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INTRODUCTION

The COVID-19 pandemic has spread rapidly across the world, causing notable disruption to the health care system as a whole. This disruption has presented new and unprecedented challenges in the care of patients with cancer—both those with curable and with noncurable forms. Providers have been forced to carefully re-examine the necessity and risk-versus-benefit ratios of even the most common and routine procedures and treatments in light of the need for physical distancing to flatten the curve of infection rates and to mitigate the risk of infection in our vulnerable patient population.

In this context, a group of expert oncologists in the field of GI oncology recently discussed and compiled recommendations for new practices as we all adapt to the quickly changing landscape. The discussion focused on balancing logistics of care with the need to practice physical distancing to mitigate risk of infection in this cancer patient population and in the health care workers who serve them and on managing each situation on a case-by-case basis—with special consideration toward differentiating between patients at high risk versus relatively lower risk of COVID-19 infection in the community—and according to the intent of treatment (intent to cure or palliative intent). As of April 1, 2020, 10 of these oncologists had reported that their centers had adopted institution-wide guidelines with some degree of formality; others also cited interpretation of the ASCO statement on the general care of patients with cancer during the COVID-19 pandemic, first posted online on March 13, 2020; much of the practice points offered for consideration via ASCO and other professional societies are predicated on direction from the Centers for Disease Control and Prevention to curtail elective surgeries and other nonurgent medical interventions in general. The situation has necessitated rapid changes to clinical practice, including accelerated adoption of telemedicine, home infusion and/or home collection of laboratory samples, and novel clinics for COVID-19 screening. Some cancer centers have created acute care clinics designed to focus on cancer-related complications, such as adverse events from chemotherapy, in an effort to minimize additional burden on already overtaxed emergency room and inpatient hospital settings and to minimize exposure of patients with cancer to potential COVID-19 infection. The risks of progression are particularly high for most cases of GI cancers, so the need to carefully weigh risks versus benefits of treatment (particularly in person) is critical. What is clear is that the risk-benefit ratio has changed dramatically because of the risks imposed by the COVID-19 virus, including inducing clinically emergent forms of morbidity and the potentially increased risk of death in the cancer population.

The suggested modifications to standard of care treatments are recommended based on multiple factors with the overarching intent to reduce harm from treatment. The recommendations can be categorized into the following broad groups of strategies:

1. Eliminate treatments with marginal benefit.
2. Reduce the time patients with cancer spend at the health care facility by employing telemedicine for clinical assessment; 
   if radiation is planned, opt for hypofractionated regimens versus conventional fractionated; 
   prefer regimens that can be self-administered at home (eg, oral, subcutaneous/intramuscular regimens over intravenous); and delay interval between treatments.

Most Commonly Offered Tips for Modifying Treatment and Practice in This Population

1. As a more general approach to patient care, regardless of tumor type, many cancer centers across the country have shifted to telemedicine approaches to patient visits to preserve physical distancing and to minimize patient interactions with potential infected persons both inside and outside of the oncology clinic setting.
2. Discontinue fluorouracil (FU) bolus/leucovorin combinations for infusional combination regimens that use FU infusions as backbones of therapy (ie, FOLFOX, FOLFIRI, FOLFIRINOX),...
3. Consider delaying or not proceeding with risk-reducing adjuvant chemotherapy for patients with resected high-risk stage II colon carcinomas; consider the same for patients at high risk of COVID-19 infection with resected stage III colon carcinomas versus shortening the duration (3 vs 6 months) and/or instituting oral chemotherapy (capecitabine in place of bolus/infusional FU-based regimens) as alternate tactics for adjuvant treatment approaches.

4. For cases of localized rectal cancer, shorten the duration of radiation treatment using the “short-course radiotherapy” approach favored in Europe.

5. Assess timing of routine surveillance imaging scans for patients with a history of treated GI malignancy and low risk of recurrence, most especially in context of scarcity of personal protective equipment that would be required by patient and/or imaging teams.

6. Case by case, discuss with patients who have metastatic incurable forms of GI malignancies currently on treatment and with stable disease and/or minimal tumor burden and consider the risks versus benefits of treatment—compared with the risk of acquiring and suffering from morbidity and related sequelae of COVID-19 infection.

**TABLE 2. Proposed Modifications Stratified by COVID-19–Related Risk of Infection**

<table>
<thead>
<tr>
<th>Risk Consideration</th>
<th>Risk Parameters</th>
<th>Proposition</th>
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<tr>
<td>Patients at high risk of COVID-19 infection</td>
<td>As defined by age, comorbidities including but not limited to cardiovascular disease and pulmonary disease; patients with diabetes, active smokers, and/or those residing in nursing facilities or group homes</td>
<td>Discuss the risk/benefit of therapy in light of evidence that patients with cancer are at a potentially greater risk of infection compared with the community.4 Lean toward delaying immunosuppressive therapy until community risk decreases.</td>
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<tr>
<td>Patients at community risk of COVID-19 infection</td>
<td>Although patients with active cancer likely have higher-than-community risk, this category includes patients without the high-risk factors detailed.</td>
<td>Proceed with treatment on a case-by-case basis after a discussion of risks and incorporation of patient preferences and values. Lean toward continuing immunosuppressive cancer-directed therapy if cancer treatment required, but institute measures to ameliorate risk of immunosuppression.</td>
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<tr>
<td>Organ</td>
<td>Oncologic Situation</td>
<td>Proposition</td>
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| Pancreas            | Unresectable (includes locally advanced cases as well as those with distant metastatic disease) | • Avoid FOLFIRINOX because of the inherently high risk of neutropenia; consider doublet regimens instead (eg, FOLFOX; otherwise gemcitabine with nab-paclitaxel if not otherwise refractory).  
• If necessary, use growth factor and reduce the dose.  
• Use every-other-week gemcitabine/nab-paclitaxel. |
| Rectum (localized) | Chemoradiation/radiation completed or ongoing                                      | • Delay the surgical intervention up to 12 weeks on observation (GRECCAR 6 [NCT01648894] showed that there is no difference in pathologic complete response with a delay of 11 or 7 weeks).  
• If the delay is beyond 12 weeks, consider restaging and guiding therapy on the basis of treatment response. |
|                     | Preoperative radiation is required                                                  | • Minimize the use of neoadjuvant chemotherapy for average-risk patients.  
• Preferably use short-course RT (5 × 5) and surgery at 12 weeks. |
|                     | Particularly high-risk cases                                                         | Proceed with neoadjuvant chemotherapy, with a preference for CAPOX over FOLFOX, followed by SBRT. |
|                     | T4 or N2: major response to chemoradiation                                           | Discuss surgical resection and consider a watch-and-wait strategy with frequent follow-up surveillance. |
| Colon (localized)   | Localized cancer < T4 (symptomatic and nonsymptomatic)                              | Surgery within the normal timeframe, if possible. |
|                     | Particular cases T4                                                                  | Proceed with or delay surgical resection; some suggest consideration of neoadjuvant chemotherapy, with preference for CAPOX, and surgery after the COVID-19 pandemic. |
|                     | Patients at high risk of COVID-19 complications                                       | Discuss delay of surgery for between 4 to 6 weeks according to the benefit-risk ratio. |
|                     | Adjuvant chemotherapy indicated, stage III and stage II (high risk)                 | • Preferably use CAPOX (3 or 6 months) instead of FOLFOX adjuvant therapy.  
• For new-onset or ongoing adjuvant therapy, consider stopping early (3 months) or switching to capecitabine or FU alone for the remainder.  
• Reassess risk v benefit in stage II colon cancer.  
• In patients already on FOLFOX, preferably drop the FU bolus and leucovorin.  
• Consider early discontinuation of oxaliplatin. If on FU alone, consider switching to capecitabine.  
• For patients at low risk, discuss the myelosuppression of oxaliplatin and the use of capecitabine monotherapy.  
• For patients at high risk of COVID-19 complications or with anticipated low absolute risk reduction with adjuvant chemotherapy, discuss not administering chemotherapy. |

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| Metastatic colorectal cancer (first and second lines) | Resectable or potentially resectable metastatic disease | • Virtual consultation with liver surgery at baseline and after neoadjuvant chemotherapy is encouraged.  
• For patients with resectable disease, delay surgery until after the COVID-19 pandemic, with or without preoperative chemotherapy according to neoplastic characteristics. |
| | | Nonresectable, multiorgan metastatic disease | • Chemotherapy: Use monotherapy (preferably capecitabine) or CAPOX with or without targeted therapies; avoid FOLFOXIRI.  
• For patients with metastatic cancer and stable/minimal disease, consider a treatment break.  
• If maintenance therapy is desired, capecitabine alone or with bevacizumab.  
• If disease is FU refractory, irinotecan with or without biologics (either bevacizumab or an EGFR inhibitor) would be preferred over FOLFIRI. |
| Metastatic colorectal cancer (beyond second-line treatment) | Nonresectable, nontrial (many centers have halted new enrollments onto therapeutic clinical trials because of the pandemic) | • Up-front goals-of-care discussions are warranted.  
• Use regorafenib and trifluridine-tipiracil (TAS-102) with prudence, given the low efficacy and potential toxicities.  
• Regorafenib is preferred over TAS-102 because of the risk of leukopenia and neutropenia.  
• For TAS-102, alternate 1 week on/1 week off to reduce the risk of myelosuppression.  
• Discuss a therapeutic pause in cases of stable disease. |
| Metastatic colorectal cancer (MSI-H on immunotherapy) | | • Double the time between infusions (eg, from pembrolizumab every 3 weeks to every 6 weeks).  
• For PD-1/PD-L1 inhibitor durations of therapy > 12 months, preferably hold immunotherapy. |
| Localized anal cancer | | • Consider oral capecitabine instead of infusional FU, concurrent with standard radiation course; if using U or capecitabine in combination with mitomycin; consider holding mitomycin for scheduled cycle 2 (day 29 of overall treatment). |
| Well-differentiated low-grade neuroendocrine tumors | | • Consider holding or increasing the interval between octreotide/lanreotide depot injections in the absence of hormone-mediated symptoms to avoid clinic visits.  
• Use of subcutaneous octreotide, telotristat, and/or other antidiarrheals in patients with functional tumors.  
• Judicious use of chemotherapy (eg, capecitabine/temozolomide) and targeted agents (everolimus, sunitinib); consider breaks in treatment in patients who are otherwise stable.  
• Consider deferring initiation of lutetium Lu177 dotatate if clinical situation allows; individualize care as needed in patients who have already initiated treatment (extending interval between cycles and/or stopping before 4 cycles if appropriate).  
• Judicious use of liver directed therapy in progressing and/or symptomatic patients. |

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TABLE 3. Proposed Modifications and Accommodations to Treatment Listed by Disease-Specific/Organ Site (continued)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Oncologic Situation</th>
<th>Proposition</th>
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<tbody>
<tr>
<td>Upper GI malignancies (esophageal, gastroesophageal junction, gastric)</td>
<td>Metastatic, and PD-L1 expression levels that meet criteria for checkpoint immunotherapy</td>
<td>• Approach similarly to the above strategies for lower GI malignancies, including: double time between infusions (eg, from pembrolizumab every 3 weeks to every 6 weeks); and for PD-1/PD-L1 inhibitor durations of therapy &gt; 12 months, preferably hold immunotherapy.</td>
</tr>
<tr>
<td>Poorly differentiated, high grade gastroenteropancreatic neuroendocrine carcinomas (NEC)</td>
<td>Localized disease</td>
<td>• Depending on co-morbidities and goals of care, consider proceeding with adjuvant (or neoadjuvant) treatment (chemotherapy with or without radiation); if necessary, use growth factor and dose reduce chemotherapy.</td>
</tr>
<tr>
<td></td>
<td>Metastatic disease—1st line setting</td>
<td>• Up-front goals of care discussion warranted. Consider proceeding with first line platinum-based therapy (stopping after max 6 cycles if stable disease or better); if necessary, use growth factor and dose reduce.</td>
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<tr>
<td></td>
<td>Metastatic disease—salvage setting</td>
<td>• Individualize therapy considering factors such as number of prior lines of therapy, likelihood of response, the patient’s tolerance of treatment, risk of COVID-19 complications, and goals of care.</td>
</tr>
</tbody>
</table>

Abbreviations: CAPOX, capecitabine, oxaliplatin; EGFR, epidermal growth factor receptor; FOLFIRINOX, leucovorin, 5-fluorouracil (no bolus; higher dose than for other FU-based regimens), oxaliplatin; FOLFOX, leucovorin, 5-fluorouracil, oxaliplatin; FOLFOXIRI, leucovorin, 5-fluorouracil (no bolus; higher dose than for other FU-based regimens), oxaliplatin, irinotecan; FU, fluorouracil; MSI-H, high microsatellite instability status; PD-1, programmed death 1; PD-L1, programmed death ligand 1; RT, radiotherapy; SBRT, stereotactic body radiotherapy.

7. For patients with metastatic, borderline resectable, or locally advanced pancreatic cancer undergoing treatment with chemotherapy of gemcitabine with nab-paclitaxel (whether for palliative or neoadjuvant intent), delete day 8 of the standard regimen and provide infusions of both drugs on days 1 and 15 of each 28-day cycle to avoid expected nadirs during that middle week. At least one previously published study suggests that this approach improves patient tolerance of this chemotherapeutic combination without notably compromising efficacy.2,3

8. Regarding empiric use of growth factor supplementation for chemotherapy regimens with a high potential for inducing neutropenia, guidance from ASCO suggests that continued use of prophylactic growth factors may be warranted. Further discussion among our experts delved into the ideal situation of avoiding additional clinic visits in this scenario—for example, through use of take-home versions of the growth factor support injections (ie, pegfilgrastim body injector); consider reduction of chemotherapy doses in an effort to further avoid neutropenia development.

9. Switch to and modify dosing, scheduling of administration and of monitoring, and overall implementation of oral chemotherapeutic or biologic agents, when feasible, in an effort to both reduce cytopenias and minimize the need for in-person clinical evaluation and exposure to potential infected individuals. Examples included less frequent evaluation of patients on regorafenib (eg, every 2 weeks rather than weekly for the first cycle), alternate-week dosing of trifluridine-tipiracil (TAS-102; 7 days on/7 days off), and implementation of capecitabine in place of bolus/infusional FU for treatment of anal carcinoma and adjuvant or metastatic colorectal carcinomas.

Tables 1, 2, and 3 categorize these and other suggested modifications by condition, risk of COVID-19 infection, and GI organ/disease site.

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**AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT**

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/OP.20.00239.
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ACKNOWLEDGMENT
The GI oncology treatment modification proposal was created with input from GI oncologists at Duke Cancer Institute, University of Minnesota, MD Anderson Cancer Center, Memorial Sloan Kettering Cancer Center, Fred Hutchinson Cancer Center, University of Wisconsin, University of Texas–Southwestern, Vanderbilt-Ingram Cancer Center, University of California, San Francisco, and the Cleveland Clinic.

REFERENCES
Authors’ Disclosures of Potential Conflicts of Interest


The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO’s conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/op/authors/author-center.

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Uncompensated Relationships: Vivor, Family Reach Foundation.

No other potential conflicts of interest were reported.