

**PHILIPPINE SOCIETY OF MEDICAL ONCOLOGY (PSMO)  
CONSENSUS RECOMMENDATIONS IN THE MANAGEMENT OF HEAD AND NECK  
CANCERS DURING COVID-19 PANDEMIC IN THE CORONAVIRUS DISEASE 2019  
(COVID-19) ERA**

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## **Background and Content:**

COVID-19 is a highly contagious disease with a mortality rate of 1-2%. Its cause, the coronavirus, may enter or reside and rapidly replicate in mucous membranes which are the sites of head and neck carcinoma (HNC).<sup>7</sup> The management of HNC might pose often potential viral exposure to the healthcare team involved and many patients with HNC are at high aerosolization risk after treatment due to dysphagia and/or airway compromise. This could potentially expose their close contacts and health care providers to the aerosolized virus. All these characterizes the unique situation in treating these cancers during this era.<sup>4</sup>

HNSCC in the Asia Pacific region has an overall incidence of approximately 300,000 new cases per year, which is more than half of the total cases worldwide.<sup>16</sup> It is a deadly disease with a mortality of 40-50% range if untreated. There is evidence of a 16% increased risk of death for every month of delay of radiation therapy. In the recommendation on the “Guidance on decisions about immediate cancer treatment during the COVID-19 crisis”, HNC belong in the high-risk category of progression should cancer care be delayed.<sup>1</sup> Similarly, concurrent chemoradiotherapy as definite curative treatment for Head and Neck has been placed at the 3<sup>rd</sup> highest level of priority in the conceptual framework for prioritizing the use of radiotherapy and systemic treatments during the COVID-19 pandemic.<sup>2</sup>

The following recommendations are composed of gathered collective recommendations modified for local use as to screening, diagnosing and managing of patient with HNC during this COVID-19 pandemic to reduce morbidity and mortality of the patients while maintaining the safety of the health care workers.

## **Goals and Objectives:**

To provide local guidance on the management of Head and Neck Cancer in the COVID-19 era

**Target Users:** These recommendations are intended for the use of medical oncologists taking care of Head and Neck cancers in the Philippines

## **Related Guidelines:**

- American Society for Radiation Oncology (ASTRO)
- American Society of Clinical Oncology (ASCO)
- Canadian Association of Head & Neck Surgical Oncology (CAHNSO)
- European Society for Medical Oncology (ESMO)

## RECOMMENDATIONS

### HEAD AND NECK CANCERS

#### DIAGNOSIS AND STAGING<sup>6,8,9</sup>

1. Who should be seen for outpatient consultations?

Outpatient, clinic and office consultations should be limited to urgent or emergent referrals or high suspicion for malignancy. Restrict all patient face to face patient assessments to urgent and emergent interactions.

2. Should a triage referral system be considered?

A triage referral system, if possible, telemedicine or virtual system, should be in place to screen for referrals with prioritization of those with a high risk of cancer and to screen for patients who should avoid the outpatient visit and must be referred to the emergency room

3. What are the considerations to be made in the diagnostic procedures?

- a. Upper aerodigestive endoscopy should be considered an Aerosol Generating Medical Procedure (AGMP), which, should only be performed when necessary and appropriate Personal Protective Equipment (PPE) should be worn.
- b. It is recommended to refrain from performing frozen sections on possible cases of 2019-nCoV unless the institution's laboratory is confident in containing aerosols in the cryostat.
- c. Diagnostic work up including imaging and biopsies should be limited to those cases with a high risk of malignancy.
- d. PET CT scan can replace the traditional workup of CT scan chest and upper abdomen for detection of distant metastases in NPC since it has proven to be the most sensitive, specific, and accurate diagnostic method, and this can be considered for at risk patients (node positive disease, especially N3 disease).

#### GENERAL CONSIDERATIONS<sup>4, 11</sup>

1. Should we consider Multidisciplinary Team discussions (MDT) during COVID-19 pandemic?

It is recommended to do MDT assessment of multilevel surgical risk and alternatives to surgery for each case followed by shared decision-making with the patient. Traditional, standard of care treatments should be observed whenever reasonable. Deviation from the traditional standard of care may be appropriate or necessary in light of the current, extraordinary circumstances. These decisions are

likely to be highly patient-, surgeon-, and institution-specific, depending on the available resources.

2. Is COVID19 testing recommended for Head and neck cancer patients about to undergo treatment or with ongoing treatment?

COVID19 testing as per institutional guidelines may be sought out for all patients undergoing treatment or pretreatment in accordance with the institution's availability, accuracy, and type of testing.

3. What is the recommendation on the health team's protection in handling patients with Head and neck cancer during the COVID19 pandemic?

The oncology chemotherapy unit and radiation unit personnel, and the surgical team for patients undergoing surgery that requires manipulation of the upper aerodigestive tract should be in appropriate personal protective equipment that would include at the least, gown, N95 masks, face shield, and gloves.

## TREATMENT

### Nasopharyngeal Cancer

<b>Table 1. Prioritization of Radiation Treatment start date based on Treatment Indication</b>		
<b>Priority</b>	<b>Description</b>	<b>Example Cases</b>
Priority I	Cases where a delay of treatment may result in a loss of life, progression of disease, or a permanent loss of neurologic or other function. These patients are to be assessed and managed accordingly.	<ol style="list-style-type: none"> <li>1. Oncologic emergencies</li> <li>2. Advanced head and neck</li> <li>3. Advanced gastrointestinal</li> <li>4. Advanced gynecologic</li> <li>5. Advanced lung</li> </ol>
Priority II	Cases that may be delayed for up to 4 weeks, and delay in treatment is unlikely to result in a loss of life or negatively affect a patient's prognosis.  If a patient's treatment is deferred, waiting lists should be created for priority II patients requiring treatment. These waiting lists will be reviewed at least weekly depending on the overall situation and the availability of treatment slots.	<ol style="list-style-type: none"> <li>1. Early stage head and neck</li> <li>2. Early stage lung</li> <li>3. Lymphoma</li> <li>4. Brain SRS of benign diseases</li> </ol>

Priority III	<p>Cases that may be delayed for 30 days or more, where such delay in radiation treatment is unlikely to result in a loss of life or negatively affect a patient's prognosis.</p> <p>If a patient's treatment is deferred, waiting lists should be created for priority III patients requiring treatment. These waiting lists will be reviewed for pending treatment accordingly and the patients contacted for follow-up as needed.</p>	<ol style="list-style-type: none"> <li>1. Early stage prostate</li> <li>2. Early stage breast</li> <li>3. Prostate on androgen deprivation</li> </ol>
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### A. Radiation therapy<sup>1, 2, 4, 5, 12, 13</sup>

1. What is the level of priority for NPC patients for radiation treatment, and when is the optimal timing for their RT?

A tiered system of prioritization (Table 1) was developed by ASTRO and Advanced HNC was given a priority 1 classification. This means, radiation or concurrent chemoradiation is of curative intent and a delay may result in a loss of life, progression of disease, or a permanent loss of function. Early HNC was given a priority 2 classification. NPC patients should receive planned RT without unnecessary delays, provided there is full compliance with the safety regulations of the institution for both patients and staff members.

2. Should RT dosing and scheduling modifications be made?

Short course hypofractionated RT is preferred when feasible to reduce the frequency of clinic visit. Conservative (smaller) RT fields are preferred, if possible, to minimize RT-induced lymphopenia and reduce mucosal toxicity.

3. What are the recommended pretreatment and on treatment management considerations for RT adverse effects?

Early interventions include weekly CBC, Early use of pain medication/management, mouth rinses, nutritional supplement shakes and dietary evaluation. To reduce hospitalizations, when dysphagia begins, IVF hydration or fluid bolus by PEG 2x/weekly during chemoradiation, NGT placement if weight loss or otherwise meeting criteria for PEG and consider treatment break of < 1 week for refractory Grade 3 symptoms.

4. What are the recommendations for palliation?

For patients receiving treatment for palliation, the recommendation is to exhaust all other options, such as maximizing analgesia, prior to pursuing radiotherapy.

**B. Chemotherapy<sup>2, 10</sup>**

1. Can the dose of IV chemotherapy concurrent with radiotherapy be reduced?

The aggregation of people in the infusion center and impaired immunity of patients undergoing radiotherapy and chemotherapy has been considered thus minimizing intravenous infusion with serious adverse reactions has been suggested.

Patients who received concurrent chemotherapy might experience severe hematologic toxicities and gastrointestinal reactions, so the completion rate of concurrent chemotherapy was lower than before.

Although current evidence reports that 200 mg/m<sup>2</sup> of concurrent Cisplatin could be the optimal cumulative dose for the NPC patients who achieved response after induction chemotherapy with patients receiving higher cumulative dose of cisplatin showing significantly improved 3-year progression-free survival (PFS) and distant metastasis-free survival (DMFS) compared with lower dose patients, other studies have also retrospectively reported that IMRT alone has achieved similar survival outcomes compared with concurrent chemoradiotherapy in locally advanced NPC patients. During COVID, the reduction of concurrent platinum dose has been suggested, but its long term effects on patients' outcome still needs to be closely followed up in future.

2. Can conversion of intravenous to oral systemic regimens be considered?

To reduce the frequency of clinic visits and inherent risks, conversion of intravenous to oral systemic regimens can be considered.

**C. Surgery**

1. How do we prioritize NPC patients for surgical procedures?

As surgical indications for NPC is conventionally recommended for recurrent disease, this premise is still to be maintained during the COVID19 pandemic. In addition, expedition of the surgical management is warranted for NPC patients presenting with impending airway compromise.

## **Head and Neck Squamous cell Carcinoma**

### **A. Surgery<sup>11</sup>**

1. What are the recommendations for Primary and recurrent mucosal SCCs traditionally treated with surgery?

In low-risk patients with oral cavity or sinonasal cancers for whom a brief postoperative admission is anticipated, the benefits of primary surgery may outweigh the risks. However, in high risk and advanced cases including laryngeal cancers and salvage surgery patients, a prolonged hospital admission and/or tracheostomy or laryngectomy and/or free-tissue transfer might be required. Intraoperative and postoperative risk of SARS-CoV-2 transmission will be high in these settings. For these patients, the risks of surgery should be weighed against the risks of traditionally substandard, alternative therapies and their corollary perceived compromises in oncologic efficacy. Primary surgery should remain the default treatment and should be chosen whenever reasonable. Conversely, multilevel surgical risks may sufficiently impair, or even prohibit, safe and efficacious surgery along with the safe care of patients postoperatively.

In these circumstances, traditionally substandard alternative therapies may be preferable. Primary radiation ± chemotherapy may be selected for oral cavity, T4a laryngeal or advanced sinonasal SCC patients. Patients opting for nonsurgical therapy must be aware of the inferior oncologic outcomes and anticipated increased morbidity of this treatment compared to primary surgery.

In certain salvage cases, definitive re-irradiation may be a reasonable alternative to surgery, particularly if the patient has experienced a prolonged disease-free interval. Re-irradiation ± chemotherapy preserves the possibility of cure, although with substantial concomitant treatment toxicity. Among some patients who later fail re-irradiation, a durable disease-free interval may allow for surgical salvage when the COVID-19-specific risks of surgery have been mitigated.

2. Are there recommendations for delays in surgery?

Urgent head and neck oncologic surgery will still be the best treatment option for many patients but during this pandemic, institutions may reasonably employ a short-term delay in all non-emergent oncologic surgeries to ensure appropriate patient screening and perioperative planning for patient and HCW safety. In this interval, surgeons and institutions should rapidly develop COVID-19-specific protocols to provide safe, quality surgical care for head and neck oncology patients.

### **B. Radiation therapy<sup>14, 5</sup>**

1. What are the recommended pretreatment strategies to be performed?

In patients who are considered candidates for RT alone, treatment may be started with hydration, minimizing the risk of hospitalization by excellent nutritional

support and social support. Pretreatment dental evaluation should be performed if possible and patients must be educated of the associated risk of osteonecrosis and worsening dentition in patients on RT. Dental guards can be used to reduce electron scatter and reduce toxicity.

2. What are recommendations for older patients (>70 years old) who are unable to undergo surgery or concomitant chemoradiation for the advanced disease?

These patients may be treated with hypofractionated RT or SBRT, 35 -44 Gy in five fractions delivered every other day. RT plans should be conformal, keeping the mandible and dental dose as low as reasonably possible. In these situations, the gross tumor should be covered as a part of the primary planning target volume (PTV) and the elective nodal region avoided to minimize the risk of severe toxicity that may result in hospitalization. Although RT should be completed in the shortest possible time, older patients that develop toxicities may need to be given a break from treatment to decrease risk of hospitalization.

3. What are the recommendations for RT for each site?

a. Oropharyngeal Cancer

- Human papillomavirus (HPV)-associated: RT alone is an option for early-stage disease (70 Gy in 2 Gy/fraction).
- HPV-negative disease: concomitant chemo-RT is standard of care, with modified chemotherapy/targeted dose regimens. If chemotherapy is not possible, RT alone (using altered fractionation, dose-escalation, or SBRT) may be appropriate

b. Laryngeal Cancer

- Supraglottic, subglottic and hypopharyngeal cancers: EBRT alone may be utilized (70 Gy in 2 Gy per fraction)
- Glottic cancers: RT to 63 Gy in 28 fractions is the standard and should be followed

c. Salivary Gland Cancer

Although primary surgery is the preferred treatment for salivary gland cancers, if the patient is unable to wait or the tumor is progressing, EBRT (70 Gy in 2 Gy/fraction) or SBRT (35 - 44 Gy in five fractions) may be utilized. Therefore, delaying treatment

d. Oral Cavity Cancer

Oral cavity cancers are primarily managed with surgery, and efforts should be made to wait if surgery cannot be performed immediately. Other options include induction chemotherapy, preoperative radiation, or definitive EBRT/SBRT. Preoperative RT is a good option if surgery is being considered within four to six weeks after completion of RT (50 Gy in 2 Gy/fraction).

4. What are the considerations in postponing initiation of RT?

Do not postpone RT by more than 4 to 6 weeks in the ff cases:

i. Oropharyngeal SCC

- ii. Laryngeal SCC, T3N1M0 with impaired vocal cord mobility
- iii. Metastatic hypopharyngeal SCC, T4aN1M1-obstructed, bleeding, with several lung metastases
- iv. Resected oral cavity SCC, pT2N2aM0 with positive margins

5. What are the recommendations on post-operative HNC?

For high-risk HNC post-resection, adjuvant RT alone may be preferred to chemoradiation to limit toxicity (54 - 66 Gy in 1.8 - 2 Gy/fraction). For patients with multiple nodes, extracapsular extension (ECE), and other high-risk features where adding chemotherapy is the standard, modified chemotherapy doses or less toxic regimens may be used. If adding chemotherapy puts the patient at risk of potential hospitalization, RT alone may be the preferred approach.

6. In the case of a patient testing positive for SARS-CoV-2 infection, what are the recommendations in delaying the initiation of radiation therapy until the patient had recovered?

In patients with COVID19 mild symptoms who had completed more than 2 weeks of treatment, there was strong agreement to continue radiation therapy. For patients demonstrating more severe symptoms (cough, chest pain, resting dyspnea and hypoxemia), the recommendation is to hold RT until the patient had fully recovered.

There might be institutional policies to interrupt RT even in patients with mild COVID symptoms and this might be considered as well, for the following reasons:

- a. concern for worsening the patient's respiratory and general condition
- b. increased likelihood of emergency admission and/or need for feeding tube insertion
- c. risk of infecting other patients and staff

### C. Chemotherapy<sup>11, 17</sup>

What are the recommendations for neoadjuvant chemotherapy in HNSCC?

Neoadjuvant chemotherapy ± Cetuximab or neoadjuvant chemotherapy ± immunotherapy may be considered, in certain settings, at this time.

While induction chemotherapy does not have a role in the routine management of primary or recurrent mucosal SCC treated with surgery, it may provide symptomatic relief and effectively delay the need for surgery for a while. Systemic therapy may successfully buy enough time to allow the patient to receive the preferred radical surgical approach.

Decisions to administer immunosuppressive therapy during a pandemic are complicated, since patients with occult SARS-CoV-2 infection would likely experience significant if not fatal complications from the disease.

Although systemic therapy without immunosuppression may seem attractive during a pandemic, there is insufficient evidence to guide the use of

induction immunotherapy without chemotherapy for primary or recurrent, resectable mucosal SCC patients at this time.

The three-drug TPF (Docetaxel, Cisplatin, 5FU) regimen has better outcomes compared to the 2 drug 5FU-platinum regimen. However, the use of both these regimens requires the administration of continuous infusion of 5FU and is associated with high risk of grade 3 or above adverse events.

Weekly paclitaxel-carboplatin regimen as NACT in HNSCC has been used in poor performance status patients and those with multiple comorbidities. This regimen was found to be safe, has a response rate of 66% and produces limited immunosuppression. Hence, this schedule appears to be a good option in the current situation.

The use of Cisplatin 30 mg/m<sup>2</sup> weekly was found to be inferior to 100 mg/m<sup>2</sup> given every 3 weeks in terms of lower locoregional control. However, the disease-free survival and overall survival were similar. The use of 3 weekly cisplatin was associated with higher in-hospital admissions and adverse events. In view of the lack of overall survival benefit and resource-consuming nature of the 3 weekly regimens, in the current pandemic, weekly cisplatin dosed at 30–40 mg/m<sup>2</sup> can be used.

## **FOLLOW-UP** <sup>3,5</sup>

What are the recommendations for follow-up?

The goal of early detection of potentially curable locoregional recurrence and/or secondary tumors with follow-up remains the same and follow-up protocols may still be followed, provided safety protocols for COVID19 are in place. The following are recommended:

- a. Patients with a scheduled follow-up visit who report suspected symptoms are encouraged to contact their physician to reschedule their visit. Physicians are also encouraged to reemphasize on giving proper education to patients on the expected side effects of treatment. This allows patients to seek consult appropriately and only when necessary.<sup>3</sup>
- b. Follow-up visits can be suspended for 2 weeks pending decisions related to the evolution of the epidemic.
- c. Patients who have recently completed radiotherapy may have their follow-up appointments safely delayed by two or more months, with telemedicine as needed.

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