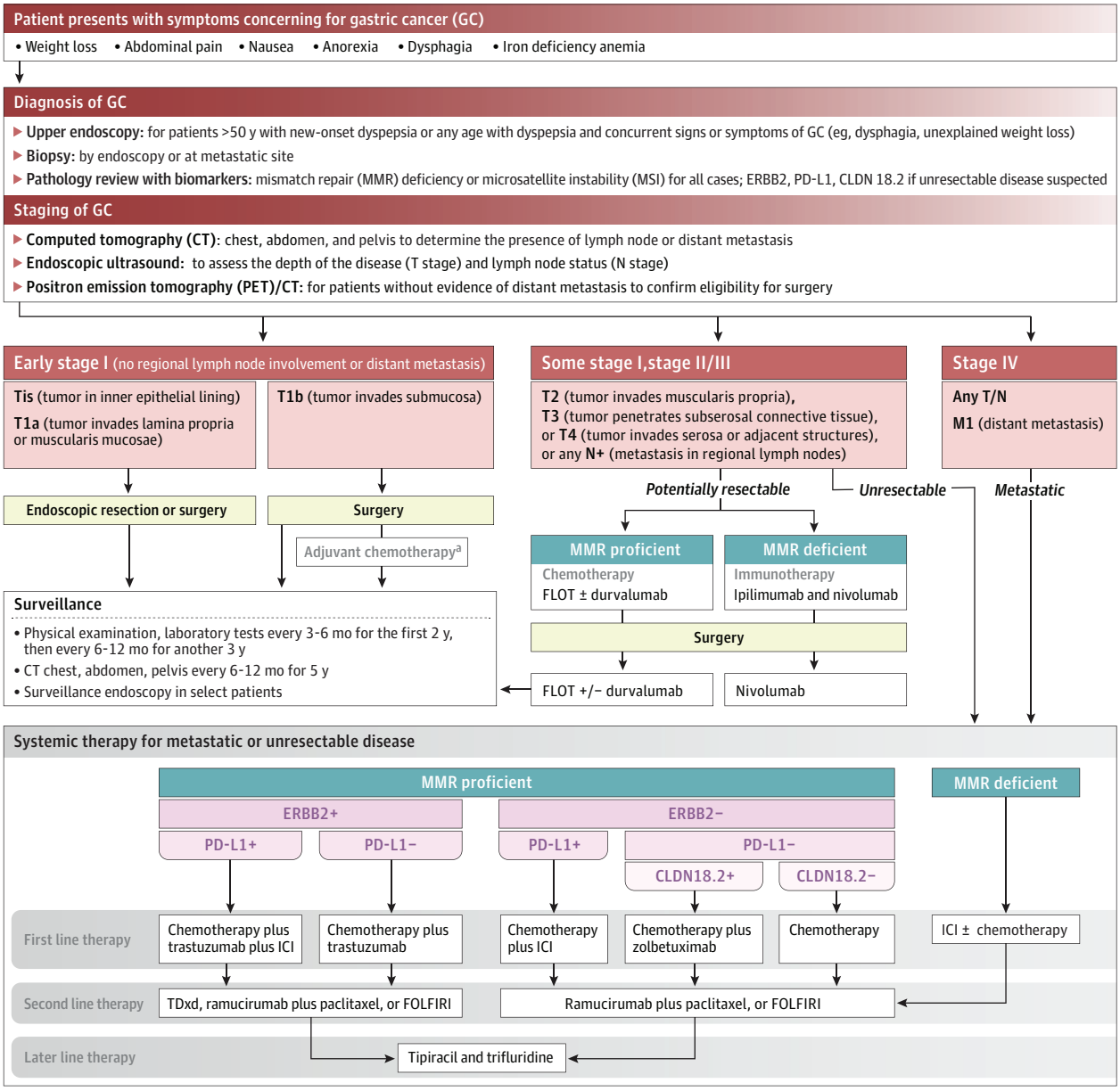
Resectable Gastric Cancer

Patients with localized disease—clinical T1a (cT1a) or cT1b—as determined by staging evaluation, including endoscopic ultrasound, should be treated with gastrectomy without neoadjuvant therapy (**Figure 2**). Endoscopic resection is reserved for patients with intestinal type cT1a disease, in which the tumor invasion is limited to the lamina propria or muscularis mucosae. After endoscopic resection, patients determined to have a higher pathological T stage (≥T2) or adverse features, such as poorly differentiated or diffuse type histology, evidence of lymphovascular invasion, or positive resection margins, should undergo gastrectomy.[4,62] NCCN guidelines recommend gastrectomy with D2 lymphadenectomy, which involves dissection of all lymph nodes along the left gastric, common hepatic, celiac, and splenic arteries.[63] Patients with pathological stage II or III disease after gastrectomy may benefit from adjuvant chemotherapy with fluoropyrimidine and oxaliplatin.[64]

Perioperative Therapy and Surgery

For patients with more advanced but potentially resectable gastric cancer (≥cT2, invading muscularis propria and beyond, and/or ≥N),

Figure 2. Overview of Diagnosis and Management of Gastric Cancer



[a]Adjuvant chemotherapy should be considered for patients who are considered candidates for upfront surgery (eg, initially thought to have early stage I disease) but are found to have pathological stage II or III disease after resection.

CLDN18.2 indicates claudin-18 isoform 2; EGFR, epidermal growth factor receptor; ERBB2, human epidermal growth factor receptor 2 (formerly HER2 or HER2/neu); FLOT, fluorouracil, leucovorin, oxaliplatin, and doxetaxel; FOLFIRI, fluorouracil, leucovorin, and oxaliplatin (FOLFOX)/fluorouracil, leucovorin, and irinotecan; ICI, immune checkpoint inhibitor; PD-L1, programmed cell death ligand 1; TDxd, trastuzumab deruxtecan.

sequential treatment with neoadjuvant chemotherapy and curative-intent surgery, followed by postoperative chemotherapy, is recommended. The FLOT4 trial[51] randomized 716 patients with advanced, potentially resectable gastric cancer to perioperative fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT, 4 cycles before and 4 cycles after surgery) or epirubicin, cisplatin, and capecitabine. Patients treated with perioperative FLOT had improved overall survival compared with the control group (median overall survival, 50 vs 35 months; HR, 0.77; 95% CI, 0.63-0.94), establishing it as the current NCCN-recommended standard perioperative chemotherapy regimen for patients with locally advanced gastric cancer. The most frequent adverse effects of the FLOT regimen were neutropenia (75%), peripheral neuropathy (71%), diarrhea (62%), and infections (35%).[51] For patients unable to tolerate the FLOT regimen, NCCN guidelines recommend using fluorouracil, leucovorin, and oxaliplatin, and omitting docetaxel.[54]

In June 2025, a phase 3 trial of 948 patients with advanced, potentially resectable gastric cancer reported a higher 2-year event-free survival of 67.4% in patients receiving durvalumab, an immune checkpoint inhibitor and monoclonal antibody against PD-L1,

plus FLOT compared with 58.5% in those receiving FLOT alone (HR, 0.71; 95% CI, 0.58-0.86).[65] The US Food and Drug Administration has granted a breakthrough therapy designation to durvalumab with FLOT to treat gastric cancer.[65]

Combined chemoradiation is not routinely recommended for patients with advanced but resectable gastric cancer. A trial that included 574 patients with gastric or gastroesophageal junction cancers reported that median survival was 46 months for those randomized to chemoradiation plus perioperative chemotherapy and 49 months for those randomized to perioperative chemotherapy only (overall survival HR, 1.05; 95% CI, 0.83-1.31).[66] However, based on studies performed in patients with esophageal cancer,[67] preoperative chemoradiation with carboplatin and paclitaxel may be considered for patients with gastroesophageal junction cancers who are not candidates for intensive perioperative chemotherapy with FLOT due to medical comorbidity.

Neoadjuvant Immunotherapy

Neoadjuvant immunotherapy is recommended for patients whose tumor has a mismatch repair-deficient or microsatellite instability–high phenotype, found in 4% to 20% of gastric cancers.[68-72] A single-group phase 2 trial of 29 patients with resectable mismatch repair-deficient or microsatellite instability–high gastric and gastroesophageal junction adenocarcinoma reported that 17 of 29 patients (58.6%) who had undergone surgery after preoperative immunotherapy with ipilimumab and nivolumab achieved a pathologically complete response, which was higher than the expected response to perioperative treatment with FLOT (16%).[73] Analyses of patients with microsatellite instability–high gastric cancer revealed that those who received perioperative chemotherapy had shorter survival time compared with those undergoing upfront surgery.[74] Based on these findings, the NCCN guidelines recommend surgery or neoadjuvant immunotherapy for patients with locally advanced mismatch repair–deficient or microsatellite instability–high gastric cancer, although randomized trials evaluating survival benefit have not been performed in this population.[54]

Systemic Therapy for Unresectable or Metastatic Gastric Cancer

First-Line Treatments | The goal of systemic therapy in patients with unresectable or metastatic gastric cancer is to prolong survival. First-line treatment involves combination chemotherapy with a fluoropyrimidine and platinum agent.[54,75] Targeted agents or immunotherapy can be added to chemotherapy based on the expression of biomarkers, including ERBB2, PD-L1, and CLDN18.2 (Figure 2). Median overall survival with these newer regimens ranges from 14 to 20 months, whereas in the comparison groups, it ranges from 11 to 16 months in the clinical trials discussed below (**Table 2**).[51,65,73,76-87]

Approximately 15% to 25% of gastric cancers have ERBB2 overexpression or amplification.[88,89] Patients with ERBB2-positive gastric cancer benefit from the addition of trastuzumab, a monoclonal antibody targeting ERBB2, to first-line chemotherapy. A trial of 594 patients with untreated, metastatic, ERBB2-positive gastric cancer reported an overall survival benefit for chemotherapy and trastuzumab compared with chemotherapy alone (median overall survival, 13.8 vs 11.1 months; HR, 0.74; 95% CI, 0.60-0.91; $P = .005$).[76] For patients with ERBB2-positive tumors also expressing PD-L1, the immune checkpoint inhibitor pembrolizumab should be added to first-line chemotherapy plus trastuzumab based on a phase 3 trial demonstrating improvements in survival with the addition of pembrolizumab vs placebo with a median overall survival in PD-L1 (combined positive score, ≥1; 20.1 vs 15.7 months; HR, 0.79; 95% CI, 0.66-0.95).[77,78]

First-line treatment for patients with ERBB2-negative gastric cancer with PD-L1 expression should include an immune checkpoint inhibitor (pembrolizumab, nivolumab, tislelizumab) in combination with fluoropyrimidine and platinum chemotherapy. A trial that randomized patients with ERBB2-negative gastric cancer to nivolumab plus fluoropyrimidine and platinum chemotherapy (n = 789) or chemotherapy alone (n = 792) reported higher median overall survival among patients with PD-L1 expression (combined positive score, ≥5) with nivolumab plus chemotherapy vs chemotherapy alone (14.4 months vs 11.1 months; HR, 0.71; 98% CI, 0.59-0.86).[79] Similar results were reported with pembrolizumab or tislelizumab.[81,90] Up to 14% of patients treated with immune checkpoint inhibitors had immune-related adverse events, including thyroid dysfunction, pneumonitis, and colitis.[79,81,90]

Zolbetuximab, a monoclonal antibody targeting CLDN18.2, can be added to first-line chemotherapy (fluoropyrimidine and platinum agent) if the tumor expresses CLDN18.2, based on 2 phase 3 clinical trials.[82,84] In a combined analysis of the 2 trials, including 1072 patients with advanced CLDN18.2-positive gastric cancer, median overall survival with zolbetuximab plus chemotherapy was 16.4 months vs 13.7 months with placebo plus chemotherapy (HR for death, 0.77; 95% CI, 0.67-0.89).[83] Vomiting was reported in 66.8% of patients receiving zolbetuximab.

Second-Line Treatments | Trastuzumab deruxtecan, an antibody-drug conjugate that delivers a cytotoxic topoisomerase I inhibitor to ERBB2-expressing tumor cells, is a second-line treatment option for patients with ERBB2-positive gastric cancer after progression with first-line therapy. A randomized phase 2 trial of 188 patients reported a median overall survival of 12.5 months with trastuzumab deruxtecan compared with 8.4 months with standard chemotherapy (HR for death, 0.59; 95% CI, 0.39-0.88).[86] Ten percent of patients treated with trastuzumab deruxtecan developed drug-related interstitial pneumonitis, which was typically mild and reversible; one patient experienced life-threatening, but not fatal, pneumonitis.

Second-line or later-line therapy can improve survival in select patients who can tolerate additional therapy. Most patients will receive chemotherapy with paclitaxel in combination with ramucirumab, a vascular endothelial growth factor receptor 2 (VEGFR-2)–targeted monoclonal antibody. A phase 3 trial of paclitaxel plus ramucirumab vs placebo in 665 patients with gastric cancer that had progressed with first-line chemotherapy reported median overall survival of 9.6 vs 7.4 months; HR for death, 0.81; 95% CI, 0.68-0.96).[85] Treatment with paclitaxel and ramucirumab was also associated with a longer time to worsening performance status of 5.7 months compared with 4.3 months in the placebo group (HR for deterioration by ≥1 performance status level, 0.802; log-rank $P = .04$).[91] In addition, quality-of-life outcomes, including emotional functioning, nausea, vomiting, and appetite loss, were either comparable or better in patients treated with paclitaxel and ramucirumab compared with paclitaxel alone.[91] Alternative later-line treatments for metastatic gastric cancer include irinotecan-based

Table 2. Summary of Selected Clinical Trials of Systemic Therapy for Gastric Cancer

Trial	Setting of therapy and biomarkers	Study regimen	Control or comparator group	Randomized patients, No. (treatment group vs control)	Primary end points and results	Common grade 3 and 4 adverse events reported in study group, % of patients
FLOT4,[51] 2019	Perioperative (no biomarkers)	FLOT	Epirubicin, cisplatin, fluorouracil	716 (356 vs 360)	Overall survival: 50 mo vs 35 mo	Neutropenia, 51; leukopenia, 27; infections, 18; diarrhea, 10; peripheral neuropathy, 7
MATTERHORN,[65] 2025	Perioperative (no biomarkers)	FLOT and durvalumab	FLOT	948 (474 vs 474)	2-y Event-free survival: 67.4% vs 58.5%	Neutropenia, 21; diarrhea, 6; leukopenia, 5; anemia, 5
NEONIPIGA,[73] 2023	Perioperative (mismatch repair deficient/microsatellite instability-high)	Ipilimumab + nivolumab, then adjuvant nivolumab	Nonrandomized	32	Pathological complete response: 58.6%	Colitis, 6; hepatitis, 6
ToGA,[76] 2010	First-line for metastatic disease (ERBB2)	FP + cisplatin + trastuzumab	FP + cisplatin	594 (298 vs 296)	Overall survival: 13.8 mo vs 11.1 mo	Neutropenia, 30; anemia, 10; vomiting, 8
KEYNOTE-811,[77,78] 2023, 2024	First-line for metastatic disease (ERBB2 and PD-L1)	FP + platinum + trastuzumab + pembrolizumab	FP + platinum + trastuzumab	698 (350 vs 348)	Progression-free survival: 10.0 mo vs 8.1 mo, all patients; Overall survival: 20.6 vs 16.8 mo, all patients	Neutropenia, 9; diarrhea, 8; thrombocytopenia, 7
CheckMate 649,[79,80] 2021, 2024	First-line for metastatic disease (PD-L1)	FP + oxaliplatin + nivolumab	FP + oxaliplatin	1581 (789 vs 792)	Overall survival in CPS ≥5: 14.4 mo vs 11.1 mo Progression-free survival in CPS ≥5: 7.7 mo vs 6.1 mo	Neutropenia, 11; anemia, 6
KEYNOTE-859,[81] 2023	First-line for metastatic disease (PD-L1)	FP + platinum + pembrolizumab	FP + platinum	1579 (789 vs 790)	Overall survival: 12.9 mo vs 11.5 mo	Neutropenia, 8; anemia, 8
SPOTLIGHT,[82,83] 2023, 2024	First-line for metastatic disease (CLDN18.2)	mFOLFOX6 + zolbetuximab	mFOLFOX6	565 (283 vs 282)	Overall survival: 18.2 mo vs 15.5 mo; Progression-free survival: 8.2 mo vs 6.8 mo	Neutropenia, 18; vomiting, 14; nausea, 13; anemia, 10; decreased appetite, 6
GLOW,[83,84] 2023, 2024	First-line for metastatic disease (CLDN18.2)	CAPOX + zolbetuximab	CAPOX	507 (254. vs 253)		
RAINBOW,[85] 2014	Second-line for metastatic disease (no biomarkers)	Ramucirumab + paclitaxel	Paclitaxel	665 (330 vs 335)	Overall survival: 9.6 mo vs 7.4 mo	Neutropenia, 41; leukopenia, 18; hypertension, 14; fatigue, 12; neuropathy, 8
DESTINY-GastricO1,[86] 2020	Second- or third-line for metastatic disease (ERBB2)	Trastuzumab deruxtecan	Chemotherapy (clinician's choice)	187 (125 vs 62)	Overall survival: 12.5 mo vs 8.4 mo	Neutropenia, 51; anemia, 38; leukopenia, 21; thrombocytopenia, 12; decreased appetite, 17
TAGS,[87] 2018	Third-line for metastatic disease (no biomarkers)	Trifluridine and tipiracil	Placebo	507 (337 vs 170)	Overall survival: 5.7 mo vs 3.6 mo	Neutropenia, 34; anemia, 19; leukopenia, 9; decreased appetite, 8; fatigue, 7

Abbreviations: CAPOX, capecitabine and oxaliplatin; CLDN18.2, claudin-18 isoform 2; CPS, combined positive score; ERBB2, human epidermal growth factor receptor 2; FLOT, fluorouracil, leucovorin, oxaliplatin, and docetaxel; FP, flouropyrimidine; mFOLFOX, modified fluorouracil, leucovorin, and oxaliplatin; PD-L1, programmed cell death ligand 1.

chemotherapy, docetaxel or paclitaxel, trifluridine and tipiracil, and ramucirumab alone; however, the expected overall survival benefit with these treatments is typically less than 2 months when compared with best supportive care.[92-96]

Novel Therapeutics for Gastric Cancer

Many novel targeted therapies for gastric cancer are in development (eTable in the Supplement). Zanidatamab, an antibody that targets 2 regions of the ERBB2 receptor, is being studied in combination with chemotherapy and immune checkpoint inhibitors. Phase 3 trials of bemarituzumab, an *FGFR2* isoform IIIb (FGFR2b)–targeted monoclonal antibody, in combination with first-line chemotherapy, are ongoing. There are multiple trials studying novel approaches targeting CLDN18.2, such as chimeric antigen receptor (CAR) T-cell and T-cell engager therapies. Novel immunotherapy targets such as TIGIT (T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain), an immune checkpoint molecule expressed on T cells, and CD73, an immunoinhibitory protein, are under investigation.

Survivorship and Supportive Care After Treatment for Gastric Cancer

Surveillance after curative treatment for gastric cancer includes physical examination and laboratory tests, such as blood counts and chemistry profiles, every 3 to 6 months for the first 2 years, then every 6 to 12 months for another 3 years, as recommended by NCCN guidelines. CT chest, abdomen, and pelvis scans with oral and intravenous contrast are recommended every 6 months for the first 2 years and then annually for another 3 years. Surveillance endoscopies are recommended every 6 months for 1 year, then annually for up to 5 years for patients with gastric cancer who had undergone endoscopic resection.

During and after treatment for gastric cancer, patients commonly experience several cancer or treatment-related symptoms. For patients with malnutrition or weight loss during the recovery from gastrectomy, enteral nutrition is preferred over parenteral nutrition.[97,98] In a retrospective study of 837 patients who had undergone curative gastrectomy, approximately 30% required a jejunostomy feeding tube. The risk of surgical site or intra-abdominal infections was higher among those who had a jejunostomy feeding tube placed (36%) than among those without (19%; $P < .001$).[99]

In addition to experiencing prolonged systemic adverse effects, such as fatigue and chemotherapy-induced neuropathy, survivors of gastric cancer may develop nutritional deficiencies after gastrectomy, such as vitamin B_{12} deficiency (64%) and iron deficiency (50%); therefore, the NCCN recommends monitoring B_{12} levels at least every 6 months with complete blood count and evaluation of iron deficiency at least annually after gastrectomy.[100,101] An observational study of 133 179 survivors of gastric cancer reported an increased risk of osteoporosis (5.85 cases per 1000 person-years) compared with 3.69 cases in matched controls (HR, 1.61; 95% CI, 1.53-1.70).[102]

Osteoporosis risk may be associated with vitamin D deficiency, which was reported in 29% to 89% of patients in a systematic review of 18 studies with 908 postgastrectomy gastric cancer survivors.[102,103] Indigestion or early satiety related to delayed gastric emptying (14%-38%), and dumping syndrome (20%-50%) are also common after gastrectomy.[104,105]

Supportive care should be incorporated early in the management of gastric cancer, with a focus on symptom management, nutritional support, psychosocial support, and palliative care for unresectable or metastatic gastric cancer. A phase 3 trial of 328 patients with metastatic esophagogastric cancer reported improved survival with early interdisciplinary supportive care, including regular nutritional and psychological assessment initiated before the start of chemotherapy, compared with standard oncological care alone (median overall survival, 14.8 vs 11.9 months; HR, 0.68; 95% CI, 0.51-0.9; $P = .02$).[106]

Limitations

This review has several limitations. First, the quality of the evidence was not formally analyzed. Second, articles were selected based on their relevance to current practice, and therefore may reflect publication bias. Third, some relevant studies may have been missed.

Conclusions

Approximately 30 300 new cases of gastric cancer are diagnosed annually in the US. Localized gastric cancer is treated with gastrectomy, and locally advanced disease is treated with surgery, immunotherapy, and chemotherapy. For patients with unresectable or metastatic gastric cancer, use of immune checkpoint inhibitors and targeted therapies, such as trastuzumab or zolbetuximab, and integration of supportive care, improves survival by several months. However, 5-year survival with metastatic gastric cancer is less than 10%.

ARTICLE INFORMATION

Accepted for Publication: October 1, 2025.

Published Online: January 7, 2026. doi:10.1001/jama.2025.20034

Conflict of Interest Disclosures: Dr Sethi reported receiving grants from Novartis, personal fees from Astrin Biosciences, and nonfinancial support from Dewpoint Therapeutics outside the submitted work and having patent US20240280561A1 pending. Dr Park reported receiving grants to her institution from Mirati Therapeutics/Bristol Myers Squibb, Exelixis, AstraZeneca, Tizona, Mersana, Bolt Biotherapeutics, StrataPATH, Chugai, Huaota, D3Bio, Amgen, Idience, Incyte, Pfizer, Alterome, and Yuhan; consultancy fees from Merck; honoraria from Medscape; meeting support from Amgen and Daiichi Sankyo; and advisory board fees from Astellas and Daiichi Sankyo outside the submitted work. No other disclosures were reported.

Additional Contributions: We thank Jennifer Thalappillil, PhD (Dana-Farber Cancer Institute), for assistance with manuscript editing and figures. Dr Thalappillil's role is supported by departmental funding. She did not receive additional compensation specifically for this project.

Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Kristin Walter, MD, at kristin.walter@jamanetwork.org.

REFERENCES

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229-263. doi:10.3322/caac.21834

2. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10-45. doi:10.3322/caac.21871

3. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. *Cancer Epidemiol Biomarkers Prev*.

2014;23(5):700-713. doi:10.1158/1055-9965.EPI-13-1057

4. Ahn JY, Jung HY, Choi KD, et al. Endoscopic and oncologic outcomes after endoscopic resection for early gastric cancer: 1370 cases of absolute and extended indications. *Gastrointest Endosc*. 2011;74(3):485-493. doi:10.1016/j.gie.2011.04.038

5. Jayakrishnan T, Ng K. Early-onset gastrointestinal cancers: a review. *JAMA*. 2025;334(15):1373-1385. doi:10.1001/jama.2025.10218

6. Arnold M, Ferlay J, van Berge Henegouwen MI, Soerjomataram I. Global burden of oesophageal and gastric cancer by histology and subsite in 2018. *Gut*. 2020;69(9):1564-1571. doi:10.1136/gutjnl-2020-321600

7. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*. 2020;8(2):e180-e190. doi:10.1016/S2214-109X(19)30488-7

8. Uemura N, Okamoto S, Yamamoto S, et al. *Helicobacter pylori* infection and the development of gastric cancer. *N Engl J Med*. 2001;345(11):784-789. doi:10.1056/NEJMoa001999

9. Chen YC, Malfertheiner P, Yu HT, et al. Global prevalence of *Helicobacter pylori* infection and incidence of gastric cancer between 1980 and 2022. *Gastroenterology*. 2024;166(4):605-619. doi:10.1053/j.gastro.2023.12.022

10. Hirabayashi M, Georges D, Clifford GM, de Martel C. Estimating the global burden of Epstein-Barr virus–associated gastric cancer: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2023;21(4):922-930.e21. doi:10.1016/j.cgh.2022.07.042

11. Vitelli-Storelli F, Rubín-García M, Pelucchi C, et al. Family history and gastric cancer risk: a pooled investigation in the Stomach Cancer Pooling (STOP) project consortium. *Cancers (Basel)*. 2021;13(15):3844. doi:10.3390/cancers13153844

12. Praud D, Rota M, Pelucchi C, et al. Cigarette smoking and gastric cancer in the Stomach Cancer Pooling (STOP) project. *Eur J Cancer Prev*. 2018;27(2):124-133. doi:10.1097/CEJ.0000000000000290

13. Ferro A, Morais S, Rota M, et al. Alcohol intake and gastric cancer: meta-analyses of published data versus individual participant data pooled analyses (STOP project). *Cancer Epidemiol*. 2018;54:125-132. doi:10.1016/j.canep.2018.04.009

14. Pelucchi C, La Vecchia C, Bonzi R, et al; STOP Project Working Group. The global gastric cancer consortium: an update from the Stomach Cancer Pooling (STOP) project. *Eur J Cancer Prev*. 2024;33(5):433-437. doi:10.1097/CEJ.0000000000000874

15. Morais S, Costa A, Albuquerque G, et al. Salt intake and gastric cancer: a pooled analysis within the Stomach Cancer Pooling (STOP) project. *Cancer Causes Control*. 2022;33(5):779-791. doi:10.1007/s10552-022-01565-y

16. Paragomi P, Dabo B, Pelucchi C, et al. The association between peptic ulcer disease and gastric cancer: results from the Stomach Cancer Pooling (STOP) project consortium. *Cancers (Basel)*. 2022;14(19):4905. doi:10.3390/cancers14194905

17. Lindblad M, Rodríguez LA, Lagergren J. Body mass, tobacco and alcohol and risk of esophageal, gastric cardia, and gastric non-cardia adenocarcinoma among men and women in a nested case-control study. *Cancer Causes Control*. 2005;16(3):285-294. doi:10.1007/s10552-004-3485-7

18. Chen Y, Liu L, Wang X, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. *Cancer Epidemiol Biomarkers Prev*. 2013;22(8):1395-1408. doi:10.1158/1055-9965.EPI-13-0042

19. Oliveira C, Pinheiro H, Figueiredo J, Seruca R, Carneiro F. Familial gastric cancer: genetic susceptibility, pathology, and implications for management. *Lancet Oncol*. 2015;16(2):e60-e70. doi:10.1016/S1470-2045(14)71016-2

20. Hansford S, Kaurah P, Li-Chang H, et al. Hereditary diffuse gastric cancer syndrome: *CDH1* mutations and beyond. *JAMA Oncol*. 2015;1(1):23-32. doi:10.1001/jamaoncol.2014.168

21. Usui Y, Taniyama Y, Endo M, et al. *Helicobacter pylori*, homologous-recombination genes, and gastric cancer. *N Engl J Med*. 2023;388(13):1181-1190. doi:10.1056/NEJMoa2211807

22. Singh AD, Gupta A, Mehta N, et al. Occurrence of gastric cancer in patients with juvenile polyposis syndrome: a systematic review and meta-analysis. *Gastrointest Endosc*. 2023;97(3):407-414.e1. doi:10.1016/j.gie.2022.10.026

23. van Lier MG, Wagner A, Mathus-Vliegen EM, Kuipers EJ, Steyerberg EW, van Leerdam ME. High cancer risk in Peutz-Jeghers syndrome: a systematic review and surveillance recommendations. *Am J Gastroenterol*. 2010;105(6):1258-1264. doi:10.1038/ajg.2009.725

24. Buckley KH, Niccum BA, Maxwell KN, Katona BW. Gastric cancer risk and pathogenesis in *BRCA1* and *BRCA2* carriers. *Cancers (Basel)*. 2022;14(23):5953. doi:10.3390/cancers14235953

25. Li S, Silvestri V, Leslie G, et al. Cancer risks associated With *BRCA1* and *BRCA2* pathogenic variants. *J Clin Oncol*. 2022;40(14):1529-1541. doi:10.1200/JCO.21.02112

26. Momozawa Y, Sasai R, Usui Y, et al. Expansion of cancer risk profile for *BRCA1* and *BRCA2* pathogenic variants. *JAMA Oncol*. 2022;8(6):871-878. doi:10.1001/jamaoncol.2022.0476

27. Choi IJ, Kook MC, Kim YI, et al. *Helicobacter pylori* therapy for the prevention of metachronous gastric cancer. *N Engl J Med*. 2018;378(12):1085-1095. doi:10.1056/NEJMoa1708423

28. Choi IJ, Kim CG, Lee JY, et al. Family history of gastric cancer and *Helicobacter pylori* treatment. *N Engl J Med*. 2020;382(5):427-436. doi:10.1056/NEJMoa1909666

29. Pan KF, Li WQ, Zhang L, et al. Gastric cancer prevention by community eradication of *Helicobacter pylori*: a cluster-randomized controlled trial. *Nat Med*. 2024;30(11):3250-3260. doi:10.1038/s41591-024-03153-w

30. Lee YC, Chiang TH, Chiu HM, et al; Collaborators of Taiwan Community-based Integrated Screening Group. Screening for *Helicobacter pylori* to prevent gastric cancer: a pragmatic randomized clinical trial. *JAMA*. 2024;332(19):1642-1651. doi:10.1001/jama.2024.14887

31. Ford AC, Yuan Y, Moayyedi P. *Helicobacter pylori* eradication therapy to prevent gastric cancer: systematic review and meta-analysis. *Gut*. 2020;69(12):2113-2121. doi:10.1136/gutjnl-2020-320839

32. Mabe K, Inoue K, Kamada T, Kato K, Kato M, Haruma K. Endoscopic screening for gastric cancer in Japan: current status and future perspectives. *Dig Endosc*. 2022;34(3):412-419. doi:10.1111/den.14063

33. Jun JK, Choi KS, Lee HY, et al. Effectiveness of the Korean national cancer screening program in reducing gastric cancer mortality. *Gastroenterology*. 2017;152(6):1319-1328.e7. doi:10.1053/j.gastro.2017.01.029

34. Park EH, Jung KW, Park NJ, et al; Community of Population-Based Regional Cancer Registries. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2022. *Cancer Res Treat*. 2025;57(2):312-330. doi:10.4143/crt.2025.264

35. Narii N, Sobue T, Zha L, et al. Effectiveness of endoscopic screening for gastric cancer: the Japan public health center-based prospective study. *Cancer Sci*. 2022;113(11):3922-3931. doi:10.1111/cas.15545

36. Shah SC, Wang AY, Wallace MB, Hwang JH. AGA clinical practice update on screening and surveillance in individuals at increased risk for gastric cancer in the United States: expert review. *Gastroenterology*. 2025;168(2):405-416.e1. doi:10.1053/j.gastro.2024.11.001

37. Lauren P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. an attempt at a histo-clinical classification. *Acta Pathol Microbiol Scand*. 1965;64:31-49. doi:10.1111/apm.1965.64.1.31

38. Cristescu R, Lee J, Nebozhyn M, et al. Molecular analysis of gastric cancer identifies subtypes associated with distinct clinical outcomes. *Nat Med*. 2015;21(5):449-456. doi:10.1038/nm.3850

39. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of gastric adenocarcinoma. *Nature*. 2014;513(7517):202-209. doi:10.1038/nature13480

40. Liu Y, Sethi NS, Hinoue T, et al; Cancer Genome Atlas Research Network. Comparative molecular analysis of gastrointestinal adenocarcinomas. *Cancer Cell*. 2018;33(4):721-735.e8. doi:10.1016/j.ccell.2018.03.010

41. Dulak AM, Schumacher SE, van Lieshout J, et al. Gastrointestinal adenocarcinomas of the esophagus, stomach, and colon exhibit distinct patterns of genome instability and oncogenesis. *Cancer Res*. 2012;72(17):4383-4393. doi:10.1158/0008-5472.CAN-11-3893

42. Bai Y, Xie T, Wang Z, et al. Efficacy and predictive biomarkers of immunotherapy in Epstein-Barr virus-associated gastric cancer. *J Immunother Cancer*. 2022;10(3):e004080. doi:10.1136/jitc-2021-004080

43. Solsky I, Rapkin B, Wong K, Friedmann P, Muscarella P, In H. Gastric cancer diagnosis after presentation to the ED: the independent association of presenting location and outcomes. *Am J Surg*. 2018;216(2):286-292. doi:10.1016/j.amjsurg.2017.10.030

44. Wanebo HJ, Kennedy BJ, Chmiel J, Steele G Jr, Winchester D, Osteen R. Cancer of the stomach: a patient care study by the American College of Surgeons. *Ann Surg*. 1993;218(5):583-592. doi:10.1097/00000658-199321850-00002

45. Tang GH, Hart R, Sholzberg M, Brezden-Masley C. Iron deficiency anemia in gastric cancer: a Canadian retrospective review. *Eur J*

Gastroenterol Hepatol. 2018;30(12):1497-1501. doi:10.1097/MEG.0000000000001251

46. Shaukat A, Wang A, Acosta RD, et al; ASGE Standards of Practice Committee. The role of endoscopy in dyspepsia. *Gastrointest Endosc*. 2015;82(2):227-232. doi:10.1016/j.gie.2015.04.003

47. Talley NJ; American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of dyspepsia. *Gastroenterology*. 2005;129(5):1753-1755. doi:10.1053/j.gastro.2005.09.019

48. Talley NJ, Vakil NB, Moayyedi P. American gastroenterological association technical review on the evaluation of dyspepsia. *Gastroenterology*. 2005;129(5):1756-1780. doi:10.1053/j.gastro.2005.09.020

49. Mranda GM, Xue Y, Zhou XG, et al. Revisiting the 8th AJCC system for gastric cancer: a review on validations, nomograms, lymph nodes impact, and proposed modifications. *Ann Med Surg (Lond)*. 2022;75:103411. doi:10.1016/j.amsu.2022.103411

50. Abdel-Rahman O. Validation of the 8th AJCC staging system for gastric cancer in a population-based setting. *Expert Rev Gastroenterol Hepatol*. 2018;12(5):525-530. doi:10.1080/17474124.2018.1413348

51. Al-Batran SE, Homann N, Pauligk C, et al; FLOT4-AIO Investigators. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial. *Lancet*. 2019;393(10184):1948-1957. doi:10.1016/S0140-6736(18)32557-1

52. Sirody J, Kaji AH, Hari DM, Chen KT. Patterns of gastric cancer metastasis in the United States. *Am J Surg*. 2022;224(1 pt B):445-448. doi:10.1016/j.amjsurg.2022.01.024

53. Riihimäki M, Hemminki A, Sundquist K, Sundquist J, Hemminki K. Metastatic spread in patients with gastric cancer. *Oncotarget*. 2016;7(32):52307-52316. doi:10.18632/oncotarget.10740

54. Ajani JA, D'Amico TA, Bentrem DJ, et al. Gastric cancer, version 2.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2022;20(2):167-192. doi:10.6004/jnccn.2022.0008

55. Lordick F, Carneiro F, Cascinu S, et al; ESMO Guidelines Committee. Gastric cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2022;33(10):1005-1020. doi:10.1016/j.annonc.2022.07.004

56. Ungureanu BS, Sacerdotianu VM, Turcu-Stiolica A, Cazacu IM, Saftoiu A. Endoscopic ultrasound vs computed tomography for gastric cancer staging: a network meta-analysis. *Diagnostics (Basel)*. 2021;11(1):134. doi:10.3390/diagnostics11010134

57. Shimada H, Okazumi S, Koyama M, Murakami K. Japanese Gastric Cancer Association task force for research promotion: clinical utility of ^{18}F-fluoro-2-deoxyglucose positron emission tomography in gastric cancer. a systematic review of the literature. *Gastric Cancer*. 2011;14(1):13-21. doi:10.1007/s10120-011-0017-5

58. Smyth E, Schöder H, Strong VE, et al. A prospective evaluation of the utility of 2-deoxy-2-[(18) F]fluoro-D-glucose positron emission tomography and computed tomography in staging locally advanced gastric cancer. *Cancer*. 2012;118(22):5481-5488. doi:10.1002/cncr.27550

59. Chen J, Cheong JH, Yun MJ, et al. Improvement in preoperative staging of gastric adenocarcinoma with positron emission tomography. *Cancer*. 2005;103(11):2383-2390. doi:10.1002/cncr.21074

60. Gertsen EC, Brenkman HJF, van Hillegersberg R, et al; PLASTIC Study Group. ^{18}F-fludeoxyglucose-positron emission tomography/computed tomography and laparoscopy for staging of locally advanced gastric cancer: a multicenter prospective Dutch cohort study (PLASTIC). *JAMA Surg*. 2021;156(12):e215340. doi:10.1001/jamasurg.2021.5340

61. Leeman MF, Patel D, Anderson J, O'Neill JR, Paterson-Brown S. Multidetector computed tomography versus staging laparoscopy for the detection of peritoneal metastases in esophagogastric junctional and gastric cancer. *Surg Laparosc Endosc Percutan Tech*. 2017;27(5):369-374. doi:10.1097/SLE.0000000000000451

62. Forbes N, Elhanafi SE, Al-Haddad MA, et al; ASGE standards of practice committee; (ASGE Standards of Practice Committee Chair). American Society for Gastrointestinal Endoscopy guideline on endoscopic submucosal dissection for the management of early esophageal and gastric cancers: summary and recommendations. *Gastrointest Endosc*. 2023;98(3):271-284. doi:10.1016/j.gie.2023.03.015

63. Mogal H, Fields R, Maithel SK, Votanopoulos K. In patients with localized and resectable gastric cancer, what is the optimal extent of lymph node dissection-D1 versus D2 versus D3? *Ann Surg Oncol*. 2019;26(9):2912-2932. doi:10.1245/s10434-019-07417-5

64. Bang YJ, Kim YW, Yang HK, et al; CLASSIC trial investigators. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. *Lancet*. 2012;379(9813):315-321. doi:10.1016/S0140-6736(11)61873-4

65. Janjigian YY, Al-Batran SE, Wainberg ZA, et al; MATTERHORN Investigators. Perioperative durvalumab in gastric and gastroesophageal junction cancer. *N Engl J Med*. 2025;393(3):217-230. doi:10.1056/NEJMoa2503701

66. Leong T, Smithers BM, Michael M, et al; Australasian Gastro-Intestinal Trials Group, National Health and Medical Research Council Clinical Trials Centre, Trans-Tasman Radiation Oncology Group, European Organisation for Research and Treatment of Cancer, and Canadian Cancer Trials Group. Preoperative chemoradiotherapy for resectable gastric cancer. *N Engl J Med*. 2024;391(19):1810-1821. doi:10.1056/NEJMoa2405195

67. van Hagen P, Hulshof MC, van Lanschot JJ, et al; CROSS Group. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012;366(22):2074-2084. doi:10.1056/NEJMoa1112088

68. Nie RC, Chen GM, Yuan SQ, et al. Adjuvant chemotherapy for gastric cancer patients with mismatch repair deficiency or microsatellite instability: systematic review and meta-analysis. *Ann Surg Oncol*. 2022;29(4):2324-2331. doi:10.1245/s10434-021-11050-6

69. Kim JW, Cho SY, Chae J, et al. Adjuvant chemotherapy in microsatellite instability-high gastric cancer. *Cancer Res Treat*. 2020;52(4):1178-1187. doi:10.4143/crt.2020.313

70. Pietrantonio F, Miceli R, Raimondi A, et al. Individual patient data meta-analysis of the value of microsatellite instability as a biomarker in gastric cancer. *J Clin Oncol*. 2019;37(35):3392-3400. doi:10.1200/JCO.19.01124

71. Tran-Minh ML, Lehmann-Che J, Lambert J, et al; for NORDICAP. Prevalence and prognosis of microsatellite instability in oesogastric adenocarcinoma, NORDICAP 16-01. *Clin Res Hepatol Gastroenterol*. 2021;45(4):101691. doi:10.1016/j.clinre.2021.101691

72. Chao J, Fuchs CS, Shitara K, et al. Assessment of pembrolizumab therapy for the treatment of microsatellite instability-high gastric or gastroesophageal junction cancer among patients in the KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062 clinical trials. *JAMA Oncol*. 2021;7(6):895-902. doi:10.1001/jamaoncol.2021.0275

73. André T, Tougeron D, Piessen G, et al. Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in localized deficient mismatch repair/microsatellite instability-high gastric or esophagogastric junction adenocarcinoma: the GERCOR NEONIPIGA phase II study. *J Clin Oncol*. 2023;41(2):255-265. doi:10.1200/JCO.22.00686

74. Smyth EC, Wotherspoon A, Peckitt C, et al. Mismatch repair deficiency, microsatellite instability, and survival: an exploratory analysis of the Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial. *JAMA Oncol*. 2017;3(9):1197-1203. doi:10.1001/jamaoncol.2016.6762

75. 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(4):666-673. doi:10.1093/annonc/mdn717

76. Bang YJ, Van Cutsem E, Feyereislova A, et al; ToGA Trial Investigators. 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(9742):687-697. doi:10.1016/S0140-6736(10)61121-X

77. Janjigian YY, Kawazoe A, Bai Y, et al; KEYNOTE-811 Investigators. Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial. *Lancet*. 2023;402(10418):2197-2208. doi:10.1016/S0140-6736(23)02033-0

78. Janjigian YY, Kawazoe A, Bai Y, et al. Pembrolizumab in HER2–positive gastric cancer. *N Engl J Med*. 2024;391(14):1360-1362. doi:10.1056/NEJMc2408121

79. Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. *Lancet*. 2021;398(10294):27-40. doi:10.1016/S0140-6736(21)00797-2

80. Janjigian YY, Ajani JA, Moehler M, et al. First-line nivolumab plus chemotherapy for advanced gastric, gastroesophageal junction, and esophageal adenocarcinoma: 3-year follow-up of

the phase III CheckMate 649 Trial. *J Clin Oncol*. 2024;42(17):2012-2020. doi:10.1200/JCO.23.01601

81. Rha SY, Oh DY, Yañez P, et al; KEYNOTE-859 investigators. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. *Lancet Oncol*. 2023;24 (11):1181-1195. doi:10.1016/S1470-2045(23)00515-6

82. Shitara K, Lordick F, Bang YJ, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. *Lancet*. 2023;401 (10389):1655-1668. doi:10.1016/S0140-6736(23) 00620-7

83. Shitara K, Shah MA, Lordick F, et al. Zolbetuximab in gastric or gastroesophageal junction adenocarcinoma. *N Engl J Med*. 2024;391 (12):1159-1162. doi:10.1056/NEJMc2409512

84. Shah MA, Shitara K, Ajani JA, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. *Nat Med*. 2023;29(8):2133-2141. doi:10.1038/ s41591-023-02465-7

85. Wilke H, Muro K, Van Cutsem E, et al; RAINBOW Study Group. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol*. 2014;15(11):1224-1235. doi:10. 1016/S1470-2045(14)70420-6

86. Shitara K, Bang YJ, Iwasa S, et al; DESTINY-Gastric01 Investigators. Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer. *N Engl J Med*. 2020;382(25):2419-2430. doi:10.1056/NEJMoa2004413

87. Shitara K, Doi T, Dvorkin M, et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2018;19(11):1437-1448. doi:10.1016/S1470-2045(18) 30739-3

88. Van Cutsem E, Bang YJ, Feng-Yi F, et al. HER2 screening data from ToGA: targeting HER2 in gastric and gastroesophageal junction cancer. *Gastric Cancer*. 2015;18(3):476-484. doi:10.1007/ s10120-014-0402-y

89. Abrahao-Machado LF, Scapulatempo-Neto C. HER2 testing in gastric cancer: an update. *World J Gastroenterol*. 2016;22(19):4619-4625. doi:10.3748/ wjg.v22.i19.4619

90. Qiu MZ, Oh DY, Kato K, et al; RATIONALE-305 Investigators. Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first line treatment for advanced gastric or gastro-oesophageal junction adenocarcinoma: RATIONALE-305 randomised, double blind, phase 3 trial. *BMJ*. 2024;385:e078876. doi:10.1136/bmj-2023-078876

91. Al-Batran SE, Van Cutsem E, Oh SC, et al. Quality-of-life and performance status results from the phase III RAINBOW study of ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated gastric or gastroesophageal junction adenocarcinoma. *Ann Oncol*. 2016;27(4): 673-679. doi:10.1093/annonc/mdv625

92. Lorenzen S, Thuss-Patience P, Pauligk C, et al. FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel—results from the phase II RAMIRIS Study of the German Gastric Cancer Study Group at AIO. *Eur J Cancer*. 2022;165:48-57. doi:10.1016/j.ejca. 2022.01.015

93. Klempner SJ, Maron SB, Chase L, Lomnicki S, Wainberg ZA, Catenacci DVT. Initial report of second-line FOLFIRI in combination with ramucirumab in advanced gastroesophageal adenocarcinomas: a multi-institutional retrospective analysis. *Oncologist*. 2019;24(4):475-482. doi:10.1634/theoncologist.2018-0602

94. Ford HE, Marshall A, Bridgewater JA, et al; COUGAR-02 Investigators. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet Oncol*. 2014;15(1):78-86. doi:10.1016/S1470-2045(13)70549-7

95. Fuchs CS, Tomasek J, Yong CJ, et al; REGARD Trial Investigators. 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(9911):31-39. doi:10.1016/S0140-6736(13) 61719-5

96. 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(2):481-488. doi:10.1007/s00280-012-2027-3

97. Jiang Z, Lin H, Huang J, et al. Lack of clinical benefit from preoperative short-term parenteral nutrition on the clinical prognosis of patients treated with radical gastrectomy for gastric cancer: a two-center retrospective study based on propensity score matching analysis. *J Gastrointest Oncol*. 2024;15(1):96-111. doi:10.21037/jgo-23-1000

98. He H, Ma Y, Liu G, et al. Early oral feeding post gastrectomy in gastric cancer: quasi-experimental study. *BMJ Support Palliat Care*. Published online February 18, 2025. doi:10.1136/spcare-2024-005183

99. Dann GC, Squires MH III, Postlewait LM, et al. An assessment of feeding jejunostomy tube placement at the time of resection for gastric adenocarcinoma: a seven-institution analysis of 837 patients from the US gastric cancer collaborative. *J Surg Oncol*. 2015;112(2):195-202. doi:10.1002/jso. 23983

100. Tovey FI, Clark CG. Anaemia after partial gastrectomy: a neglected curable condition. *Lancet*. 1980;1(8175):956-958. doi:10.1016/S0140-6736(80) 91406-3

101. Bae JM, Park JW, Yang HK, Kim JP. Nutritional status of gastric cancer patients after total gastrectomy. *World J Surg*. 1998;22(3):254-260. doi:10.1007/s002689900379

102. Yoo SH, Lee JA, Kang SY, et al. Risk of osteoporosis after gastrectomy in long-term gastric cancer survivors. *Gastric Cancer*. 2018;21(4):720-727. doi:10.1007/s10120-017-0777-7

103. Muszyński T, Polak K, Frątczak A, Miziołek B, Bergler-Czop B, Szczepanik A. Vitamin D—the nutritional status of post-gastrectomy gastric cancer patients—systematic review. *Nutrients*. 2022;14(13):2712. doi:10.3390/nu14132712

104. Cobani E, Al Hallak MN, Shields AF, et al. Gastric cancer survivorship: multidisciplinary management, best practices and opportunities. *J Gastrointest Cancer*. 2024;55(2):519-533. doi:10. 1007/s12029-023-01001-7

105. Kubo M, Sasako M, Gotoda T, et al. Endoscopic evaluation of the remnant stomach after gastrectomy: proposal for a new classification. *Gastric Cancer*. 2002;5(2):83-89. doi:10.1007/ s101200200014

106. Lu Z, Fang Y, Liu C, et al. Early interdisciplinary supportive care in patients with previously untreated metastatic esophagogastric cancer: a phase III randomized controlled trial. *J Clin Oncol*. 2021;39(7):748-756. doi:10.1200/JCO.20.01254