

Gastrointestinal Cancer Guidance

The American Society of Clinical Oncology offers the following clinical guidance on treatment alternatives during shortages of antineoplastic agents. Decisions should be based on specific goals of the therapy where evidence-based medicine has shown survival outcomes and life-extending benefits in both early and advanced stages. For more information on ASCO's general principles during drug shortages, please visit ASCO's [Clinical Guidance page](#). For further consideration of ethical guidance, please visit ASCO's [Ethical Principles and Implementation Strategies page](#).

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The following agents are recommended substitutes when treating patients with gastrointestinal malignancies during a drug shortage.

1. Capecitabine is a reasonable substitute for 5-fluorouracil (5-FU; please see FDA insert for [potential contraindications](#))
2. Oxaliplatin is a reasonable substitute for cisplatin
3. Oxaliplatin is a reasonable substitute for carboplatin **but must be provided in conjunction with 5-FU (or capecitabine if 5FU is unavailable)**
4. 5-FU should be **prioritized for patients with dysphagia**.

1. Upper Gastrointestinal Malignancies

- a. Esophageal and/or Gastroesophageal Junction Cancer
 - i. Resectable disease (adenocarcinoma or squamous cell carcinoma)
 1. For the treatment of resectable disease, radiotherapy plus chemotherapy with either paclitaxel and carboplatin or 5FU plus cisplatin or FOLFOX are the recommended standard of care. Reasonable alternatives may include:
 - a. Perioperative approach, with chemotherapy with oxaliplatin, leucovorin, fluorouracil (FOLFOX) or docetaxel, oxaliplatin, leucovorin, fluorouracil (FLOT) for gastroesophageal junction cancer if 5FU is available.
 - b. Neoadjuvant chemoradiation approach with FOLFOX plus radiotherapy for esophageal cancer or gastroesophageal junction cancer. If 5-FU is unavailable and the patient can

swallow, treatment with capecitabine and oxaliplatin (CapeOx) with concurrent radiation would be the alternative.

- ii. Unresectable or advanced-stage disease
 - 1. Use 5-FU plus oxaliplatin (FOLFOX) with or without nivolumab/pembrolizumab) if 5FU is available. If 5-FU is unavailable and the patient can swallow, treat with CapeOx with or without nivolumab/pembrolizumab. If the patient cannot swallow, treat with irinotecan plus oxaliplatin.
 - 2. For patients with squamous cell carcinoma, treat with either FOLFOX plus nivolumab or pembrolizumab if 5FU is available. If 5FU is not available, nivolumab plus ipilimumab can be used.

b. Gastric Cancer

- i. Resectable disease
 - 1. Perioperative chemotherapy with oxaliplatin, leucovorin, fluorouracil (FOLFOX) or docetaxel, oxaliplatin, leucovorin, fluorouracil (FLOT) are recommended standards of care for patients with resectable gastric cancer. Reasonable alternatives include:
 - a. Perioperative chemotherapy with CapeOx
- ii. Unresectable or Stage IV Disease
 - 1. Treat with FOLFOX or CapeOx with or without nivolumab/pembrolizumab.

2. Pancreato-Biliary Malignancies

a. Biliary Cancers

- i. For patients with resectable disease, treat with adjuvant capecitabine.
- ii. For advanced disease, treat with gemcitabine, cisplatin, durvalumab if cisplatin is available. There is no prospective data supporting the substitution of oxaliplatin, but consideration could be given to giving gemcitabine alone as the chemotherapy backbone.
- iii. For refractory disease, treat with FOLFOX if fluorouracil is available or CapeOx if fluorouracil is unavailable.
- iv. For refractory disease, treat with FOLFIRI or 5-FU/ nanoliposomal irinotecan if fluorouracil is available. Capecitabine can substitute for 5-FU with caution; **consider dose reductions** due to the high risk of diarrhea and dehydration.

b. Pancreatic cancer

- i. In the perioperative setting, treat with gemcitabine plus nab-paclitaxel or with FOLFIRINOX (5-FU, oxaliplatin, irinotecan, and leucovorin) if 5-FU is available.
- ii. For advanced disease, treat with gemcitabine plus nab-paclitaxel or FOLFIRINOX if fluorouracil is available.
- iii. For patients with a pathogenic *BRCA* mutation, treat with FOLFIRINOX in resectable or metastatic disease. If cisplatin is not available, consider FOLFOX or GEMOX depending on availability.

3. Small Intestine Malignancies

- a. Consider the substitution of capecitabine for fluorouracil in combination with oxaliplatin.

- b. FOLFIRI (fluorouracil, leucovorin, irinotecan) could be used second-line. Capecitabine can substitute for 5-FU with caution; **consider dose reductions** due to the high risk of diarrhea and dehydration.
- 4. Colorectal Cancer
 - a. For resectable/unresectable treatment of colon/rectal cancer, FOLFOX or CapeOx are standards of care. Reasonable alternatives include:
 - i. Consider substituting capecitabine for fluorouracil in combination with oxaliplatin.
 - b. Metastatic colorectal cancer
 - i. Consider substituting capecitabine for 5-FU in combination with oxaliplatin.
 - ii. FOLFIRI could be used second-line Capecitabine can substitute for fluorouracil with caution; **consider dose reductions** due to the high risk of diarrhea and dehydration.
- 5. Anal Cancer
 - a. Locally advanced anal cancer is treated with curative intent chemoradiation
 - i. 5-FU in combination with mitomycin C is the standard of care. Reasonable alternatives include:
 - 1. Capecitabine may be substituted for fluorouracil in combination with mitomycin C.
 - b. Treatment naïve metastatic anal cancer
 - i. There is no prospective data to support the substitution of oxaliplatin for carboplatin or cisplatin. At the provider's discretion, consider starting paclitaxel as a single agent (if off protocol) and it is determined by the provider that treatment should be initiated as soon as possible.

