

# Newly diagnosed metastatic gastric cancer

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This column is based on the format of an Elsevier textbook entitled *Hematology and Oncology Pearls*, by Dr. Danso and Ethan Basch. In each column we will present updated case studies with a clinical photograph and challenge readers to formulate a diagnosis and treatment plan. Dr. Danso then discusses the correct diagnosis, the disorder, its clinical course, and the patient's outcome, concluding with clinical pearls distilled from the case.

**A** 64-year-old man with a history of a Billroth II procedure for peptic ulcer disease presented to his primary care physician with a 4-month history of intermittent abdominal discomfort, fatigue, and a 35-pound weight loss. The patient's symptoms progressed to frequent nausea and vomiting over 2 weeks. Endoscopic findings demonstrated an 8 cm × 5 cm ulcerated mass in the stomach extending from the proximal lesser curvature to the posterior wall.

## Physical examination

Physical examination revealed an obese man with a temperature of 37.2°C, a pulse of 86, and a blood pressure of 140/80 mm Hg. HEENT (head, eyes, ears, nose, and throat) assessment indicated anicteric sclerae and dry mucous membranes. Moderate epigastric tenderness was present on abdominal examination, with no shifting dullness. There was no edema detected in the extremities.

## Laboratory findings

The biopsy from the gastric mass indicated invasive poorly differentiated adenocarcinoma. The biochemistry profile yielded normal electrolyte levels, with normal renal and hepatic function. Computed tomographic (CT) scans of the chest, abdomen,

and pelvis were notable for mediastinal and hilar lymphadenopathy, numerous pulmonary nodules, and ascites (Figure 1).

*Question:* What is the appropriate treatment option for this patient?

*Answer:* Cisplatin-based chemotherapy is the treatment of choice for patients with metastatic gastric cancer.

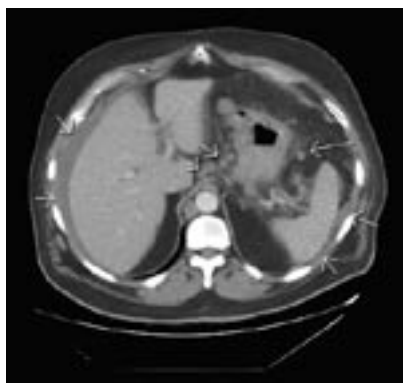
## Discussion

After lung cancer, gastric cancer is the second most common cancer worldwide. The disease is most prevalent in Japan, Chile, and Scandinavia. In the United States, there are approximately 22,000 new cases of gastric cancer each year.<sup>1</sup> At presentation, 80% of patients have advanced

inoperable disease. For these patients, chemotherapy is a useful palliative option that has been demonstrated to improve median survival when compared with best supportive care.<sup>2</sup> Several single-agent chemotherapy drugs have been studied in advanced gastric cancer (Table 1). These agents result in a response rate of 8%–30%. Responses are generally incomplete and of short duration.

The low therapeutic activity of single-agent chemotherapy has led to the development of combination regimens. Combination chemotherapy results in higher responses and longer median survival than do single agents. In phase II trials of some common combinations, such as fluorouracil (5-FU), doxorubicin, and high-dose methotrexate (FAMTX); epirubicin (Ellence), cisplatin, and 5-FU (ECF); etoposide, leucovorin (LV), and 5-FU; and cisplatin and 5-FU (CF), response rates have ranged from 20%–60%.<sup>3</sup> To define the optimal regimen in metastatic gastric carcinoma, several randomized trials of combination chemotherapy have been performed (Table 2).

Although considerable debate remains as to which regimen is the best one, many investigators agree that cisplatin and 5-FU-based therapy is a standard reference regimen. Other front-line regimens include weekly



**FIGURE 1** Computed tomographic scan of the abdomen demonstrating ascites and extensive perigastric, splenic hilar, gastrohepatic, and celiac lymphadenopathy (arrows).

**TABLE 1**

Response rates with single-agent chemotherapy in advanced gastric cancer

Agent	Number of patients	Response
Mitomycin	211	30%
Uracil and tegafur (UFT)	188	28%
Irinotecan	60	23%
Fluorouracil	416	21%
Docetaxel	86	20%
Cisplatin	139	19%
Doxorubicin	221	18%
Etoposide	26	17%
Paclitaxel	55	11%
Carboplatin	41	8%

**TABLE 2**

Combination chemotherapy for advanced gastric and gastroesophageal junction carcinoma

Agents	Number of patients	Response	Median survival, mo
ELF vs FAMTX vs CF	245	9% 12% 20%	7.2 6.7 7.2
FAMTX vs ECF	274	21% 46%	6.1 8.7
MCF vs ECF	580	44% 42%	8.7 9.4
DC vs DCF	148	25% 37%	8.6 9.2

ELF = epirubicin, cisplatin, and fluorouracil; FAMTX = fluorouracil, doxorubicin, and high-dose methotrexate; CF = cisplatin and fluorouracil; ECF = epirubicin, cisplatin, and fluorouracil; MCF = mitomycin, cisplatin, and fluorouracil; DC = docetaxel and cisplatin; DCF = docetaxel, cisplatin, and fluorouracil

irinotecan (Camptosar) with cisplatin. In phase II trials, this regimen resulted in response rates from 30%–60%.<sup>4</sup> In the UK and Europe, ECF is the preferred regimen.

Researchers at M. D. Anderson Cancer Center have been instrumental in incorporating docetaxel (Taxotere) into the treatment regimen for metastatic gastric cancer, with the favored first-line regimen being docetaxel, cisplatin, and 5-FU (DCF); the regimen has been

shown to produce significant improvement in response rates and time to disease progression.<sup>5</sup> The overall confirmed response rate was significantly higher with DCF than with CF (37% vs 25%;  $P = 0.01$ ). The median overall survival was also significantly longer with DCF than with CF (9.2 months vs 8.6 months;  $P = 0.02$ ). However, DCF is a highly toxic regimen, with 82% of patients developing grade 3 or 4 neutropenia and 68% developing nonhematologic grade 3 or 4 adverse events. Concerns about the toxicity of DCF have limited its general use in the oncology community. Nonetheless, docetaxel has now received regulatory approval for use in patients with metastatic gastric cancer.

In recent years, emerging data suggest that oxaliplatin (Eloxatin) may have a useful role in treating metastatic gastric cancer. Oxaliplatin has a higher preclinical antitumoral potency than does cisplatin in gastric cancer cell line models. As this agent has a more favorable toxicity profile than does cisplatin, investigators have explored 5-FU, LV, and oxaliplatin (FOLFOX) in combination for advanced gastric cancer.

In a phase II trial reported by Louvet et al,<sup>6</sup> FOLFOX6 resulted in a 44% response rate. The median time to disease progression and overall survival were 6.2 months and 8.6 months, respectively. Although hematologic toxicity was modest, grade 3 peripheral neuropathy occurred in 21% of patients. These early data suggest that the FOLFOX6 regimen is an attractive treatment for patients with advanced or metastatic gastric cancer.

### Patient outcome

The patient presented here was treated with combination chemother-

apy with irinotecan and cisplatin. He achieved a good partial response that was maintained for 6 months, but subsequently his disease progressed. He was placed on second-line treatment with a taxane, but unfortunately, disease progressed soon thereafter.

### Clinical pearls

1. Cisplatin-based chemotherapy is the treatment of choice for patients with metastatic gastric cancer.
2. In phase II trials, weekly cisplatin with irinotecan produces response rates of 30%–60%.
3. Randomized trials have demonstrated that the addition of epirubicin or docetaxel to cisplatin and 5-FU improves response rates and survival. The improved efficacy is, however, associated with significantly higher toxicity.

### References

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