

## **Recommendations of Systemic Treatment of Cancer Patients During COVID-19 Pandemic**

*Department of Medical Oncology, KCCC*

*13/May/2020*

# Table of Contents

<i>General Recommendations .....</i>	<i>1</i>
<i>Breast Cancer During COVID-19 Pandemic.....</i>	<i>2</i>
<i>Gastrointestinal Cancers During COVID-19 Pandemic .....</i>	<i>4</i>
<i>Lung Cancers and Sarcomas during COVID-19 Pandemic.....</i>	<i>8</i>
<i>Other Cancers During COVID-19 Pandemic .....</i>	<i>10</i>

# General Recommendations for Systemic Treatment of Common Cancers During COVID-19 Pandemic

*Department of Medical Oncology, KCCC*

## Overview & purpose

A group of expert oncologists from different treating units in the department of medical oncology in Kuwait Cancer Control Center (KCCC) compiled recommendations for systemic treatments of common cancers. These recommendations intend to mitigate the challenges facing cancer patients and healthcare providers amidst the global pandemic of COVID-19 infection. Cancer patients are at heightened risk of complications from COVID-19 infection. Special consideration is given toward patients' risk of infection and the galls of treatment. These recommendations still respect the management of each situation on a case-by-case basis and in line with major international recommendations.

## General recommendations

The following recommendations aim to assist physicians to calculate the benefit to risk ratios in their daily practices while respecting the means to reduce the risk of infection:

1. Special consideration should be given to patients at high risk of COVID-19 infection (i.e. Old age, comorbidities or active smokers).
2. Treatment in the curative setting and for patients with aggressive biology disease is considered a higher priority.
3. Consider substituting IV medications with PO or SC options.
4. Consider prescribing protocols requiring less frequent visits over more demanding ones as appropriate.
5. Consider substituting protocols requiring longer durations with shorter duration ones if possible.
6. Contemplate watchful waiting, treatment de-escalation and treatment holiday approaches if appropriate.
7. Telemedicine approaches are more preferable to patient visits.
8. Consider re-filling the electronic prescriptions for stable patients on long term medications.
9. Home delivery of medications is a viable option to reduce patients' traffic and risk of infection.
10. Consider reducing the amount and frequency of investigations as appropriate.
11. Optimize the preservation of healthcare resources to prevent unforeseeable shortages.

# Recommendations for Systemic Treatment of Breast Cancer During COVID-19 Pandemic

*Breast Cancer Unit, KCCC*

## Chemotherapy

1. Priority of treatment is for the curative neoadjuvant then adjuvant and followed by palliative chemotherapy.
2. Triple negative and her2 positive disease are urgent and treatment should be commenced as usual. 4 cycles AC followed by 3 weekly docetaxel with Herceptin SC and peruzumab (only neoadjuvant) and GCSF cover throughout.
3. Avoid dose dense chemotherapy.
4. Weekly taxol should be substituted with 3 weekly docetaxel.
5. Highly myelosuppressive chemotherapy agents should be covered with GCSF support to reduce risk of neutropenia including palliative chemotherapy e.g. Doxorubicin, Docetaxel and cisplatin where myelosuppression is >20%.
6. Herceptin should be given subcutaneously to reduce time of delivery.
7. Adjuvant herceptin should be given for 6 months instead of 12 months, except the very high risk (i.e. LN+ve and ER-ve).
8. Prescribe Adjuvant Pertuzumab only if it was not given in the neoadjuvant setting and for high risk patient only (i.e. LN+ve).
9. Herceptin should be stopped in Any patient with a stable disease for more than 2 years
10. Consider oral navelbine as an option in the treatment of metastatic disease, patients can be prescribed 2 cycles and avoid hospital visits. Patients should have their CBC and LFT checked outside the hospital.

## Hormonal therapy

1. Avoid bringing patients to hospital to continue their prescription.
2. Physicians should only prescribe oral medication If means are available to deliver their medication at home.
3. For any patient on hormonal therapy who is struggling with side effects or other problems like clotting or endometrial abnormality It is a good time to have a break from hormonal therapy. It is proven to be safe to stop hormonal therapy even for up to 6 months.

## Systemic therapy

1. CDK4/6 therapy should only be continued if the patient has been well on it with no neutropenia or G3 side effects. Avoid bringing patients for blood tests in order to decide. If in doubt, do not continue the prescription.

2. Consider prescribing oral medication for 3 months instead of one month if appropriate.
3. Xeloda therapy should only be continued if the patient is well with no G3 side effects.
4. Monthly Xgeva and zometa therapy should be changed to 3 monthly therapy.
5. Monthly 3.6 mg Zoladex injection should be changed to 10.8 mg three monthly.

## Disease monitoring

Use your clinical judgment to assess disease response. If the patient clinically responding, then avoid requesting 3 monthly PET scans. This is crucial to reduce patient visits. If scans are required to restage the disease because of suspected disease progression, then request ultrasound or CT scan instead of PET.

Do not request an annual mammogram for now, we can restart this service once we are out of the pandemic.

## Other issues

The list is non comprehensive and there is no replacement for physician judgment in outweighing the risk and benefit for each patient separately. Physicians should practice their common-sense clinical judgment in decision making, if in doubt please consult with your colleagues. There will be situations where physicians may choose other nonstandard therapy in order to avoid risk of hospital exposure. For example, oral lapatinib over hospital herceptin in the metastatic setting.

## References

1-<https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/breast-cancer-in-the-covid-19-era>

2-[https://www.nccn.org/covid-19/pdf/The\\_COVID-19\\_Pandemic\\_Breast\\_Cancer\\_Consortium\\_Recommendations.pdf](https://www.nccn.org/covid-19/pdf/The_COVID-19_Pandemic_Breast_Cancer_Consortium_Recommendations.pdf)

# Recommendations for Systemic Treatment of Gastrointestinal Cancers During COVID-19 Pandemic

*Gastrointestinal cancer Unit, KCCC*

## General Considerations

1. Aim to eliminate treatments with marginal benefit.
2. Re-evaluate the risk/benefit of continuing treatment in heavily pretreated patients.
3. Adjust investigations requests (Obtain closer to home, reduce frequency to every other cycle if appropriate).
4. Consider doubling dosing time of immunotherapy [i.e. Pembrolizumab 400 mg Q 6 weeks and Nivolumab 480 mg Q 4 weeks]

## I. Colon cancer

### A. Colon cancer: Adjuvant regimens

1. Reassess risk vs. benefit in stage II colon cancer.
2. Consider fluoropyrimidine based treatment for high risk stage II colon cancer instead of platinum doublet.
3. Consider Capecitabine instead on bolus/infusional 5FU
4. Consider CAPOX instead of FOLFOX.
5. For new or ongoing adjuvant therapy, consider early stop (3 months) or switch to capecitabine for the remainder of the duration if possible.
6. In patients already on FOLFOX, dropping the FU bolus is preferable.
7. Consider early discontinuation of oxaliplatin if possible.
8. For patients at high risk of COVID-19 complications, discuss not administering chemotherapy.

### B. Colon cancer: Metastatic setting

#### Colon cancer patients on palliative regimens

1. Case by case, review patients with metastatic incurable disease. observation or low intensity treatment may be considered for stable disease and/or minimal tumor burden.
2. Consider less frequent evaluation for patient on oral chemotherapy and decreased lab investigations for those deemed fit if possible.
3. Encourage to start all regimens with palliative intent with dose reduction (i.e. 25%) to reduce possible toxicity and need for hospital admissions.
4. Discontinue FU infusions in favor of changing to oral capecitabine when possible. For example: consider XELERI in replace for FOLFIRI. Also, CAPOX instead of FOLFOX.
5. Discontinue fluorouracil (FU) bolus/leucovorin combinations for infusional regimens especially when given with palliative intent or aggressive regimens with expected 50% rate of neutropenia (i.e. FOLFIRNOX)

6. For chemotherapy regimens with a high neutropenia potential, consider continued use of prophylactic growth factors or dose reduction to avoid neutropenia.
7. For High-risk chemotherapy (triplet chemotherapy), consider shifting to doublet chemotherapy and/or dose reduction if possible.
8. For oral targeted agents (i.e. regorafenib, sorafenib), consider telemedicine follow up, decrease labs and break from therapy if otherwise stable.

- **Resectable or potentially resectable metastatic disease**

Review case virtually with Hepato-biliary team at baseline & after neoadjuvant chemotherapy, delay surgery until after pandemic or as agreed by MDT.

- **Non-resectable, multiorgan metastatic disease:**

- A. Use monotherapy (capecitabine) or CAPOX ± targeted therapies.
- B. FOLFOXIRI should be reserved for highly selected fit patients (i.e. border line resectable disease or BRAF mutant).
- C. Consider treatment break if stable/minimal disease.
- D. Chemotherapy breaks preferable compared to maintenance treatment.
- E. If maintenance therapy is desired, capecitabine alone is preferred (+/- targeted agent).
- F. If disease is FU refractory, irinotecan ± biologics would be preferred over FOLFIRI.

- **Metastatic colorectal cancer (beyond second-line treatment)**

- A. Consider treatment break if stable disease.
- B. Discuss limited benefit of 3<sup>rd</sup> line vs Covid infection risk.
- C. Regorafenib is preferred over TAS-102 because of the risk of leukopenia and neutropenia and possibility of TAS-102 unavailability.

### **C. Colon cancer patients on active surveillance**

consider tele-medicine review, postpone all routine visits and decrease scans as possible with increase follow up interval (Q6M blood test and Q1year CT for the 5 years surveillance).

## **II. Upper Gastrointestinal malignancies (esophageal, gastroesophageal junction, gastric)**

In the curative setting: discuss cases in MDT about the best sequence of treatment modalities given the risk evaluation of each patient.

## **III. Pancreas**

- 1- Palliative intent: For patients with metastatic, locally advanced pancreatic cancer consider omission of D8 of gemcitabine with nab-paclitaxel with maintaining both drugs on days 1 and 15 to avoid nadir expected with D8.

- 2- FOLFIRINOX should be reserved for highly selected fit patients (i.e. border line resectable disease, young and fit)

#### **IV. Liver Cancer**

- 1- Most of patient on oral medications can be reviewed through phone.
- 2- Consider treatment break for stable patients.
- 3- Evaluate patient comorbidities, risk of COVID-19 infection vs benefit from treatment.  
Discuss Best supportive care with patient especially with Child Pugh score C.

#### **V. Neuroendocrine tumors**

##### **1- Well-differentiated low-grade**

- A. Consider holding or increasing injection intervals to avoid clinic visits if no symptoms.
- B. Use Subcutaneous octreotide, and/or other anti-diarrheal medications in patients with functional tumors.
- C. Consider breaks in stable patient.
- D. Defer Lu177 dotatate if clinical situation allows.
- E. If treatment is already initiated, extend intervals between cycles and/or stop around 4 cycles if appropriate).
- F. Judicious use of liver directed therapy in progressing and/or symptomatic patients.

##### **2- Poorly differentiated, high grade gastroenteropancreatic neuroendocrine carcinomas (NEC)**

###### **A. Localized disease**

Depending on comorbidities & goals of care, consider adjuvant or neoadjuvant treatment. Use growth factor and reduce chemotherapy dose if necessary.

###### **B. Metastatic 1<sup>st</sup> Line**

Proceed with platinum-based therapy, maximum 6 cycles if stable. Use growth factor and dose reductions if necessary.

###### **C. Beyond 1<sup>st</sup> Line [Salvage Setting]:**

Individualize therapy considering, likelihood of response, Patient's tolerance & risk of COVID-19 complications.

#### **VI. Gall bladder carcinoma and cholangiocarcinoma**

##### **Adjuvant setting**

Adjuvant capecitabine is preferable

##### **Metastatic disease**



Options may include: Gemcitabine plus cisplatin, capecitabine plus gemcitabine, Capecitabine plus oxaliplatin or Capecitabine alone.

## References

1. American Society of Clinical Oncology : General care of patients with cancer during the COVID-19 pandemic. [https:// www.asco.org/asco-coronavirus-information/care-individuals-cancer-during-covid-19](https://www.asco.org/asco-coronavirus-information/care-individuals-cancer-during-covid-19).
2. Ahn DH, Krishna K, Blazer M, et al: A modified regimen of biweekly gemcitabine and nab-paclitaxel in patients with metastatic pancreatic cancer is both tolerable and effective: A retrospective analysis. *Ther Adv Med Oncol* 9(2):75-78, 2017.
3. Kokkali S, Tripodaki E-S, Drizou M, et al: Biweekly gemcitabine/nab-paclitaxel as first-line treatment for advanced pancreatic cancer. *In Vivo*. 32(3): 653-657, 2018
4. Gonzalez H, Hagerling C, Werb Z: Roles of the immune system in cancer: From tumor initiation to metastatic progression. *Genes Dev* 32(19-20):1267-1284, 2018
5. Lefevre JH, Mineur L, Kotti S, et al: Effect of interval (7 or 11 weeks) between neoadjuvant radiochemotherapy and surgery on complete pathologic response in rectal cancer: A multicenter, randomized, controlled trial (GRECCAR-6). *J Clin Oncol* 34:3773-3780, 2016.
6. Capecitabine plus oxaliplatin versus gemcitabine plus oxaliplatin as first-line therapy for advanced biliary tract cancers: a multicenter, open-label, randomized, phase III, noninferiority trial S. T. Kim. *Annals of Oncology* 30: 788–795, 2019  
doi:10.1093/annonc/mdz058 Published online 20 February 2019

# Recommendations for Systemic Treatment of Lung Cancers and Sarcomas during COVID-19 Pandemic

*Thoracic and Sarcoma Unit, KCCC*

## I. LUNG CANCER:

1. Curative-intent systemic therapy (i.e.: adjuvant, neoadjuvant, concurrent) should continue uninterrupted for patients with Non-Small Cell Lung Cancer (NSCLC) as well as chemotherapy +/- immunotherapy for small cell lung cancer.
2. Use of extended interval immunotherapy for (Nivolumab & Pembrolizumab) given the visit frequency and duration for Nivolumab every 4 weeks and for pembrolizumab every 6 weeks instead of 2- or 3-weekly and this should carefully be discussed with the patient.
3. For patients ongoing with immunotherapy from more than 12/18 months, delaying the next cycle, omitting some scheduled cycle or generally enlarging intervals should be considered.
4. Holding immunotherapy for responders after 2 years in frontline metastatic NSCLC, as per the frontline clinical trials.
5. For patients ongoing with immunotherapy having stopped due to toxicity, resuming might be delayed in absence of disease progression
6. For unresectable stage III NSCLC patients treated with concurrent definitive chemo/RT, consider delaying consolidation immunotherapy with durvalumab, for up to 6 weeks following completion of chemoradiation.
7. With respect to the systemic therapy bookings, priority should be given to patients who achieved disease control by standard of care modalities.
8. Weekly Taxol and Docetaxel should be substituted with 3-weekly schedule provided that the patient tolerates this schedule.
9. Appropriate use of neutrophil growth factor support in high-risk patients should continue and might be liberalized to include those with intermediate risk.
10. All targeted therapies should be supplied for at least 2 months and avoid unnecessarily clinic visits if there is no new medical reasons or issues.
11. Treatment interval prolongation or deferring doses may be more reasonable in the metastatic setting, although efforts should be made to continue treatment on schedule.

## II. Sarcoma:

1. Chemotherapy schedules may be modified to reduce clinical visits (for instance, using 3-weekly dosing instead of weekly dosing for selected agents when appropriate).
2. Patients should receive G-CSF/EPO growth factor and, eventually, antibiotic support to minimize neutropenia.
3. Dexamethasone use should be limited as appropriate.
4. Curative intent systemic therapy (the adjuvant and neoadjuvant chemotherapy) is considered a higher priority than palliative intent treatment.
5. After failure of second line treatment, Oral systemic therapy (i.e. pazopanib) should be considered over IV chemotherapy if possible.

6. Consider managing some of the predictable and manageable toxicities from oral systemic therapy via telemedicine.
7. Refilling of TKIs for longer durations may be considered for stable GIST patients without symptoms or toxicities.
8. Still we are considering hospital admission for patients who are allocated for VIDE protocol.
9. We are considering restarting the multidisciplinary tumor board for the sarcoma team through virtual meeting and to involve all the required specialties.

## References

1. National comprehensive cancer network. Coronavirus Disease 2019 (COVID-19) Resources for the Cancer Care Community. Available at: <https://www.nccn.org/covid-19/> (1st April 2020, date last accessed).
2. <https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/lung-cancer-in-the-covid-19-era>.

# Recommendations for Systemic Treatment of Other Cancers During COVID-19 Pandemic

*Other Cancers Unit, KCCC*

## General Considerations

1. Highest priority for chemotherapy treatment is in the curative setting and for aggressive biology disease with the rapid tumor turn over (i.e. Germ Cell Tumors, gestational trophoblastic disease and choriocarcinoma, bulky, symptomatic and high-volume disease burden).
2. Asymptomatic patients with non-aggressive and minimal disease burden could be postponed for a month with no expected negative impact on disease outcome.
3. Delay all treatments beyond first-line therapy with expected modest efficacy (unless there are urgent clinical reasons), maintenance therapies and treatments in patients with low disease burden and slow progression
4. Delay imaging procedures to monitor treatment response (unless there are urgent clinical reasons)
5. Consider the usage of longest interval among the standard protocols.
6. Consider doubling dosing time of Immunotherapy [i.e. Pembrolizumab 400 mg Q 6 weeks and Nivolumab 480 mg Q 4 weeks].
7. Monthly Xgeva and zometa therapy should be changed to 3 monthly therapy.

### I. Prostate Cancer:

Oral antiandrogen preferred instead of docetaxel for mHSPC and mCRPC (abiraterone or enzalutamide)

mCRPC: docetaxel with G-CSF Q3week preferred instead of docetaxel Q2 weeks

### II. Ovarian cancer

chemotherapy paclitaxel + carboplatin Q 3 weeks preferred to weekly.

No further maintenance bevacizumab

### III. Uterine cancer

Adopted PROTEC 2 result for adjuvant where chemotherapy is equal to CT/RT in subgroup of patient with intermediate risk factor uterine cancer.

### IV. Cervix cancer

Palliative chemotherapy had the strongest evidence for Avastin with carboplatin and Taxol so the priority to keep it or delay for later cycles sessions after Covid -19

crisis subsidence.

## **V. Bladder cancer**

In the neoadjuvant setting, consider giving cisplatin and gemcitabine with G-CSF  
carboplatin is more preferred in the palliative setting due to its relatively favorable toxicity profile

## **VI. Glioblastoma multiforme**

Consider best supportive care beyond the failure of second line treatment

## **VII. Head and neck squamous cell carcinoma**

For recurrent and metastatic disease, consider replacing ETREME protocol with TPEx protocol. use carboplatin plus paclitaxel or carboplatin plus capecitabine as preferable choices for induction chemotherapy instead of TPF.

## **References:**

1. <https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic>
2. Masumi Ueda MD, MA et al: Managing Cancer Care During the COVID-19 Pandemic: Agility and Collaboration Toward a Common Goal Online Publication Date: Apr 2020 DOI: <https://doi.org/10.6004/jnccn.2020.7560>
3. Lambertini M, Toss A, Passaro A, et al. Cancer care during the spread of coronavirus disease 2019 (COVID-19). <https://esmoopen.bmj.com/content/esmoopen/5/2/e000759.full.pdf>