

**PHILIPPINE SOCIETY OF MEDICAL ONCOLOGY (PSMO)  
CONSENSUS RECOMMENDATIONS IN THE MANAGEMENT OF COLORECTAL  
CANCER DURING COVID-19 PANDEMIC IN THE CORONAVIRUS DISEASE 2019  
(COVID-19) ERA**

**Section of Medical Oncology  
Department of Internal Medicine  
Veterans Memorial Medical Center  
2020**

**Fellows**

Lasam, Jesus Toedoro B.  
Lopez, Stephen E.  
Patacsil, John Marvin T.  
Rebugio, Jaarmy Flor

**Consultants**

Baguino, Anna Mie V.  
Cornel, Annielyn O.  
Ferrerias, Cherelina S.  
Galvez, Christina G.  
Ganzon, Domingo E.  
Kindipan, Mercy Grace G.  
Ortines, Gerardine R.  
Pua, Paul Francis B.  
Querol, John P.  
Resuello, Dana Colleene DM.  
Sandoval, Sharon G.

## **I. Background and Context**

The outbreak of coronavirus disease 2019 (COVID-19) posed a lot of threats in the healthcare system. Globally, COVID-19 has afflicted over six million individuals with a mortality rate of about 6%.<sup>3</sup> According to the Centers for Disease Control and Prevention (CDC), older adults and people of any age who have serious underlying medical conditions (i.e. asthma, HIV, immunocompromised, hypertension, diabetes), might be at higher risk for severe illness from COVID-19.<sup>1</sup> Since most cancer patients belong to the elderly age group and are among the immunocompromised, COVID-19 certainly presents a major concern to oncologic care.

Colorectal Cancer (CRC) is the third most commonly diagnosed cancer worldwide in males and the second in females, with 1.8 million new cases and almost 861,000 deaths in 2018 according to the World Health Organization GLOBOCAN database.<sup>2</sup> In the Philippines, it is also the third most common cancer in terms of incidence.<sup>4</sup> CRC management is multidisciplinary. During this pandemic, we have to adapt to the current situation without compromising treatment outcomes, hence the need to modify existing guidelines.

## **II. Rationale**

Our healthcare system was challenged by this pandemic. Colorectal Cancer still exists even during the COVID-19 season, causing a major area of oncologic concern. There is therefore an urgency of local consensus recommendations in the prioritizing, screening, diagnosing, treating and surveillance of colorectal cancer patients who are negative for COVID-19-related illness. Since this is a new situation we are in, we are limited by the lack of experience to provide sufficient evidence.

## **III. Objective**

These recommendations aim to provide local guidance on the management of colorectal cancer not suspected to have COVID-19-related illness in time of COVID-19 Pandemic.

## **IV. Target Users**

These recommendations are intended for the use of medical oncologists taking care of colorectal cancer patients in the Philippines.

## **V. Related Guidelines**

This guideline primarily localizes to the Philippine setting the recommendations by the European Society of Medical Oncology (ESMO) as published in *ESMO management and treatment adapted recommendations in the COVID-19 era: colorectal cancer*.

## VI. Recommendations

### A. Prioritization

**Q: In general, how should colorectal cancer patients be prioritized during the COVID-19 pandemic?**

A: The tiered approach of ESMO in delivering a guidance for cancer patients during the COVID-19 pandemic is designed across three levels of priorities, namely: tier 1 (high priority intervention), 2 (medium priority) and 3 (low priority):<sup>5</sup>

**High priority:** Patient's condition is immediately life threatening, clinically unstable, and/or the magnitude of benefit qualifies the intervention as high priority (e.g. significant overall survival [OS] gain and/or substantial improvement in quality of life [QoL]);

**Medium priority:** Patient's situation is non-critical but delay beyond 6 weeks could potentially impact overall outcome and/or the magnitude of benefit qualifies for intermediate priority;

**Low priority:** Patient's condition is stable enough that services can be delayed for the duration of the COVID-19 pandemic and/or the intervention is non-priority based on the magnitude of benefit (e.g. no survival gain with no change nor reduced QoL).

### B. Outpatient visits

**Q: Among patients with colorectal cancer, who should be prioritized for outpatient visits?**

A: The ESMO Guidelines classified colorectal cancer patients coming in for out-patient visits into high, medium and low priority:<sup>5</sup>

Patients classified as **High Priority** include for out-patient visit include:

- Potentially unstable (acute abdominal pain, intestinal occlusion, ascites, complications after surgery/endoscopy or radiological interventions, diarrhea, severe skin toxicity, new symptoms, clinical progression)
- Symptomatic new patients (symptomatic ascites, intestinal occlusion, chronic diarrhea)

Patients classified as **Medium Priority** for out-patient visit include:

- Newly diagnosed asymptomatic patients, no prior surgery
- Newly diagnosed asymptomatic patients after surgery for treatment strategy planning in case of adjuvant and first-line treatment
- Chemo/radiotherapy-related serious side effects
- Established patients with new problems or symptoms from treatment;
  - Convert as many visits as possible to telemedicine appointments

Patients classified as **Low Priority** for out-patient include:

- Second opinion
- Secondary prevention of CRC;
  - If possible, schedule blood tests and imaging close to home and convert to telemedicine
- Follow-up visit out of study
- Re-staging in metastatic setting when the goal is not to perform surgery with curative intent on metastatic and primary lesions
- Re-staging in third- and fourth-line treatment
- Follow-up visit on maintenance treatment;
  - If possible, schedule blood tests and imaging close to home and convert to telemedicine

### C. Diagnostics/Imaging/Surveillance

**Q: Among patients with colorectal cancer, how do we prioritize imaging and radiological/endoscopic intervention?**

**A:** The ESMO guidelines classified imaging and radiological/endoscopic intervention into high, medium and low priority<sup>5</sup>.

Imaging and radiological/endoscopic intervention classified as **High Priority** include:

- Radiological confirmation of intestinal occlusion, bleeding, perforation, post-surgical complications and post-interventional procedures
- Radiological confirmations of bone fractures due to metastasis

Imaging and radiological/endoscopic intervention classified as **Medium Priority** include:

- Diagnostic imaging/endoscopy for clinically-suspected CRC (clinical, biomarkers, family history)
- Diagnostic imaging/endoscopy for high-risk categories (familial cases of CRC, serrated polyps)

Imaging and radiological/endoscopic intervention classified as **Low Priority** include:

- Secondary prevention of CRC.
  - In these cases, it is preferred to perform occult test; and if possible, schedule blood tests and imaging close to home and convert to telemedicine
- Follow-up visit out of study
- Re-staging in metastatic setting when the goal is not to perform surgery with curative intent on metastatic and primary lesions
- Re-staging in third- and fourth-line treatment

**Q: Among patients on routine surveillance, should we consider delaying surveillance scans, carcinoembryonic antigen (CEA) monitoring and surveillance colonoscopy?**

**A:** Strongly consider several months delay of routine surveillance scans, CEA monitoring and surveillance colonoscopies until the pandemic has resolved. Use telephone or telemedicine visits to evaluate patient and assure clinical stability<sup>6</sup>.

**Q: Among asymptomatic patients in whom single-agent capecitabine is being given, should we consider management without routine labs?**

**A:** For patients receiving capecitabine, consider management without routine labs in the absence of symptoms requiring investigation. This would permit treatment at home without extra exposure<sup>6</sup>.

#### **D. Surgical Intervention**

**Q: Among patients with colorectal cancer, how do we prioritize surgical intervention?**

**A:** The ESMO guidelines has classified patients needing surgical intervention<sup>5</sup>.

Patients classified as **High priority** include:

- Radiologically-confirmed intestinal occlusion in newly diagnosed patients
- Patients having bowel perforation and peritonitis
- Patients presenting with massive gastrointestinal bleeding
- Patients presenting with post-surgical complications such as perforation or anastomotic leak
- Patients presenting with post-colonoscopy complications
- Patients with post-interventional procedure complications
- Patients with bone fractures especially those with spinal cord compression due to metastasis

Patients classified as **Medium priority** include:

- Patients who are clinical stage I, II and III colon cancer
- Patients who are clinical stage I rectal cancer
- Patients who are stage II-III rectal cancer after neoadjuvant treatment
- Patients who will undergo resection of metastasis in oligometastatic patients with curative intent as front line or after neoadjuvant treatment

Patients classified as **Low priority** include:

- Patients who are early stage rectal cancer after complete radiological response following radiotherapy
- Patients who will undergo prophylactic surgery
- Patients who will undergo biopsy of metastatic lesions for molecular analysis for late-line treatments. The recommendations are to start last-line options and wait until the end of the COVID-19 pandemic for such for such evaluation and when possible, use liquid biopsies rather than tissue biopsy.

## **E. Treatment: Early Stage Colorectal Cancer**

**Q: How do we prioritize patients needing medical oncologic care?  
How do we address the needs of these patients?**

**A:** The ESMO guidelines has classified patients needing medical oncologic care<sup>5</sup>.

Patients classified as **High priority** include:

- Patients having severe complications due to chemotherapy, radiation, or surgical treatment that will require hospitalization. It is recommended to avoid outpatient visit appointments and should be admitted the earliest possible time.

Patients classified as **Medium priority** include:

- Patients diagnosed as stage II with high risk features who will undergo adjuvant treatment. Fluoropyrimidine treatment should be considered for this group. Capecitabine is preferred over infusional Fluoropyrimidine in order to minimize hospitalization<sup>5</sup>. In patients with very high risk features addition of Oxaliplatin may be considered<sup>14</sup>. In patients with high risk stage II colon cancer, giving Capecitabine plus Oxaliplatin for 3 months may be considered based on the IDEA pooled analysis which showed of 6 months<sup>15</sup>. Molecular testing for MSI and DPD are suggested for treatment decisions.
- Patients diagnosed as stage III with either low and high risk features for adjuvant treatment. The current standard of care for the adjuvant therapy in a stage III colon cancer is a combination of fluoropyrimidine and oxaliplatin<sup>14,16</sup>. Capecitabine plus Oxaliplatin is recommended in order to minimize hospital admission for chemotherapy infusion<sup>5</sup>. The length of oxaliplatin-based adjuvant treatment for stage III colon cancer based on the IDEA data may be tailored to 3 months for Capecitabine plus Oxaliplatin (T1-3 N1 disease), 6 months for Capecitabine plus Oxaliplatin (T4 or N2 disease) or 6 months for FOLFOX (T4 or N2 disease)<sup>14</sup>.

Patients classified as **Low priority** include:

- Patients needing weekly blood tests except in cases where their clinical conditions require them to do so.
- Patients requiring radiological evaluation where risk/benefit ratio should be considered.

## **F. Treatment: Metastatic Colorectal Cancer**

**Q: Among patients with metastatic colorectal cancer, what treatment option can be used as first line?**

**A:** For metastatic disease, consider single agent capecitabine when at all times reasonable, and consider Capecitabine and Oxaliplatin on a 21 day cycle over other 14 day cycle regimen, to reduce contact of the patient with the clinic and chemotherapy unit. Given the added risks of toxicity, leucovorin/fluorouracil/oxaliplatin/irinotecan (FOLFOXIRI) use during this pandemic should only be used in extenuating circumstances<sup>6</sup>. By changing from push-and-pump 5FU to capecitabine for the vast majority of patients, there will be reduction in rates of neutropenia and decrease throughput in chemotherapy outpatient units, reducing requirements for the weekly line flushing, pump disconnections, and other routine maintenance<sup>7</sup>.

If FOLFOXIRI +/- anti-VEGF or anti-EGFR is chosen as first line, it should be administered in the outpatient clinic and given with maximum support to prevent side effects. Consider the application of pegfilgrastim in higher risk patients to prevent neutropenia and hospitalization<sup>5</sup>.

For metastatic MMR deficient (dMMR)/microsatellite instability-high cancer, upfront anti-PD1 therapy instead of cytotoxic chemotherapy. The NCCN Colon/Rectal/Anal/Small Bowel Panel has determined that a standard pembrolizumab dose of 200 mg over an extended dosing interval of every 6 weeks (rather than every 3 weeks) may be feasible. However, it acknowledges that the FDA-approved pembrolizumab regimen for an extended dosing interval is 400 mg flat dose every 6 weeks is recommended<sup>6</sup>.

**Q: Among patients with metastatic colorectal cancer whom maintenance therapy is indicated, what chemotherapeutic options are preferred?**

**A:** Administration of capecitabine instead of infusional 5FU using a 3 week interval is recommended<sup>5</sup>.

**Q: Among patients with metastatic colorectal cancer on chemotherapy who develop grade 3/4 toxicities, what dose adjustments can be made to prevent its recurrence?**

**A:** To reduce the frequency of grade 3/4 toxicities, fortunately in colorectal cancer, there is evidence that dose intensity carries a survival advantage. Therefore, it is to be recommended that for those patients that are being



continued on more intensive regimens, dose modifications by as much as 25% should be made proactively, particularly in the first few cycles<sup>8</sup>.

**Q: Among patients with metastatic colorectal cancer, who are currently on 5FU based chemotherapy, can they continue receiving this combination?**

**A:** Discontinue 5- fluoracil (5FU) bolus/leucovorin combinations for infusional combination regimens that use 5FU infusions as backbone therapy (ie, FOLFOX, FOLFIRI, FOLFIRINOX), most especially when given with palliative intent<sup>9</sup>.

**Q: Among patients with metastatic colorectal cancer with documented disease progression after receiving chemotherapy, what specimen may be used for molecular analysis?**

**A:** When possible, use liquid biopsy for analyses rather than tissue biopsies. If not, start late line options and wait until the end of the COVID 19 pandemic for such evaluation<sup>5</sup>.

## **G. Radiation Treatment**

**Q: Among patients with early and locally advanced colorectal cancer requiring pre-operative radiotherapy, what are treatment options are acceptable as first line?**

**A:** Using only short course pelvic RT is strongly recommended during this pandemic<sup>5,6,10</sup>. Treatment in 5 fractions instead of 28 dramatically decreases the patient's exposure and risks of contracting the virus, and as resources becomes constrained due to technicians and other staff becoming ill, many more patient can be accommodated if the 5-treatment approach is further used<sup>6</sup>. In terms of time gained in the treatment pathway, the 5x5 Gy strategy in short course RT reduces active treatment time to must 5 days compared with the 5-6 weeks with long course chemoradiation, effectively allowing patient and clinician to recover over 30 days of treatment time<sup>10</sup>.

Then, radiotherapy response should be evaluated in the 8th week after radiotherapy. If there is regression with radiotherapy, it will be feasible to prolong waiting period up to 12 weeks or even 16 weeks. In the stage II and III rectal cancer cases, during the waiting period, the consolidation chemotherapy protocol should be discussed in the MDT board<sup>11</sup>. Additional 2-4 cycles of CapeOx may be scheduled for selected rectal cancer patients to increase the odds of pCR when awaiting for the surgery<sup>12</sup>.

**Q: Among patients with metastatic colorectal cancer, who has clear contraindications to systemic therapy but requires management of local symptoms, what treatment options can be offered?**

**A:** Palliative radiotherapy (single fraction or hypofractionated schemes) or stent placement can be offered for symptomatic relief<sup>5,13</sup>. Newer technologies including stereotactic radiosurgery have enabled much shorter treatment schedules and we recommend using these techniques for palliative radiation where available<sup>8</sup>.

#### **H. Multidisciplinary Team Meetings**

**Q: How should we conduct multidisciplinary team (MDT) meetings for colorectal cancer patients during the COVID-19 pandemic?**

**A:** Communication and discussion with other professionals by phone rather than face-to-face is strongly recommended<sup>5</sup>. With this, cancer multidisciplinary team meetings should continue and it is strongly recommended to be done via a virtual platform during this time of pandemic.

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