Cancer in the context of COVID-19: Summary of emerging evidence (9)

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The CRI presents a selection of emerging research articles and clinical practice guidelines related to cancer and COVID-19, with a summary of their key findings/recommendations (links to the articles are embedded as hyperlinks in the titles). This is the ninth of our weekly compilation, which we plan to update and disseminate as the pandemic evolves globally and nationally.

This week, we highlight latest research related to oncology services in COVID-19 outbreak contexts, including in resource-constrained settings. We hope that insights from these pieces of evidence will help guide how we rethink cancer prevention, treatment and care in the context of the ongoing pandemic, in view of its unprecedented implications for patients, healthcare providers and the community in general. We are keen to include research and guidelines from African settings and will profile these as they become available. Previous weeks' editions can be found on the **CRI website,** as well as on **our Twitter page (@UctCri).**

Pino et al. Cancer Center Recommendations to Mitigate COVID-19 Impact in Patients With Cancer: Low-Resource Settings Version. JCO Global Oncology. DOI: 10.1200/GO.20.00093

Country context: Global

In this letter to the editor, the authors recommend ways by which cancer centers in low-resource settings can mitigate the incidence and impact of COVID-19 in their contexts. The recommendations are summarised below:

1. Social containment is the key. Cancer centers must move to virtual assistance through technological platforms to give telemonitoring and tele-assistance, especially to controlled and older patients, to ensure they stay at home.
2. Tumor boards and scientific meetings must move to virtual modalities
3. Prioritise and switch noncurative medical and surgical treatments. This means a change of immunotherapy schedules to 4 weeks (nivolumab, pembrolizumab) or even 6 weeks (pembrolizumab off-label) for selected patients. Switch to oral therapies for advanced cases with intravenous treatments. Temporarily discontinue noncritical therapies, such as bisphosphonates or denosumab, and optimise devices such as on-body injector pegfilgrastim to avoid the return of the patients the next day to the clinic.
4. Use strict selection of patients for in-hospital chemotherapy. This must be offered only to curative-intent treatments with higher-toxicity combinations (acute leukemias, high-grade lymphomas, soft tissue sarcomas).

5. Give long-term (6 months) formulations to patients in long-term oral treatment, such as hormonal therapies. For patients with prostate cancer using oral therapies, the follow-up can move to every 2 months.
6. All patients attending the cancer center must enter into a COVID-19 protocol to measure body temperature before entrance and to initiate the diagnostic process in case of symptoms. Cancer centers must have COVID-19 diagnostic tests on site.
7. Optimise protective measures for the health care team.
8. Standardise with the infectious disease, bioethics, and intensive care unit departments the entry criteria of patients with cancer according to their prognosis. Patients and their families must be informed about institutional protocols to step down medical interventions and prioritise support and palliative care in-house.
9. In hospices, where available, this infrastructure can be adapted as expansion for critical oncological care for selected patients who will be treated according to protocols and entry criteria.
10. Create a population registry of this cohort of COVID-19–positive patients with cancer to define clinical characteristics, disease dynamics, response to therapies, and outcomes that can enhance data about this special group of patients and refine institutional protocols.
11. Where available, cancer centers must create a digital platform to enhance patient, caregiver, health authority, and health care team integration; data and information flow; and even telemedicine to accomplish the previous activities in a better way.

Marron et al. Ethics and Resource Scarcity: ASCO Recommendations for the Oncology Community During the COVID-19 Pandemic. Journal of Clinical Oncology. DOI: 10.1200/JCO.20.00960 Journal of Clinical Oncology

Country context: USA

This paper provides an ethical framework for guiding the allocation of cancer and other health care resources during the COVID-19 pandemic, such as the rationing of ventilators, critical and intensive care beds, and medications for patients with cancer. The recommendations are summarised as follows:

- Allocation of scarce resources in a pandemic should be based on maximising health benefits.
- A fair and consistent prioritisation and allocation policy should be developed before allocation becomes necessary.
- The Hastings Center's "Ethical Framework for Health Care Institutions & Guidelines for Institutional Ethics Services Responding to the Coronavirus Pandemic" should be used as a model for approaching ethical decision making in the context of COVID-19 and resource shortages.
- Another useful framework, which provides practical guidance for those making difficult decisions under conditions of severe shortage, is the University of Pittsburgh's "Allocation of Scarce Critical Care Resources During a Public Health Emergency" with the following clarification regarding multiprinciple scoring systems:

        - If a policy takes preexisting life-limiting diseases into account, it should do so consistently across types of disease and should consider evidence-based information regarding life expectancy.
        - All cancer diagnoses and prognoses should be considered individually, with input from the treating oncologist. Cancer diagnosis alone should not be considered terminal, even for patients living with advanced or metastatic disease. Consideration of cancer as either a major or severely life-limiting comorbidity should reflect evidence-based factors, including the individual patient's clinical status and prognosis.
- Decisions regarding allocation of scarce resources should be separated from bedside decision making. The oncologist caring for a patient should not make scarce resource allocation decisions about that patient.
- Oncologists should work with their institutions on how best to use scarce resources for care and support of patients with cancer.
- Oncologists should communicate allocation plans and decisions to their patients with compassion and honesty, and health care institutions should offer support to oncologists in these communications.
- Oncologists should engage in advance care planning discussions with their patients and carefully document patient preferences for goals of care, particularly end-of-life care.

Issaka et al. Colorectal Cancer Screening and Prevention in the COVID-19 Era. JAMA Health Forum

Country context: USA

This opinion piece highlights the problems that may result from delaying colorectal cancer screening, including delayed diagnoses, worse clinical outcomes and higher mortality. To avert these problems, the authors recommend that cancer care organisations and providers should leverage the mailed fecal immunochemical test (FIT), which is an inexpensive, at-home colorectal cancer screening method that checks for blood in stool and can be returned by mail.

To ensure that mailed FIT outreaches do not increase existing colorectal cancer screening disparities, it is recommended that implementation strategies should proactively apply a health equity lens in the following ways:

1. Prioritise mailed FIT outreach for individuals who are not up to date with screening.
2. Ensure mailed FIT outreach includes all individuals within a health care system regardless of health plan or associated incentives, and
3. Support passing policies waive co-insurance for follow-up colonoscopy completion after abnormal FIT results.

It is also recommended that primary care physicians and gastroenterologists maintain momentum in decreasing colorectal cancer mortality within health care organisations by taking the following steps:

1. Advocate for establishing mailed FIT outreach programs, with an eye toward health equity, that can be executed by medical administration with modest physician oversight (Gupta et al, unpublished data, 2020).
2. Set clear expectations that follow-up colonoscopies for abnormal FIT results will receive priority scheduling after the moratorium on screening colonoscopies is lifted.
3. Create workflows to track patients with abnormal FIT results until colonoscopy is completed.
4. Increase gastroenterology staffing to accommodate the expected surge in procedural demand.
5. Offer evening or weekend colonoscopy sessions to enable patients and gastroenterologists to alleviate colorectal cancer screening and surveillance backlogs.

Sean Ong et al. Safety first: evidence for delay of radical prostatectomy without use of androgen deprivation therapy during COVID-19. Future Oncol. Doi: 10.2217/fon-2020-0388

Country context: Global

This paper reviews available evidence on the delay of radical prostatectomy in patients with prostate cancer. It summarises findings from the literature, showing that low risk prostate cancer can be safely monitored without intervention; which can be explored in a crisis setting like the COVID-19 pandemic. However, it also notes that intermediate risk and high risk cancers pose a different challenge. For patients who have more than 10 years life expectancy, the authors note that studies have shown that receiving either radical prostatectomy or radiation therapy reduces mortality, when compared with watchful waiting. In addition, they recommend approaches to prostate cancer prioritization and treatment modification.

Boulad et al. COVID-19 in Children With Cancer in New York City. JAMA Oncology. Doi: 10.1001/jamaoncol.2020.2028

Country Context: USA

This study presents findings from the screening and testing of children and their caregivers at a large paediatric cancer centre. Of the children who were screened for exposure and symptoms of COVID-19, the rate of positivity for SARS-CoV-2 was 29.3%. By comparison, in the 120 asymptomatic patients without known exposure, the rate of SARS-CoV-2 positivity was only 2.5%. Only 1 child with COVID-19 illness required noncritical care hospitalisation for COVID-19 symptoms. Three other patients without significant COVID-19 symptoms were admitted for concomitant fever and neutropenia, cancer morbidity, or planned chemotherapy. All other paediatric patients had mild symptoms and were managed at home. The table below presents a summary of key findings:

Table 1. Results of COVID-19 Testing at Memorial Sloan Kettering (MSK)

Variable	No.	SARS-CoV-2 positive, No. (%)
March 10-April 12, 2020		
Total pediatric outpatient visits	1267	
Total unique patients	505	
Total pediatric patients swabs	244	25 (10.2)
Total pediatric unique patients	178	20 (11.2)
Total unique patients screen positive or symptom positive	58	17 (29.3)[a]
Total unique patients screen negative and symptom negative	120	3 (2.5)[a]
Total adult caregiver swabs	91	15 (16.5)
Total unique adult caregivers	74	13 (17.6)
Total unique caregivers screen positive or symptom positive	6	3 (50.0)
Total adult caregivers screen negative and symptom negative	68	10 (14.7)
Total patients tested at MSK, April 12, 2020	2932	608 (20.7)

Abbreviation: COVID-19, coronavirus disease 2019.

[a] *P*<.001, Fisher exact test comparing [screen positive or symptom positive] to [screen negative and symptom negative].

Braunstein et al. Breast Radiation Therapy Under COVID-19 Pandemic Resource Constraints—Approaches to Defer or Shorten Treatment From a Comprehensive Cancer Center in the United States. Advanced Radiation Oncol. Doi: 10.1016/j.adro.2020.03.013

Country Context: USA

In this review article, the authors present evidence-based guidelines for omitting or modifying breast cancer radiation therapy, where appropriate, in an effort to mitigate risk to patients and optimise resource utilisation. Recommendations for the safe application of hypofractionated and abbreviated radiation regimens are highlighted in the table below:

Target	Total dose/no. of fractions	Technique/contours	Dose constraints (for shortest regimen only)	Notes
Partial breast	30 Gy/5 every other day (preferred) or daily (acceptable) 40 Gy/10 daily	IMRT/VMAT (preferred) 3D-CRT GTV (clips∗) to PTV ~2 cm (1.5 cm to CTV with 5 mm PTV margin)	30 Gy in 5 fractions: D_{max} <110% V105%(31.5 Gy) <5% of breast volume Ipsi breast-PTV V15Gy <50% Contra breast D_{max} <1Gy Lung (ipsi) V10Gy <20% Lung (contra) V5Gy <10%	Florence PBI trial http://econtour.org/cases/47 MSK prospective http://econtour.org/cases/108 • ∗ Clips strongly preferred for targeting and daily setup • ∗ Daily kv match to clips vs CBCT match to seroma

Target	Total dose/no. of fractions	Technique/contours	Dose constraints (for shortest regimen only)	Notes
Whole breast	26 Gy/5 daily ± 5.2 Gy × 1 boost 40 Gy/15 daily 42.4 Gy/16 daily	3D-CRT For left-sided, DIBH (preferred) and/or heart block	26 Gy in 5 fractions: D_{max} <110% V107% <2% of breast volume V105% <5% of breast volume Lung V8Gy <15% (<17% acceptable) Heart V7Gy <5%, V1.5Gy <30%	UK FAST FORWARD http://econtour.org/cases/117
Postmastectomy (PMRT)	42.56 Gy/16	3D-CRT or IMRT	42.56 Gy in 16 fractions: D_{max} <115% V107% <10 cm^3 of PTV Contra breast V3Gy <10% (preferred), V5Gy <10% (acceptable) Lung V18Gy ≤35% (≤40% acceptable) Heart mean ≤3 Gy (preferred), ≤5 Gy (acceptable) Heart V22.5Gy <10% (left-sided), V22.5Gy <2% (right-sided)	RTCHARM (NCT03414970) http://econtour.org/cases/110
Breast and RNI	42.56 Gy/16 with SIB to tumor bed 48 Gy/16 (3 Gy/fx) 40 Gy/15 with SIB† to tumor bed 48 Gy/15 (3.2 Gy/fx)	3D-CRT or IMRT 3D CRT SIB involves a separate electron plan delivered after photon plan Seroma/clips 7-10 mm for CTV, then another 5-7 mm for PTV. NOTE: expansions can be smaller for SIB.	(see PMRT constraints)	UK START B and extrapolation from RTOG 1005 • †SIB: EQD2 57Gy for a/b 3

Abbreviations: 3D-CRT = 3D conformal radiation therapy; CBCT = cone beam computed tomography; CTV = clinical target volume; DIBH = deep inspiration breath hold; GTV = gross tumor volume; IMRT = intensity modulated radiation therapy; MSK = Memorial Sloan Kettering; PBI = partial breast irradiation; PMRT = post-mastectomy radiation; PTV = planning target volume; RNI = regional nodal irradiation; RTOG = Radiation Therapy Oncology Group; SIB = simultaneous integrated boost; VMAT = volumetric modulated arc therapy.

Chaves et al. Emergency changes in international guidelines on treatment for head and neck cancer patients during the COVID-19 pandemic. Oral Oncology. Doi: org/10.1016/j.oraloncology.2020.104734

Country context: Global

Given the critical need to share skills and expertise to propose recommendations for the diagnosis and treatment of head and neck squamous cell carcinoma (HNSCC) patients during the COVID-19 pandemic, the authors draw on their expertise to offer a set of emergency guidelines. Their recommendations aim to reduce the risk of patient harm, by reducing their risk of exposure to SARS-CoV-2, without compromising their treatment and outcomes. The proposed emergency guidelines are summarised below:

Do not postpone or interrupt HNSCC treatment in SARS-CoV-2 negative patients unless there are significant clinical reasons that prevent the patient from being treated: Multidisciplinary management continues to be essential for optimal decision making and treatment planning of HNSCC patients and, due to the inability to have in-person meetings, web-based meetings should be encouraged. HNSCC usually has a high proliferation rate and it is also associated with a significant tumor-associated symptom burden. Therefore, delay to initiate oncologic treatments or applying treatment interruptions can cause disease progression and may negatively impact survival outcomes.

Flexible fiberoptic endoscopy should be done only if necessary, to make a decision on treatment: Fiberoptic endoscopy examination is a high risk procedure for head and neck

surgical oncologists and otolaryngologists because of the high nasal viral loads in COVID-19 patients. This exam must be performed only for initial diagnostic or staging purposes and not for follow-up of asymptomatic patients. The recommendations for endoscopic examination vary because of the lack of availability of adequate Personal Protective Equipment (PPE) to the staff involved in patient care in all institutions.

Multidisciplinary support must be kept during patient's treatment: Nutrition assessments, swallowing evaluation and oral care are mandatory during HNSCC treatment. The use of prophylactic procedures (e.g., low-level laser therapy) in the oral cavity should be avoided for patients with high risk of mucositis (e.g., oral cavity and oropharynx cancers) due to the risk for healthcare professionals, and it may be considered as an analgesic procedure only in selected cases.

Treatment of early stage HNSCC patients should be individualised: For patients with early stage HNSCC primaries located in the larynx, oral cavity or oropharynx, treatment options usually involve single-modality surgery or radiation therapy. These two approaches are normally associated with similar clinical outcomes

Concurrent chemoradiation with cisplatin is the standard of care for patients with locoregionally advanced HNSCC: In those patients who are treated with concurrent chemoradiation, two high-dose cycles of cisplatin (100 mg/m^2 each cycle) should be administered, with the third cycle being suspended (survival benefit with a cumulative cisplatin dose of 200 mg/m^2 for HPV-unrelated tumors and in stage III HPV-related squamous cell carcinoma of the oropharynx has been documented).

Induction chemotherapy should not be routinely used as an option to postpone upfront surgery or radiation therapy: Induction chemotherapy with the standard TPF (docetaxel, cisplatin, 5-FU) regimen has a significant risk of immunosuppression and when followed by cetuximab-radiation showed a higher risk of mortality compared with concomitant cisplatin-radiation. Therefore, the risk of COVID-19 infection and subsequent severe complications requiring hospitalisation may worsen the patient's prognosis. Therefore, it should not be considered as an option to postpone upfront surgery or radiation therapy, but may be indicated in well-established clinical scenarios, like larynx preservation.

Cisplatin with postoperative radiation therapy should be used only for patients with high-risk disease with major factors (extranodal extension and/or positive margins): Patients who are treated with surgery with curative intent, including radical resection with neck dissection of an advanced stage tumor may be at high risk of disease relapse. Although several factors have been related to an increased risk of locoregional relapse after head and neck surgery (e.g., stages T3/T4, lymphovascular space invasion, perineural invasion, positive/close resection margins, positive lymph nodes)

Recurrent/metastatic disease: The treatment objectives for patients with recurrent or metastatic HNSCC during the COVID-19 pandemic remain the same: optimise overall survival and quality of life, accomplish symptom control, and minimise toxicity. However, in the present situation it seems pertinent to avoid severe neutropenia, because there are data of a higher risk in neutropenic patients and SARS-CoV-2 infection. To reduce frequent contact with the hospital, regimens with longer treatment intervals between cycles or the use of oral medication seems preferable.

Hypofractioned radiation therapy may be considered for palliative care (shorter schedule as possible): In patients with incurable disease, best supportive care typically results in life expectancy of approximately 100 days, versus five months with palliative radiation therapy. A variety of different dose schedules are reported in the literature for palliative radiation therapy in patients with locally advanced HNSCC.
Treated patients in follow-up: The COVID-19 pandemic is overburdening health care systems worldwide due to extensive and rapid consumption of supplies necessary for acute care, the inability of supply chains to keep up with demands, and the losses and exhaustion of human resources

Editorial. COVID-19: Global consequences for oncology. Lancet Oncology. Doi: 10.1016/S1470-2045(20)30175-3.

Country context: Global

This article highlights challenges facing oncology care, service delivery and research globally due to the COVID-19 outbreak. It illustrates how health-care systems are under increasing pressure as the pandemic escalates and countries struggle to contain the virus; how emergency departments and intensive care units are nearing breaking point, and how medical resources are being diverted to tackle the crisis. In terms of research, it highlights how conferences are being cancelled, and cancer research trials are grinding to a halt.

Sites:

PUB COVID-19. Resource page. May 2020.

Country context: Global

This is a public repository of journal articles, guidelines and other published resources related to cancer and COVID-19.

Econtour. Cancer and COVID-19 Resource Page

Country context: Global

This page offers access to clinical guidelines, protocols and other resources for the safe application of hypofractionated and abbreviated radiation regimens in COVID-19 outbreak settings.