

# Complete pathologic response with combination oxaliplatin and 5-fluorouracil chemotherapy in an older patient with advanced gastric cancer

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**Management of gastric cancer in older adults is challenging. Perioperative treatment with epirubicin, cisplatin, and 5-fluorouracil combination chemotherapy and surgery is considered the standard treatment of locally advanced gastric adenocarcinoma. However, this chemotherapy regimen is not well tolerated in older adults. Here, we report a case of an older patient with locally advanced gastric cancer who was treated with modified FOLFOX-6 (oxaliplatin, leucovorin, and 5-fluorouracil) regimen and achieved a complete pathological response. *Anti-Cancer Drugs* 22:1024–1026 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

*Anti-Cancer Drugs* 2011, 22:1024–1026

**Keywords:** elderly, gastric cancer, perioperative chemotherapy

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Received 8 May 2011 accepted 22 June 2011

## Introduction

Gastric cancer is the world's fourth leading cause of cancer, behind lung, breast, and colorectal cancer and is the second most common cause of mortality from cancer worldwide, contributing to over 700 000 deaths annually [1]. In the USA, there are 21 000 new cases diagnosed each year, and approximately 10 500 die of this disease annually [2]. Although gastric cancer mortality continues to decline, it is currently the 10th leading cause of cancer-related death in the USA [2]. Incidence of gastric cancer increases with age, with a median age of 70 years for men and 74 years for women. The relative five-year survival rate continues to be poor, averaging approximately 22% for all stages.

The pivotal MAGIC trial showed the benefit of perioperative chemotherapy treatments in patients with gastroesophageal cancers [3]. In this study, patients with advanced gastroesophageal cancer were randomized to receive either surgery alone or surgery with perioperative chemotherapy {epirubicin, cisplatin, and 5-fluorouracil (5-FU)[ECF regimen]}. Addition of perioperative chemotherapy showed significant improvement in five-year overall survival (36 vs. 23%,  $P = 0.009$ ) [3]. The majority of the patients in the MAGIC study were younger than 60 years (more than 40%). The median age was 62 years, and only 20% of the patients in this study were older than 70 years.

Although ECF has a likely survival benefit in older adults with locally advanced gastric cancer, this treatment is usually not well tolerated in this age group. Combination chemotherapy with ECF regimen can result in severe hematologic side effects. Rates of grades 3–4 neutropenia in ECF have been reported as high as 82% [4].

More recently, other combinations of chemotherapeutic agents have been used for the treatment of locally advanced gastric cancer with equal or greater efficacy and improved safety. Phase II trials using modified FOLFOX-4 (oxaliplatin, leucovorin, and 5-FU) regimens found these chemotherapeutic agents in combination to be both efficacious and well tolerated in elderly patients with metastatic gastric cancer [5–7]. In one study involving older patients (median age 71), modified FOLFOX-4 showed an overall response rate of 45.6% with a median overall survival of 9.8 months in patients with metastatic gastric cancer [5]. There were no grade 4 toxicities reported and grade 3 toxicities were lower as compared with triple-drug regimens such as ECF. Another similar study involving modified FOLFOX-4 regimen in the elderly reported a median overall survival of 10 months with mild toxicities including grade 3 hematologic toxicities of neutropenia, anemia, and thrombocytopenia (6.8, 2.3, and 4.5% respectively) with no grade 4 hematologic toxicities [7]. There are no studies available to this date examining the usefulness of preoperative chemotherapy treatments with combination oxaliplatin and 5-FU in older patients with locally advanced gastric cancer.

In this study, we report a case of an older patient with locally advanced gastric adenocarcinoma who was treated with combination oxaliplatin and 5-FU chemotherapy (modified FOLFOX-6 regimen) and achieved a complete pathological response.

## Case history

The patient is a 79-year-old Korean woman who was diagnosed with gastric adenocarcinoma in July 2008 after presenting with nonspecific abdominal discomfort, dyspepsia,

and early satiety beginning several months previously. Her medical history was significant for gastroesophageal reflux disease, hypothyroidism, and a pancreatic neuroendocrine tumor, which was biopsied and confirmed as a pancreatic islet cell tumor. Medical workup began with an initial upper endoscopy in July 2008 revealing a concentric mass in the antrum. Biopsy of the mass was performed, and pathology was consistent with poorly differentiated gastric adenocarcinoma. The tumor was found to have invaded through the lamina propria. Giemsa stain was negative for *Helicobacter pylori*. Endoscopic ultrasound confirmed concentric involvement of the antrum in the prepyloric region. Suspicious lymph nodes were seen near the tumor. She was staged T3N1Mx on the basis of the endoscopic ultrasound finding. Computed tomography (CT) scans of her abdomen and pelvis were negative for metastasis. A positron emission tomography/CT study confirmed a metabolically active tumor in the gastric antrum but was negative for local or distant metastatic disease. One small (1 cm) lymph node was detected in the aortopulmonary window and prevascular space. A 1.3 cm hypodense lesion in the head of the pancreas was detected and consistent with islet cell tumor diagnosed previously. The final stage was determined to be T3N1M0.

At the completion of the initial staging workup, the patient was started on treatment with preoperative chemotherapy in September 2008 with modified FOLFOX-6 regimen: oxaliplatin ( $85 \text{ mg/m}^2$ ), leucovorin ( $400 \text{ mg/m}^2$ ), 5-FU ( $400 \text{ mg/m}^2$ ) intravenous pyelogram, followed by 5-FU ( $2400 \text{ mg/m}^2$ ) over 46 h. The patient received a total of six cycles preoperatively. Endoscopy with ultrasound was repeated before her surgery in November 2008, revealing a normal esophagus and a distorted gastric antrum without focal obstruction. There was no evidence of perigastric or celiac lymphadenopathy. The stomach wall layers at the antrum were of normal thickness with no focal masses detected. She underwent exploratory laparotomy the following week with distal subtotal gastrectomy and en bloc omentectomy with no surgical complications. Pathological evaluation of the surgical specimen showed no dysplasia or malignancy, and only some intestinal metaplasia with an ulcer was detected. Both proximal and distal margins were negative for tumor with no evidence of gross disease. No malignancy was seen in the lymph nodes, and there was no evidence of lymphatic or omental involvement. Postoperatively, the patient received two additional cycles of planned six cycles of FOLFOX-6. Following the second cycle of postoperative chemotherapy, the patient presented to the clinic with increased abdominal bloating, decreased hearing, and grade 1 neuropathy in the hands and feet. In April 2009, the patient presented with bacteremia secondary to Port-A-Cath infection. The Port-A-Cath was removed and the infection resolved after antibiotic treatments. A follow-up CT scan was performed during this time showing no evidence of recurrent gastric

adenocarcinoma. Upper endoscopy performed in July 2009 revealed a normal esophagus and a visible gastroesophageal junction with a small hiatal hernia. The gastrojejunal anastomosis was identified without abnormalities. Endoscopic ultrasound showed no endosonographic abnormalities of the gastric wall and perigastric tissues. There was no evidence of mediastinal lymphadenopathy.

To this date, the patient continues to remain active, and her most recent upper endoscopic evaluation in February 2011 was negative with no evidence of recurrence.

## Discussion

Perioperative chemotherapy with ECF regimen and surgery is considered the current standard treatment for locally advanced gastric adenocarcinoma. However, the toxicity with the combination of three chemotherapy agents brings further challenges in the treatment of older adults with gastric cancer. Here, we have reported a case of poorly differentiated gastric carcinoma in an older patient who was treated with modified FOLFOX-6 regimen and achieved a complete pathologic response. The patient in this case experienced some complications after her surgery and was not able to complete the planned postoperative chemotherapy treatment.

Further clinical trials are necessary to test the efficacy of the modified FOLFOX-6 regimen in the perioperative treatment of locally advanced gastric cancer, specifically for older adults. Ideally, chemotherapy treatments for advanced gastric cancer need to be given preoperatively because most patients, such as in this case, would have a more difficult time tolerating chemotherapy treatments if given postoperatively. One of the potential hazards of using preoperative chemotherapy is the risk of having no significant response or disease progression. A follow-up endoscopic evaluation after 8–10 weeks of chemotherapy can show early signs of response to the treatments. If there is response evident by reduction of the tumor size and/or depth of invasion, the preoperative chemotherapy treatments can continue as planned. If there is no sign of significant response, other preoperative approaches such as combination chemoradiotherapy can be considered in the design of the future clinical studies.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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