COVID-19 in THORACIC ONCOLOGY PATIENTS

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5.26.20



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



WHAT ARE WE IN FOR?

- > Part I Important background data
- > Part II Important Articles
- > Part III Available guidelines

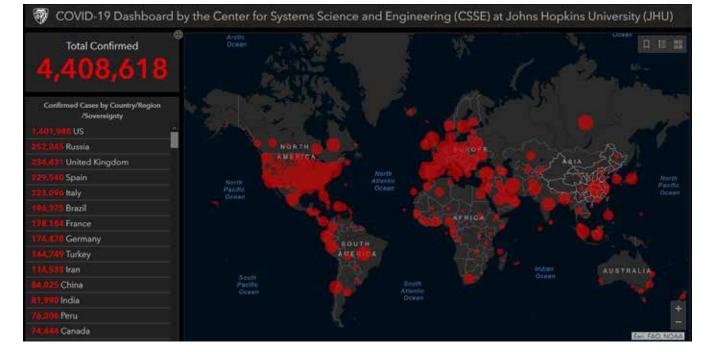
PART I – BACKGROUND



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

WHAT IS A PANDEMIC?

- A global outbreak of a novel virus which can infect people easily and spread from person to person in an efficient and sustained way.
- > What affects the impact of a pandemic?
 - > Clinical Severity
 - > Transmissibility





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WHAT IS THE SARS-COV-2?



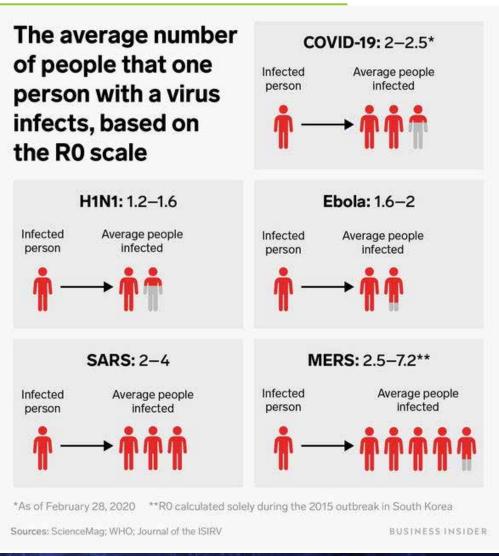
> Member of the Coronaviridae family

HOW IS IT SPREAD?

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- Spread through respiratory tract by droplets, respiratory secretions, and direct contact
 - Half life of aerosols ~ 1.1 hours, steel 5.6 hours, plastic 6.8 hours
- Virus RNA has been identified in samples from stool, GI tract, saliva, tears, semen, and urine
 - > Fecal oral transmission has not been ruled out
- Median incubation period is reported to be 3-5 days (range 1-14 days)
- > 95% experience symptoms by day 12.5 of contact
- Asymptomatic cases are common, and patients can transmit virus prior to symptom development
 - > Infectiousness begins 2.3 days before symptom onset
- > WHO estimates R0 to be 2.0-2.5



Guo et al, Military Medical Research, March 2020 | Feng et al, Journal of Medical Virology, March 2020 | Liu et al, Lancet ID,

March 2020 Van Doremalen et al, NEJM, March 2020 Wang et al, International Journal of Antimicrobial Agents, March 2020 Xi al, Nature Medicine, April 2020

HOW DO PATIENTS PRESENT?



- Clinical presentations can range from asymptomatic to severe respiratory failure
 - > In China
 - > 81% mild
 - > 14% severe
 - > 05% critical
- > Primary symptoms
 - Fever, cough, shortness of breath
- Additional common symptoms
 - > Myalgias, fatigue, sore throat, nausea/vomiting, diarrhea, headache, anosmia, dysgeusia
 - GI symptoms frequently occur prior to respiratory symptoms
- Some patients have GI symptoms prior to fever/respiratory symptoms
- Spectrum of neurological symptoms has been described ranging from CVA, skeletal muscle injury, headache, depressed consciousness, dizziness, seizure

Table 2 Clinical Symptoms associated with COVID-19.	
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Clinical types		Symptoms
	Mild type	nonpneumonia or mild pneumonia
	Severe type	dyspnea, respiratory frequency ≥ 30/min, blood oxygen
		saturation \leq 93%, partial pressure of arterial oxygen to fraction
		of inspired oxygen ratio < 300, and/or lung infiltrates >50% within 24 to 48 hours
/		
	Critical type	respiratory failure, septic shock, and/or multiple organ dysfunction or failure

Feng et al, Journal of Medical Virology, March 2020 | Wang et al, International Journal of Antimicrobial Agents, March Conquering Thora 2020 Onder et al, JAMA, March 2020 ACP guide on clinical presentation and course of COVID-19

HOW IS IT DIAGNOSED?



- Current standard is nucleic acid detection via samples from nasopharyngeal swabs by real time PCR
 - > Accuracy is dependent on specimen collection, pre-test probability, and timing since onset of symptoms
 - > False negative rates are higher earlier in the disease course, repeat testing should be considered in the right clinical scenario
 - Sensitivity and specificity assessments vary based on the specific assay, how it is processed, and whether best practices were followed
- > Rapid fluorescent immunoassay antigen detection
 - Test results in 15 min
 - > Detects SARS-COV-2 nucleocapsid protein antigen
 - Sensitivity 80% of PCR, negative predictive value ~88%, 100% specificity
- Serology

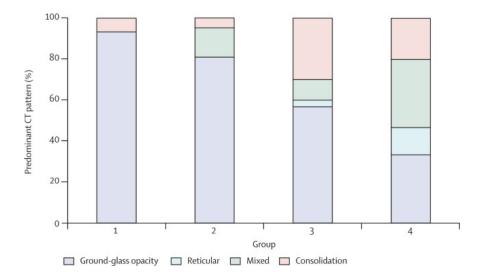
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- > Reflects prior exposure and cannot be used to independently diagnose current infection
- > Can be helpful in evaluate late sequelae (i.e. "covid toes syndrome") when RT-PCR can be negative
- > May cross react with other human coronaviruses
- CT scans
 - Can increase sensitivity when added to RT-PCR
 - Can also be done alone if RT-PCR not available
 - > Sensitivity of CT in suspected patients was found to be 97% based on positive RT-PCR
- PET/CT
 - Case series from Italy have shown that asymptomatic patients can have signs of interstitial pneumonia with FDG uptake and later develop COVID19

WHAT ARE THE IMAGING FINDINGS?

- All lung segments can be involved, slight predilection for the RLL
- > 79% of patients had bilateral lung involvement
- > 54% showed peripheral distribution
- > 44% showed diffuse distribution
- > Most common patterns
 - › 65% GGO
 - > 81% III defined margins
 - > 35% Smooth or irregular interlobular septal thickening
 - > 47% Air bronchograms
 - > 10% Crazy-paving pattern
 - > 32% thickening of adjacent pleura

Shi et al, Lancet ID, February 2020 | Feng et al, Journal of Medical Virology, March 2020



group 1 (scan before symptom onset; n=15),

group 3 (scan >1 week to 2 weeks after symptom onset; n=30), and group 4 (scan >2 weeks to 3 weeks after symptom onset; n=15).



Figure 5 Transverse thin-section serial CT scans from a 77-year-old man





- Radiation pneumonitis and immunotherapy induced pneumonitis can often present and appear like COVID-19 pneumonia on imaging studies
- The Chinese guidelines recommend a multidisciplinary team of radiologists, radiation oncologists, medical oncologists, and infectious disease physicians to help triage these patients when diagnostics are confounding
- > Tumor progression, obstructive pneumonia, lymphangitic metastases, cancer associated pleural effusions can all cause fevers and associated imaging findings
- > Do not forget cancer associated medical conditions in our differential diagnosis
- > Pulmonary embolism, CHF, myocarditis, other viral/bacterial/fungal causes of pneumonia
- Co-infection with other viral pneumonias as well as bacterial super-infections have been reported and are associated with more serious illness

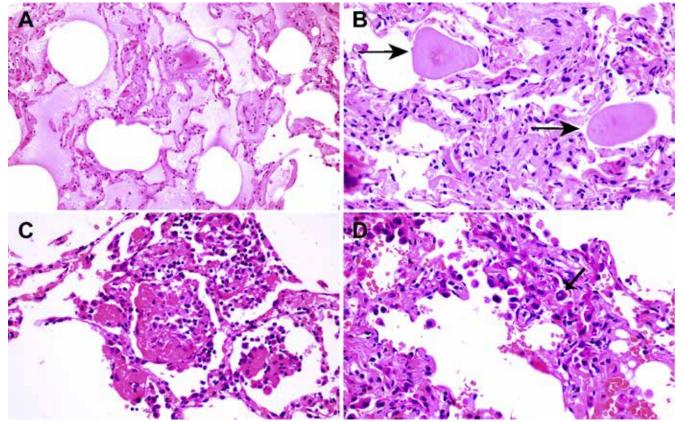




WHAT IS SEEN UNDER THE MICROSCOPE?

- Two cases of asymptomatic patients, undergoing lobectomy for lung cancer, had findings consistent with exudative and proliferative phases of acute lung injury
- Postmortem biopsies are consistent with diffuse alveolar damage and organizing pneumonia

Feng et al, Journal of Medical Virology, March 2020 | Tian et al, Journal of thoracic Oncology, March 2020 | Zhang et al, Annals of Internal Medicine, March 2020



Histologic changes from case 1. () Proteinaceous exudates in alveolar spaces, with granules; () scattered large protein globules (arrows); () intra-alveolar fibrin with early organization, mononuclear inflammatory cells, and multinucleated giant cells; () hyperplastic pneumocytes, some with suspected viral inclusions (arrow).

HOW DO I MANAGE THESE PATIENTS?



- > Implementation of infection control practices
- > Oxygen support, when needed, favoring non-aerosolizing tools
 - > Limit non-invasive mechanical ventilation and high-flow nasal cannula
- Minimize steroids, unless being used for alternative diagnosis (sepsis, ARDs) due to concern for increased viral shedding
- > Prophylaxis for venous thrombosis, due to increased thrombotic risk in these patients
- > Consider non-intubated hypoxemic patients to assume a prone position when practical
- Ongoing studies are assessing the role of various pharmacologic and immunologic interventions
 - > Interim analysis of a placebo controlled RCT of remdesivir involving 1063 patients
 - > Patients on the intervention arm had a 31% faster time to recovery (11 days vs. 15 days) (p<0.001)
 - > Patients on the intervention arm had a 8% mortality rate vs. 11.6% in the placebo arm (p=0.059)

Further up to date information on treatment options for COVID-19



ACP review-Treatment COVID-19

HOW DO PATIENTS DO?



- The most reported predictors of severe prognosis in patients with COVID-19 included: age, sex, features derived from CT scans, CRP, LDH, and lymphocyte count
 - > Other proposed labs: D-dimer, ANC:ALC ratio, troponin T, NT-proNP
- > Patients who are active smokers, older, and have co-morbidities have a higher disease severity and mortality
 - Active smokers have a 1.5 times higher risk of severe symptoms and 2.4 times higher risk of ICU admission, mechanical ventilation or death

HOW DO PATIENTS DO?



- > 14% develop severe disease requiring hospitalization and oxygen
- > 5% require ICU admission
 - > 25-30% of hospitalized patients require ICU admission
 - > Essentially all secondary to hypoxic respiratory failure
- > Mortality can reach 62% for patients in critical care
- > Case fatality rate 2.3% china
 - > Cases aged 70-79 8.0%
 - > Cases older than 80 14.8%
- > Case fatality rate 7.2% Italy
 - > 20% had active cancer

HOW DO CANCER PATIENTS DO?



> Meta analysis of 11 studies

- > 2% of COVID cases were in cancer patients
- > Higher likelihood of severe events (35-54%)
 - Mortality 28.5% in one study, case fatality rate 5.6% vs. 2.3% in the general population
 - > Patients with more advanced cancer are more likely to have severe disease
 - Recent treatment (within 14 days) associated w/ development of severe events (HR=4.079)

PART II – JOURNAL ARTICLES



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., Yu Hu, M.D., Wen-hua Liang, Ph.D., Chun-quan Ou, Ph.D., Jian-xing He, M.D., Lei Liu, M.D., Hong Shan, M.D., Chun-liang Lei, M.D., David S.C. Hui, M.D., Bin Du, M.D., Lan-juan Li, M.D., <u>et al.</u>, for the China Medical Treatment Expert Group for Covid-19*



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- > Median age 47 years, only 0.9% under-age of 15
- > 41.9% female
- > 23.7% had at least one coexisting illness
 - > 0.9% (10 pts) had cancer of any kind
- > Patients with severe disease
 - > Older by median 7 years
 - > Presence of any coexisting illness (39.7% vs. 21.0%)
 - > Of the 10 cancer patients 7 had mild disease, 3 severe

Guan et al, NEJM, February 2020

*Please see supplemental document

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HOW DO THEY PRESENT?



- > Median incubation period is 4 days
- > Symptoms
 - > 43.8% Fever on admission with 88.7% developing fever during their hospitalization
 - > 67.8% cough, 38.1% fatigue, 33.7% sputum production
- > Lack of typical physical exam findings associated with URI
- > Imaging
 - > 86.2% CT findings, 59.1% CXR findings
- > Labs (medians)
 - > WBC 4.7 (severe 3.7)
 - > Lymphocyte count 1.0 (severe 800)
 - > PLT 168 (severe 137.5)
 - > Hgb 13.4 (severe 12.8)

Guan et al, NEJM, February 2020

*Please see supplemental document

WHAT ARE THE CLINICAL OUTCOMES?



- > 67/1099 (6.1%) of all patients met composite outcome of ICU admission, mechanical ventilation, or death
 - > 43/173 (24.9%) of patients who presented with severe disease met composite endpoint
- > Other important complications
 - > 12% septic shock
 - > 37% ARDS
- > Treatments
 - > 58% IV antibiotics, 35.8% oseltamivir, 31% antifungals
 - > 18.6% systemic glucocorticoids
 - > 13.1% IVIG
 - > 41.3% required oxygen
 - > 6.1% mechanical ventilation
 - > 0.5% ECMO
 - > 0.8% CRRT
- > 55/1099 patients required ICU level care (5%)
- > 15/1099 patients died (1.4%)

Guan et al, NEJM, February 2020

*Please see supplemental document

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THE LANCET Oncology

COMMENT | VOLUME 21, ISSUE 3, P335-337, MARCH 01, 2020

Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China

Wenhua Liang ^{†, ‡} • Weijie Guan [†] • Ruchong Chen [†] • Wei Wang [†] • Jianfu Li • Ke Xu • et al. Show all authors • Show footnotes

Published: February 14, 2020 . DOI: https://doi.org/10.1016/S1470-2045(20)30096-6 .



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WHAT DID THESE PATIENTS LOOK LIKE?

- > 18 (1%) had a history of cancer
- > 5 (28%) had a history of lung cancer
- 4/16 (25%) had received chemotherapy or surgery within the past month
- > Median age 63 years
- > 4/18 (22%) prior smoking history

Table S2. Baseline characteristics between cancer patients and non-cancer patients

Characteristics	Cancer patients	Non-cancer patients	P value
Age	63.1±12.1	48.7±16.2	<0.001
Sex (Male%)	61.1%	57.2%	0.814
Known smoking history	22.2%	6.8%	0.032
Any other comorbidity*	22.2%	24.2%	1.000
Abnormality in X-ray	22.2%	15.2%	0.504
Abnormality in CT-scan	94.4%	70.8%	0.033
Polypnea#	47.1%	23.5%	0.039

*, other comorbidities include chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, coronary heart disease, cerebrovascular disease, viral hepatitis type B, malignant tumor, chronic kidney disease and immunodeficiency. #other symptoms being compared but found no difference include fever, cough, expectoration, stuffy nose, conjunctival congestion, headache, sore throat, dyspnea, fatigue, nausea and vomiting, hemoptysis, diarrhea, muscular pain, arthralgia, shivering.

Liang et al, Lancet Oncology, February 2020

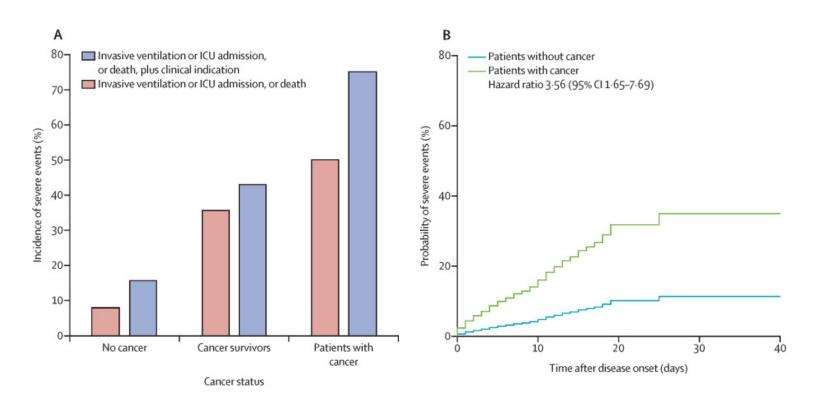
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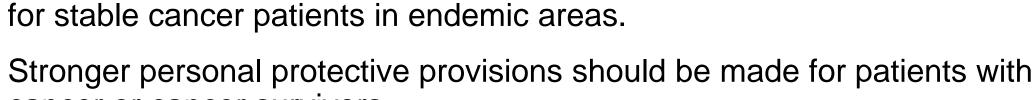
WHAT HAPPENED TO THESE PATIENTS?

- Higher risk for severe events
- Recent treatment associated with more severe events
- Age was only risk factor for severe events
- Cancer patients appear to deteriorate more rapidly

Liang et al, Lancet Oncology, February 2020



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 More intense surveillance or treatment should be considered when cancer patients are infected with SARS-CoV-2, especially for older patients or in those with co-morbidities.

1. An intentional postponing of adjuvant chemotherapy or elective surgery

Liang et al, Lancet Oncology, February 2020

cancer or cancer survivors.

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ANNALS OF ONCOLOGY driving innovation in oncology

Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China

L. Zhang, F. Zhu, L. Xie, C. Wang, J. Wang, R. Chen, P. Jia, H.Q. Guan, L. Peng, Y. Chen, P. Peng, P. Zhang, Q. Chu, Q. Shen, Y. Wang, S.Y. Xu, J.P. Zhao, M. Zhou



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

CLINICAL CHARACTERISTICS OF CANCER PATIENTS WITH COVID-19



- > 28 hospitalized COVID-19 infected cancer pts from 3 hospitals in Wuhan, China
- > 17 (60.7%) male, median age 65
- > 25.0% Lung cancer patients, 14.3% esophageal, 10.7% breast
- > 28% acquired infection in the hospital
- > 82% fever, 81% dry cough, 50% SOB
- > 82% lymphopenia, 82% CRP elevation, 75% anemia, 89% hypoproteinemia
- > 75% GGOs, 46% patchy consolidation on CT chest
 - > Patchy consolidation as associated with a higher risk of severe events (HR 5.438, 95% CI 1.498-19.748, p=0.010)

CLINICAL CHARACTERISTICS OF CANCER PATIENTS WITH COVID-19



- > 70% of patients with stage IV disease developed severe symptoms vs.
 44.1% of non-stage IV patients (not statistically significant **)
- Recent treatment (within 14 days) was associated with severe events HR 4.079 (95% CI 1.086-15.322, p=0.037)
- > 53.6% of all cancer patients had a severe event
 - > 21.4% ICU admission, 35.7% had life threatening complications
- > 78.6% required oxygen, 35.7% required invasive mechanical ventilation
- > 71.4% received some type of antiviral medication
 - > arborol (50%), lopinavir/ritonavir (35.7%), ganciclovir (32.1%), ribavirin (3.6%)
- > 82% received antibiotics
- > 80% received steroids
- > 28.6% died

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ORIGINAL REPORTS

Outcome of Oncology Patients Infected With Coronavirus

Abdul-Rahman Jazieh, MD, MPH¹ ^{Cod}; <u>Thamer H. Alenazi</u>, MD¹; <u>Ayman Alhejazi</u>, MD¹; <u>Faisal Al Safi</u>, MD¹; and <u>Ashwaq Al Olayan</u>, MD¹





ONCOLOGY PATIENTS WITH MERS 2015

- > 19 patients with confirmed cancer diagnosis
- > Median age 66, 63% male
- > 47% hematologic malignancy, 21% colorectal cancer, 16% lung cancer, 3% other
 - > For solid tumors (10/19 pts), 50% were stage IV
 - > 90% active disease
 - > Active disease was significantly associated with a high fatality rate
 - > 1/3 were receiving active treatment
 - > No difference in outcomes
- Most common comorbidities included diabetes (52%), hypertension (58%), cardiac disease (47%)
- > 80% required ICU admission
 - > 81% ÅRDS, 69% intubated, 56% had renal injury of which 19% required dialysis
- > 84% fatality rate, 100% of those with hematologic malignancies and advanced cancer vs. 39% in the general population

TABLE 4. Patient Outcomes (N = 19) Outcome	No.	%	
Survival			
Dead	16	84.2	
Alive	3	15.8	
Cause of death			
Multi-organ failure	6	37.5	
Septic shock	4	25.0	
Cancer related	4	25.0	
Cardiac arrest	2	12.5	
ARDS	2	12.5	
Other®	3	18.75	
Median No. of days from hospital admission to death (min-max)	23 (23 (10-78) 12 (1-76) 10 (1-25)	
Median No. of days from hospital admission to ICU admission (min-max)	12		
Median No. of days from ICU admission to death (min-max)	10		

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit; max, maximum; min, minimum.

³Severe metabolic acidosis, no code (kidney injury), severe community-acquired pneumonia.



Research Letter

ONLINE FIRST

March 25, 2020

SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China

Jing Yu, MD^{1,2,3}; Wen Ouyang, MD^{1,2,3}; Melvin L. K. Chua, MBBS, PhD^{1,4,5}; et al

» Author Affiliations | Article Information

JAMA Oncol. Published online March 25, 2020. doi:10.1001/jamaoncol.2020.0980



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



CANCER PATIENTS IN WUHAN CHINA

- > 1524 patients with cancer who were admitted to the Department of Radiation and Medical Oncology, Zhongnan Hospital of Wuhan University from 12/30/2019-02/17/2020
- > 12 were diagnosed with COVID19
- Infection rate of SARS-CoV-2 with cancer was 0.79% (cumulative incidence of COVID-19 reported in the city of Wuhan 0.37%)
- > Median age 66, 66% older than 60
- > 58.3% NSCLC
 - Patients with NSCLC older than 60 had a higher incidence of COVID 19 than those younger 4.3% vs. 1.8%
- > 42.7% on active treatment
- > with immunotherapy or without immunotherapy (n=3) or radiation therapy (n=2)
- > 3/12 had serious illness,1/12 required ICU level care, 6/12 discharged, 3/12 died

Yu et al, JAMA Oncol, March 2020



- > Case report from China was published in JTO
- > 57 M with advanced EGFR L858R mutant NSCLC on Osimertinib presented with fever, cough, SOB, myalgia, and diarrhea with known exposure to COVID19 and was found to be positive for SARS-CoV-2
- > Treated with lopinavir/ritonavir
- > Continued Osimertinib
- > Improved and was discharged after 1 month of hospitalization

Zhang et al, Journal of Thoracic Oncology, March 2020

Case report of NSCLC on nivolumab

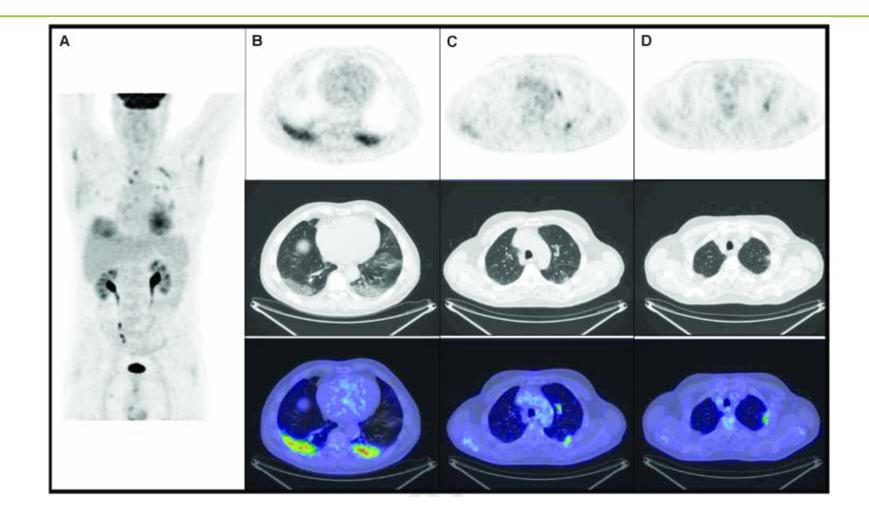


- > 65 yo M w/ emphysema and NSCLC dx in 2012 s/p surgical removal of cerebral mets as well as WBRT and systemic carboplatin/pemetrexed until in 7/2013 when he was found to have progressive disease and was started on nivolumab in the s/o clinical trial. He has remained on this since with stable disease.
- On 3/4/2020 he p/w SOB, fever, and mental confusion. Labs on presentation were notable for normal leukocytes with lymphopenia, elevated CRP, transaminases, and LDH. Nasal swab was positive for COVID 19. Within 24 hours he required 15 L/min of supplemental oxygen and sedation for agitation. He passed on 3/9/2020.
- > He was not treated with more advanced procedures likely due to his cancer and emphysema history
- Highlights need for oncologist to be involved in the care of their patients sick with COVID for advocacy as well as alternative treatment strategies –the authors in this case offered steroids as a consideration

18F-FDG uptake in Asymptomatic SARS-CoV-2 (COVID-19) pt, IASLC referred to PET/CT for Non-Small Cells Lung Cancer restaging

- > 73 yo M w/ pT2aN0 NSCLC s/p lobectomy in 2016 was noted to have a centimetric nodule in the left superior lobe suspected for malignancy.
- > PET/CT was ordered and scheduled for 3/18/2929 in Italy
- > Patient had no symptoms, COVID19 exposures, and was afebrile
- > PET/CT revealed bilateral diffuse intense FDG uptake in the lower lobes, mediastinal lymph nodes, and less intense uptake in the remaining lobes. Uptake corresponded to peripheral predominant GGOs.
- > Pt was tested w/ RT PCR resulted positive later requiring ICU admission with rapid disease progression and ARDS.







Original InvestigationONLINE FIRST FREEApril 6, 2020Baseline Characteristics and
Outcomes of 1591 Patients Infected
With SARS-CoV-2 Admitted to ICUs of
the Lombardy Region, Italy

Giacomo Grasselli, MD^{1,2}; Alberto Zangrillo, MD^{3,4}; Alberto Zanella, MD^{1,2}; et al

Series of 1591 patients with COVID19 requiring ICUs



- > Median age 63, 82% male
- > 68% had at least 1 comorbidity, 49% HTN, 8% cancer
- > 99% required respiratory support
 - > 88% mechanical ventilation, 11% non-invasive ventilation
 - Median of FIO2 was lower for younger patients and median PaO2/FiO2 was lower in younger patients
- > 1581 had disposition information
 - > 58% still in ICU
 - > 16% discharged from the ICU
 - > 26% died in the ICU
 - > Older patients had a higher mortality 36% vs. younger patients 21%





COVID-19 in the perioperative period of lung resection: a brief report from a single thoracic surgery department in Wuhan, China



- From Jan 1-22 the thoracic oncology dept of Tongji Hospital continued routine operations
- > 139 underwent lung resection among these 7 were laboratory confirmed COVID-19 post op
- > Median age 69, 5 males
- > Co-morbidities included COPD (2), ILD (1), HL (1)
- > 6/7 NSCLC, 1/7 pulmonary sclerosing pneumocytoma
- > All 7 had successful, uneventful surgeries
 - > 4 VATs lobectomy, 1 VATS segmentectomy plus wedge, 1 thoracotomy sleeve lobectomy 1 lobectomy plus bronchus reconstruction



> Pathology

- > 7 patients had typical malignant pathology
- Patient 1- wide range of lung interstitial inflammation w/ numerous infiltrating immune cells (predominantly plasma cells/macrophages), thickened alveolar septum and fibrous connective tissue proliferation was noted. Large number of macrophages and fam cells in the alveolar cavities but no evidence pneumocyte hyperplasia was observed, no obvious viral inclusions.
- > Other 6 patients did not have evidence of inflammation
- > Clinical history
 - Oseltamivir was used for all 7, addition of umifenovir in 2 and lopinavir and ritonavir in 1 patient
 - > 4 received steroids
 - > 3 patients required intubation and ultimately died
 - > 2 cured and discharged from the hospital
 - > 2 hospitalized and stable



> Presentation

- > All 7 presented with fever after surgery, ranging 0-23 days post op
- > 5 endorsed SOB, 4 nonproductive cough, 2 fatigue, 1 productive cough, 2 myalgia, 1 diarrhea

> Labs

- > Decline in lymphocyte count was observed in all 7, 5 had frank lymphopenia
- > 1 had transaminitis
- > Elevated CRP and procalcitonin was found in all 7
- > 5/7 had elevated d-dimers and fibrinogen

Imaging

- > All 7 had emerging GGOs w/ (4) or w/o (3) reticulation
- > 3 progressed to bilateral findings



CANCER DISCOVERY

Research Briefs

Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System

Vikas Mehta, Sanjay Goel, Rafi Kabarriti, Daniel Cole, Mendel Goldfinger, Ana Acuna-Villaorduna, Kith Pradhan, Raja Thota, Stan Reissman, Joseph A. Sparano, Benjamin A Gartrell, Richard V. Smith, Nitin Ohri, Madhur Garg, Andrew D. Racine, Shalom Kalnicki, Roman Perez-Soler, Balazs Halmos, and Amit Verma

DOI: 10.1158/2159-8290.CD-20-0516 (I) Check for updates

		Alive	Deceased
	Total	157 (72%)	61 (28%)
218 PTs with cancer and COVID-19 infection treated in	Solid tumors	123(75%)	41 (25%)
Montefiore Health System from March 18-April 8	Genitourinary	39 (85%)	7 (15%)
Montenere riedaan eyetein non Maren re April e	Breast	24 (86%)	4 (14%)
Median age 69, 58% male	Colorectal	13 (62%)	8 (38%)
Median age 05, 5070 male	Gynecologic Lung	8 (62%) 5 (45%)	5 (38%) 6 (55%)
28% died	Head and Neck	7 (88%)	1 (13%)
	Neuro	7 (88%)	1 (13%)
> 25% of solid tumor patients	Upper GI	5 (63%)	3 (38%)
•	Hepatobiliary	5 (71%)	2 (29%)
> 55% of lung cancer patients	Bone / Soft Tissue	4 (80%)	1 (20%)
> 37% of hematologic malignancy patients	Neuro-endocrine	3 (100%)	0 (0%)
	Pancreas Skin	1 (33%)	2 (67%)
Active disease (< 1 year) and advanced metastatic	экш	2 (67%)	1 (33%)
Active disease (< 1 year) and advanced metastatic disease showed trend toward increased mortality	Hematologic malignancies	34 (63%)	20 (37%)
A stirre all sus ather ways and an all ather the ways are not	NHL	10 (67%)	5 (33%)
Active chemotherapy and radiation therapy were not associated with increased case fatality	MDS	2 (40%)	3 (60%)
associated with incréased case fatality	MPN	5 (71%)	2 (29%)
accordiated main meredecia cace ratanty	ALL AML	4 (100%) 1 (100%)	0 (0%) 0 (0%)
Are and concomitant heart and lung disease were	MM	8 (62%)	5 (38%)
Age and concomitant heart and lung disease were associated with increased mortality	CML	0 (0%)	1 (100%)
associated with increased mortality	Hodgkin's	2 (40%)	3 (60%)
-	CLL	2 (67%)	1 (33%)
61% of those who died had frequent exposure to health		0.(570())	6 (100)
61% of those who died had frequent exposure to health care system often due to either living in a nursing home	Myeloid Malignancy Lymphoid Malignancy	8 (57%) 26 (65%)	6 (43%) 14 (35%)
or frequent hospitalizations	Lymphoid Manghancy	20 (0576)	14 (5576)

 Case fatality rates (see table 4) are higher in all age groups when compared to NYC COVID 19 cases Abbreviations: MDS: Myelodysplastic syndromes, ALL: Acute Lymphoblastic Leukemia, AML: Acute Myeloid Leukemia

MPN: Myeloproliferative neoplasm; MM: Multiple myeloma; CML: Chronic Myeloid Leukemia; CLL: Chronic Lymphoid Leukemia

Table 2: Disease characteristics of cancer patients with COVID-19 and association with mortality

•	Alive	Deceased	P Val
Total	157 (72%)	61 (28%)	
Males	91 (72%)	36 (28%)	0.6
Females	66 (73%)	25 (27%)	0.6
1 cillaics	00(7576)	25 (2176)	0.0
Median Age (Range)	66 (10-92)	76 (10-92)	0.0006
Race			0.602
Caucasian	14 (64%)	8 (36%)	
Hispanic	58 (76%)	18 (24%)	
African American	67(73%)	25 (27%)	
Asian	5 (71%)	2 (29%)	
Other	13 (62%)	8 (38%)	
	N/Total Alive (%)	N/Total Deceased (%)	
ICU admission	8 (5%)	15 (24%)	9.10E-05
Ventilator support	10 (6%)	35 (57%)	1.74E-15
Hemodialysis	10 (6%)	6 (10%)	0.37
Metastasis (Solids only)	27 (22%)	15 (37%)	0.06
Active Cancer (<1yr)	60 (38%)	32 (52%)	0.09
Active ChemoTx	34 (22%)	8 (13%)	0.2
Immunotherapy	4 (3%)	1 (2%)	1
Radiation Therapy	38 (24%)	11 (18%)	0.33
DM	53 (34%)	27 (44%)	0.116
HTN	100 (64%)	47 (77%)	0.047
Chronic Lung Dis	34 (22%)	28 (46%)	0.0003
Chronic Kidney Dis	33 (21%)	21 (34%)	0.052
Coronary Artery Dis	24 (15%)	19 (31%)	0.012
CHF	18 (11%)	15 (25%)	0.019



	Alive	Deceased	P Val
Total	157 (72%)	61 (28%)	
Pre-COVID-19 (Means)			
Hemoglobin	11.99	11.22	0.048
Platelet Count	225	256	0.16
WBC	7.33	7.55	0.12
ANC	4.9	5.8	0.18
Fotal Lymphocyte Count	1.6	1.7	0.5
Post-COVID-19 (Means)			
Hemoglobin	10.7	9.9	0.047
Platelet Count	177	171	0.7
WBC	5.8	8.8	0.01
ANC	4.4	6.6	0.017
Total Lymphocyte Count	0.7	0.6	0.6
Ferritin	1491	2136	0.21
D Dimer	4.1	8.8	0.002
Lactate	2	4	0.001
LDH	438	683	0.01

Conquering Thoracic Cancers Worldwide



Table 4: Comparison of Cancer and COVID-19 mortality with all NYC cases (official NYC numbers up to 5pm, April 12th, 2020) and a control group from the same healthcare facility. The NYC cohort and the control group were compared independently to the Cancer-COVID-19 cohort and the P Values and Odds ratio are shown.

Age Groups	Cancer COVID- 19 Cases	Cancer COVID- 19 Deaths	%	Control Group Cases	Control Group Deaths	96	Odds Ratio	P Val	NYC Cases	NYC Deaths	%	Odds Ratio	P Val
Total	218	61	28%	1090	149	14%	2.45	8.46E-07	104185	6182	6%	6.160	< 2.2e- 16
0-17	3	1	33%	5	0	0%	na	0.375	2025	3	0%	304.66	0.006
18-44	13	1	8%	75	2	3%	2.99	0.38466	39704	284	1%	11.56	0.088
45-64	64	10	16%	320	13	4%	4.35	0.00161	37851	1449	4%	4.65	0.0001
65-74	59	13	22%	282	41	15%	1.66	0.169939	13128	1511	12%	2.17	0.020
>75	79	36	46%	408	93	23%	2.83	7.34E-05	11477	2935	26%	2.44	0.0001



CANCER DISCOVERY

RESEARCH BRIEF

Patients with Cancer Appear More Vulnerable to SARS-COV-2: A Multicenter Study during the COVID-19 Outbreak №

Mengyuan Dai^{1,23}, Dianbo Liu⁴⁵, Miao Liu⁶, Fuxiang Zhou^{2,37}, Guiling Li⁸, Zhen Chen⁹, Zhian Zhang¹⁰, Hua You¹¹, Meng Wu¹², Qichao Zheng¹², Yong Xiong¹³, Huihua Xiong¹⁴, Chun Wang¹⁵, Changchun Chen¹⁶, Fei Xiong¹⁷, Yan Zhang¹⁸, Yaqin Peng¹⁸, Siping Ge¹³, Bo Zhen²⁰, Tingting Yu²¹, Ling Wang²², Hua Wang²³, Yu Liu^{2,27}, Yeshan Chen⁹, Junhua Mei¹⁰, Xiaojia Gao¹⁵, Zhuyan Li²⁴, Lijuan Gan^{1,2,3}, Can He^{1,2,3}, Zhan Li^{1,2,3}, Yuying Shi^{1,2,3}, Yuwen Qi^{1,2,3}, Jing Yang^{1,2,3}, Daniel G. Tenen^{25,25}, Li Chai⁶, Lorelei A. Mucci²⁷, Mauricio Santillana⁴⁵, and Hongbing Cai^{1,2,3}



- > 105 cancer patients and 536 non-cancer patients treated for COVID-19 in Hubei Province China January 22-February 24, 2020
- > Lung cancer was most frequent canter type 20.95%
- > Treatments
 - > 13 radiation, 17 chemotherapy, 8 surgery, 4 targeted therapy, 6 immunotherapy
- > Outcomes
 - > Higher death rates OR 2.34 (95% CI 1.15-4.77 p=0.03)
 - > ICU admission OR 2.84 (95% CI 1.59-5.08 p=<0.01)
 - > Risk of 1 severe or critical symptom OR 2.79 (95% Cl 2.79 Cl 1.74-4.41 p<0.01)
 - > Patients with hematologic malignancies had highest death rate, ICU admission rate, risk of severe/critical symptoms, and need for mechanical ventilation followed by lung cancer patients
 - > Patients with advanced/metastatic disease similarly had higher adverse outcomes
 - > Pts with on immunotherapy tended to have high rates of death (2/6) and development of critical symptoms 4/6
 - > Pts s/p surgery tended to have high rates of death (2/8), need for ICU admission (3/8), and need for invasive ventilation (2/8)
 - > Patients who received radiation did not show statistically significant differences in having any severe events when compared to non-cancer patients





Review

The experience on coronavirus disease 2019 and cancer from an oncology hub institution in Milan, Lombardy Region



- > Analysis of 909 patients who died of COVID-19 in Italy
- More than 50% had 3 or more comorbid conditions, only 2% had no comorbid conditions
- > 16.5% were cancer patients (defined as having been treated within the last 5 years)
 - > 95.5% experienced ARDs
 - > 25.7% had acute renal failure
 - > 11.2% diagnosed with a secondary superinfection
 - > 11.6% diagnosed with cardiac injury
- > Analysis of 9 patients with COVID-19 and cancer
 - > 3 managed as inpatients (2/3 with severe disease), 6 outpatients
 - > None required ICU
 - > All patients either former or current smokers
 - > Median age 68, median 1 comorbidity
 - > 8/9 on active cancer therapy (3-curative, 5-palliative)
 - > 4-chemotherapy, 2- experimental immunotherapy, 2 small molecule
 - > None of the immunotherapy patients experienced an adverse outcome



CANCER DISCOVERY

Research Briefs

Impact of PD-1 blockade on severity of COVID-19 in patients with lung cancers

Jia Luo, Hira Rizvi, Jacklynn V Egger, Isabel R Preeshagul, Jedd D. Wolchok, and Matthew D. Hellmann

DOI: 10.1158/2159-8290.CD-20-0596 🖲 Check for updates

Tables

Table 1. Baseline characteristics and clinical course of patients with lung cancers and +SARS-CoV-2 test

- 69 consecutive patients with lung cancer between March 12-April 13, 2020
- > Median age 69
- > 80% active or metastatic disease
- 64% had at least a 5-year pack year smoking history
- > 62% required hospitalization
- > 24% died
- No significant difference in disease severity regardless of PD-1 blockade exposure when accounting for smoking history
- Smoking history was associated with severe COVID-19

	Patients (n = 69)
D-fi-t-shf-i-fi-	1
Patients characteristics	no./total no.* (%)
Age	
Median (range) - yr	69 (31-91)
Sex	22/22 (22/2)
Female	36/69 (52%)
Male	33/69 (48%)
Race	10100 (5001)
White	40/69 (58%)
Black	12/69 (17%)
Asian	11/69 (16%)
Other	2/69 (3%)
Unknown	4/69 (6%)
Ethnicity	
Hispanic or Latino	8/69 (12%)
Non-Hispanic or Latino	57/69 (82%)
Unknown	4/69 (6%)
Prior smoking history ^a	
< 5 pack years	25/69 (36%)
≥ 5 pack-years	44/69 (64%)
Lung cancer specific features	
Non-small cell lung cancer	64/69 (93%)
Small cell lung cancer	5/69 (7%)
Metastatic or active lung cancer ^b	55/69 (80%)
Prior thoracic surgery or radiation therapy	32/69 (46%)
Comorbid conditions	, , ,
Chronic obstructive pulmonary disease (COPD) ⁶	12/69 (17%)
Non-COPD lung disease ^d	14/69 (20%)
Obesity (BMI≥30)	23/69 (33%)
Hypertension	38/69 (55%)
Congestive heart failure®	5/69 (7%)
Diabetes mellitus	21/69 (30%)
Clinical course	
Hospitalization	42/67* (63%)
Admission of ICU/Receipt of Intubation/Transition to DNI	24/65* (37%)
Admission to intensive care unit (ICU)	15/65* (23%)
Receipt of intubation and mechanical ventilation	13/64* (20%)
Transition to do not resuscitate/do not intubate (DNR/DNI) [†]	10/65* (18%)
Death	16/67* (24%)

Conquering Thoracic Cancers Worldwide

TERAVOLT Data Reveal presented at AACR Virtual Meeting 4/24/2020



- > Presented by Marina Chiara Garassino, MD
- > 34.6% death rate (66/191) among patients with thoracic cancers
- > Most frequent complications
 - > Pneumonia and pneumonitis: 79.6% (125/157)
 - > ARDS: 26.8% (42/157)
 - > Multiorgan failure: 7.6% (12/157)
 - > Sepsis: 5.1% (8/157)
- > No cancer treatment was associated with a higher mortality
- > No comorbidities were significantly associated to a higher risk of death

Outcome of cancer patients with COVID-19 at Gustave Roussy Cancer Center, presented at ACCR virtual meeting 4/24/2020

Cancer characteristics

- Presented by
 Fabrice Barlesi
 MD
- Images taken from his presentation

		N=137 (%)
Solid tumor, n=119	Breast Gastro Intestinal (GI) Head and Neck Genito-urinary (GU) Gynecological Thoracic Dermatology Others (endocrine, CNS, ACUP)	23 (19.3%) 18 (15.1%) 17 (14.3%) 17 (14.3%) 17 (14.3%) 12 (10.1%) 9 (7.6%) 6 (5%)
Hematology, n=24	Mature B cell neoplasms/Myeloma Acute Myeloid Leukemia (AML) Hodgkin Lymphoma Others (MDS)	15 (62.5%)/4 (16.7%) 4 (16.7%) 3 (12.5%) 2 (8.4%)
Current Status (Unk, n=2)	Remission/Curative intent Active advanced disease	56 (41.5%) 79 (58.5%)

Outcome of cancer patients with COVID-19 at Gustave Roussy Cancer Center, presented at ACCR virtual meeting 4/24/2020

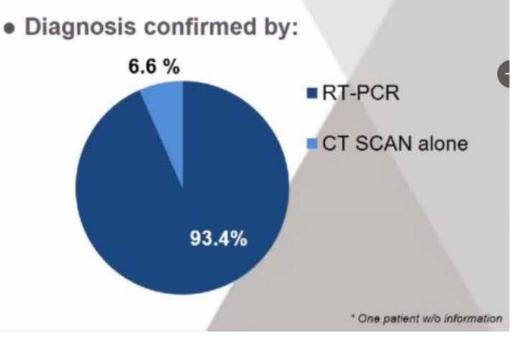
SARS-CoV-2 diagnosis and characteristics

- Diagnosis suspected / symptoms*:
 - > Fully asymptomatic pts, n=31 (23%)
 - > Self-reported symptoms, n=105 (77%)

Symptoms at diagnosis (after medical assessment)	N=111 (83%)
Fever	65 (47)
Dry cough	63 (46)
Fatigue	47 (34)
Dyspnea	45 (33)
Diarrhea	15 (11)
Anosmia	13 (9.5)

> Median time to admission, 4 days

- Contact with a known Covid-19 patient:
 - > N=26 (20.5%)



Outcome of cancer patients with COVID-19 at Gustave Roussy Cancer Center, presented at ACCR virtual meeting 4/24/2020

- > 12% incidence was comparable to global population 80% of patients are symptomatic
- > 11% required ICU admission
- > 14.8% died (compared to 18.3% in France)
- > Factors that affect outcomes
 - > Frail (ECOG >1)
 - > Hematologic malignancies
 - Patients with advanced disease and treated with cytotoxic chemotherapy within 3 months

PART III – AVAILABLE GUIDELINES



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



- > Guidelines from JTO
- > Guidelines from ESMO
- Solution Strain Stra

Management of Lung Cancer during the COVID-19 Pandemic



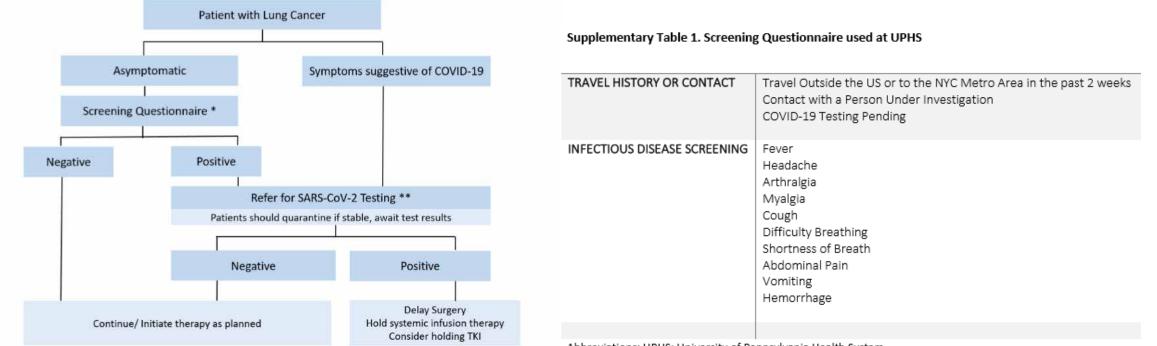


Figure 1. Algorithm for treating patients with Lung Cancer during the COVID-19 pandemic. *Screening Questionnaire detailed in Supplemental Table 1, ** Drive through testing preferred (if Abbreviations: UPHS: University of Pennsylvania Health System available) for stable patients, in-hospital evaluation for patients with severe symptoms or hypoxia

Management of Lung Cancer during the COVID-19 Pandemic

Table 1. Management recommendations and additional considerations for patients with NSCLC by stage of disease

STAGE	RECOMMENDATIONS	ADDITIONAL CONSIDERATIONS
 STAGE I	Defer surgery for lung nodules < 2cm, GGO, carcinoid tumors Follow ACS guidelines, and decisions must be based on institutional resources	Consider SBRT/ Ablation
STAGE II/III	Delay adjuvant chemotherapy to 3-4 months post- operatively	Consider withholding adjuvant chemotherapy for patients > 75 years of age or with significant comorbidity Consider Neo-adjuvant/ Induction if surgery not immediately feasible
STAGE III	Delay start of consolidation durvalumab up to 6 weeks from completion of concurrent Chemo Radiation Hypo-fractionated RT schedules should be used with concurrent chemotherapy, when feasible No consolidation chemotherapy should be administered	Consider delaying start of concurrent Chemo Radiation on case-by-case basis, discuss with Radiation Oncology about sequential chemotherapy followed by Concurrent Chemo Radiation Consider using Q3W chemotherapy regimens, instead of QW chemotherapy to minimize exposure
STAGE IV	after completion of concurrent Chemo Radiation After initial induction chemo-immunotherapy, consideration should be made to space out interval between maintenance infusions, especially for those who have been on therapy for > 6 months and those with an excellent clinical/ radiographic response Stop immunotherapy for patients who have completed 2 years of treatment	For patients on TKI: Do not routinely hold TKI for Covid-19 positive patients unless symptomatic If symptomatic and concern for pneumonitis, advise testing for Covid-19 before making a
		decision about stopping therapy

Abbreviations: GGO: ground glass nodules, ACS: American College of Surgeons, SBRT: Stereotactic Body Radiation Therapy, TKI: Tyrosine Kinase Inhibitor

Management of Lung Cancer during the COVID-19 Pandemic

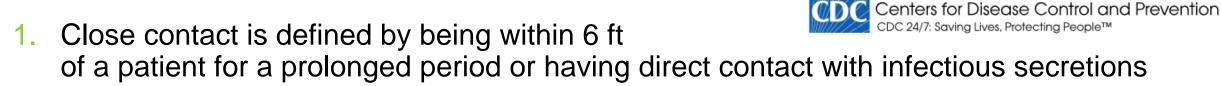


Table 2. Management recommendations and additional considerations for patients with SCLC by stage of disease

STAGE	RECOMMENDATIONS	ADDITIONAL CONSIDERATIONS
LS-SCLC	Continue with therapy as planned	Consider BID Radiation Therapy to minimize duration and exposure Start Radiation Therapy with cycle 2 of chemotherapy PCI should be recommended for patients < 75 years of age
ES-SCLC	Use oral instead of intravenous etoposide on days 1-3 of chemotherapy	Consider oral therapies such as PO temozolomide or PO topotecan for second line platinum resistant, refractory SCLC
	After induction chemo-immunotherapy, maintenance immunotherapy should be dosed Q4W (atezolizumab 1680 mg or durvalumab 1500 mg IV)	Refrain from PCI in consultation with radiation oncology

Abbreviations: BID: Twice Daily, PO: Oral, IV: Intravenous, PCI: Prophylactic Cranial Irradiation

WHAT THE CDC THINKS YOU SHOULD KNOW!



- 2. Patients with confirmed COVID19 or concern for infection should be isolated in private rooms with a mask and door closed
- 3. Practice hand hygiene before and after all patient contacts
- 4. PPE
 - 1. Respiratory or facemask (respirator for any aerosol generating procedures)
 - 2. Eye protection
 - 3. Gloves
 - 4. Gowns
- 5. Routine cleaning and disinfection procedures are appropriate for SARS-COV-2
- 6. You should contact occupational health with any unprotected exposure to a confirmed or possible case or if you develop symptoms yourself.

IASLO

WHO SHOULD WE BE TESTING?



UNITEDSA

IDSA:

- > Tier 1
 - > Critically ill patients receiving ICU care with unexplained viral pneumonia or respiratory failure regardless of travel/contact history
 - > Any person with fever or signs/symptoms of lower respiratory tract illness and close contact with a confirmed patient within 14 days of symptom onset
 - > Any person with fevers or signs/symptoms of lower respiratory tract illness and travel to an endemic area within 14 days
 - > Individuals with fevers or signs/symptoms of lower respiratory tract illness who are critical to the pandemic response (i.e.- healthcare workers, public health officials, or essential leaders)
- Tier 2: hospitalized (non-ICU) patients and long-term care residents with unexplained fever and sighs/symptoms of lower respiratory tract infection.
- > Tier 3: Patients in outpatient setting who meet the criteria for influenzas testing.
 - > Co-morbid DM, COPD, CHF, age >50, Immunocompromised hosts
 - > Pregnant women and symptomatic children with similar risks is encouraged
- > Tier 4: Community surveillance as directed by public health and/or ID authorities.

WHO SHOULD WE BE TESTING?





Centers for Disease Control and Prevention CDC 24/7: Saving Lives, Protecting People™

CDC:

- Hospitalized patients who have signs and symptoms compatible with COVID-19 in order to inform decisions related to infection control.
- > Other symptomatic individuals such as, older adults and individuals with chronic medical conditions and/or an immunocompromised state that may put them at higher risk for poor outcomes (e.g., diabetes, heart disease, receiving immunosuppressive medications, chronic lung disease, chronic kidney disease).
- Any persons including healthcare personnel, who within 14 days of symptom onset had close contact with a suspect or laboratory-confirmed COVID-19 patient, or who have a history of travel from affected geographic areas within 14 days of their symptom onset.

CHINA'S GUIDELINES FOR CANCER MANAGEMENT



- > Early stage cancer patients
 - > Postpone surgery/radiation if able
 - > Provide appropriate psychological counseling around treatment delay to patient and family via telemedicine
 - Recommend consideration of target therapy in adjuvant therapy to avoid side effects of chemo, repeated hospital visits, and immunosuppression
- > Patients infected with SARS-CoV-2 can resume care after 2 weeks of clinical stability
- > Prior to surgery or initiation of chemo/radiation a 2-week isolation is required with daily fever and symptom checks
- > Defer any unnecessary infusions (i.e. zoledronic acid)
- > Move any possible treatments into the "Day ward" (infusion suite) vs. hospital
- > Visits and labs to be done at remote centers and telemedicine if possible
- > Policies to mitigate wait times, PPE available to patients while in the health care system, appropriate barricades to entice patients to travel in low risk parts of the hospital

F



ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY



- > They do not offer their own set of guidelines, but refer the CDC's guidelines
- > Limit access to the facility through one point of entrance
- Triage stations should be set up outside the facility, clinic, or office with social distancing 6 ft apart to screen patients/visitors for COVID-19 symptoms and fever before entering
- > All patients seen in clinic should be screened for potential exposures or symptoms
- > All clinics, infusion suites, and waiting rooms should be redesigned with social distancing in mind
- > All patients should be informed on COVID 19 associated symptoms and instructed on appropriate hand hygiene
- > In the setting of fever a comprehensive fever work up should be performed
- > For most patients it is appropriate to continue or initiate routine treatment without anticipatory intensity modifications
- > If a patient is confirmed or presumed to be infected, standard treatment delays in the setting of infection should be performed.
 - > These patients should be given PPE and separated from other patients if they must be seen in clinic
- Minimize non-essential staff in clinic and ensure adequate supplies of PPE





- > There is no evidence for prophylactic antiviral therapy for immunosuppressed patients
- > Delivering as much care as possible remotely
 - > Conduct remote check ins for high risk patients
- > Limit visitors –allow only if essential for care delivery
- > Recommended strategic use of growth factor to mitigate treatment induced neutropenia
- > No evidence to support use of PPE in cancer patients on treatment who are not infected
- > Postpone cancer screening that requires inpatient evaluation (i.e. colonoscopy, mammogram)
- > Mental health services in the community should be identified and readily made available to patients/providers
- To consider:
 - > Holding chemo for patients in deep remission on maintenance
 - > Switching to oral chemo when possible to minimize clinic visits
 - > Arranging infusions at unaffected satellite sites or in the home if possible
 - > Holding chemo for 2 weeks for sites within an "infectious hub"
 - > Modifying or delaying chemo for high risk patients after a comprehensive risks/benefits analysis





- > Italy created new clinical pathways for cancer patients
 - > All for profit elective health care activity was stopped to increase health care access
 - > Hub and spoke networks established so cancer patients can be triaged to a parallel health system separated from the COVID 19 care centers
 - > Public and private care centers have combined their workforce, care-lines, resources
 - > Concentrate resources
 - > Care is driven by expert consultations
- > Like prior guidelines
 - > Delay treatments and direct clinical care when able and appropriate
 - > Aggressive disease prevention



Considerations from the SSCA experience

- > Disease prevention through screening, patient/provider education, and appropriate PPE use/training
- > Multilayer coverage system for clinics
- > Extending clinic hours and acute evaluation capabilities to triage patients away from ERs
- > Delay all non-essential care and rapidly expand telemedicine
 - > Defer non-essential consultations (i.e.- second opinions)
- > Treatment delays in the non-curative setting
- Treatment delays for cancer surgery when safe alternative neo-adjuvant options are available (i.e.endocrine therapy in early stage breast cancer)
- > Pro-active end of life care discussions with patients who are at high risk for serious illness
 - > with input from palliative care, ethics, and other disease site experts when appropriate.
- Remember provider and leadership well-being





- > Editorial article
- > Emphasized the "distraction effect" of the pandemic
 - The potential negative effect of shifting total attention away from standard clinical care to COVID-19 only
 - > Potential back-log of delayed and rescheduled cancer care
- Avoid, if possible, delaying any curative interventions (surgery, chemo, radiation)
- Emphasized the potential negative impact of delaying palliative chemo in terms of symptom control and survival time
- > Encouraged trying to continue screening activities like mammogram

Francesco et al, Annals of Oncology, March 2020





Ensure the continuum of care

- Cancer service should be delivered but all steps should be taken to protect patients from infection with SARS-CoV-2
 - For most patients the benefit of following a well-planned and well-controlled anti-cancer treatment plan will outweigh the risk of coronavirus infection
- > Utilization of new practice models including telemedicine
- Modifying regimen schedules to reduce number of clinic visits (i.e.- three or two weekly as opposed to weekly, oral or subcutaneous vs. IV)
- > A "previous day" telephone encounter should be recommended to identify flu-like symptoms
- > Good hygiene and use of PPE
- > Emotional support for cancer patients will be critical

NICE National Institute for Health and Care Excellence



- Communicate with patients and support their mental wellbeing, and help alleviate any anxiety and fear they may have about COVID19
- Minimize face to face contact and practice standard universal precautions and screen all patients for exposures and symptoms
- > Ask patients to attend appointments without family
- > Minimize time in the waiting area:
 - Encourage patients not to arrive early, text patients when you are ready to see them so they can wait in their car
- Note: symptoms of COVID19, neutropenic sepsis, and pneumonitis may be difficult to differentiate on presentation
- > Use table 1 to help inform priority for systemic treatment considering:
 - level of immunosuppression associated with treatment, patient specific risk factors, capacity issues, risk of cancer not being treated optimally with risk of being immunosuppressed and becoming ill from COVID19

Table 1 Prioritising patients for systemic anticancer treatment

Priority level	Categorisation based on treatment intent and risk:benefit ratio of treatment
1	Curative treatment with a high (more than 50%) chance of success
2	Curative treatment with an intermediate (15% to 50%) chance of success
3	Non-curative treatment with a high (more than 50%) chance of more than 1 year extension to life
4	Curative therapy with a low (0% to 15%) chance of success or non- curative therapy with an intermediate (15% to 50%) chance of more than 1 year extension to life
5	Non-curative therapy with a high (more than 50%) chance of palliation or temporary tumour control and less than 1 year expected extension to life
6	Non-curative therapy with an intermediate (15% to 50%) chance of palliation or temporary tumour control and less than 1 year expected extension to life





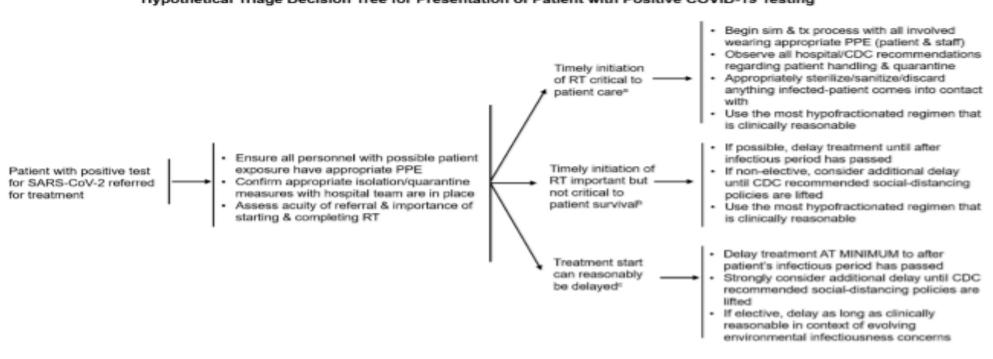
- > Try to deliver anti-cancer treatment in different and less immunosuppressive ways
 - > IV versus oral regimens
 - > Shorter treatment regimens
 - > Decrease frequency of immunotherapy regimens
 - > Providing repeat prescriptions
 - > Deferring infusions for long term prophylaxis (i.e. zoledronic acid)
 - > Utilize home delivery of prescriptions
 - > Using treatment breaks for long term treatments
- > Decisions should be made in a multi-disciplinary team

The Impact of COVID-19 on Radiation Oncology Clinics and Cancer Patients in the U.S.

Rivera et al.

Accepted to Advances in Radiation Oncology on March 19, 2020





Hypothetical Triage Decision Tree for Presentation of Patient with Positive COVID-19 Testing

^a cord compression, significant hemorrhage, very high α/β intact cancers (locally adv gyn, H&N, lung)

adjuvant RT after R0 or microscopically positive margins in grossly resected cancers, medium α/β intact cancers

^c elective cases (thalamotomies, BNI ≤ IV TGN), low α/β intact cancers (GG2-3 prostate ca, longstanding LGG/meningioma)



French Guidelines



> Applies to adult patients with solid tumors

> Prevention

- > Medical and radiation oncology should remain "COVID19 sanctuaries"
- Oncology patient's presence at hospitals/clinics should be minimized due to their increased susceptibility
 - Home infusions, IV-> Oral substitutions, telemedicine, regimen timing adjustment, temporary holidays for patients with metastatic disease
- In the hospital/clinic COVID19 patients should be isolated and treated separately from cancer patients

> Prioritization (esp. if hospital/clinical resources limited)

- (1) patients with cancer managed with curative intent (favoring those <60 yo and/or life expectancy >5 years)
- (2) patients with cancers managed with non-curative intent treatments and <60 and/or life expectancy >5 years
- (3) other patients with cancer managed with non-curative intent treatments, favoring those who if their disease progresses are at high risk for rapid mortality



COVID-19: global consequences for oncology

- Highlights the high-risk nature of cancer patients during the COVID-19 pandemic
 - > Need for significant healthcare resources in a time of healthcare overextension
 - > Increased vulnerability to infection
 - > Many clinical trials are halted
 - Challenges for collaboration and dissemination of new knowledge due to halting research conferences

Editorial

How we treat patients with lung cancer- review



- > All regimens with a survival benefit should be prioritized
- > Risk : benefit assessment for adjuvant treatments
- > RT concurrent or sequential to chemo with curative intent should be reserved for those with adequate respiratory function
 - > Stage III NSCLC RT should start on day 1 of chemo so only 2 cycles will be needed
- > Palliative or ablative RT should not be denied if it does not require multiple visits.
 - Txt to the lung should be limited to cases with compression of airways or bleeding
- > If patient is COVID19 positive but asymptomatic a 28-day delay should be considered
- > 2 negative tests 1 week apart should be performed before restarting treatment
- > Regimens with longer intervals and shorter duration should be preferred
- > Oral chemo should be considered for high risk patients (ECOG 2, elderly)
- > Use of prophylactic granulocyte colony stimulating factor

How we treat patients with lung cancer- review

Open access

Table 1 Practical suggestions to treat patients with lung cancer during the SARS-CoV-2 pandemic			
	Non-small cell lung cancer	Small cell lung cancer	
1. Should be started when possible*†	 NACHT for locally advanced resectable disease Sequential/concurrent CHT/RT§¶ for stage III disease First-line treatment for metastatic disease Palliative or ablative radiotherapy (SBRT) outside the lung** 	 disease Concurrent CHT/RT§ for limited-stage disease 	
2. Should not be stopped without justification	 NACHT for locally advanced resectable diseaset Sequential/concurrent CHT/RT§¶ for stage III disease First-line treatment for metastatic disease Maintenance ICI* 	 Concurrent CHT/RT§ for limited-stage disease First-line treatment for metastatic disease 	
3. Can be given preferentially	 CT/RT for stage III disease Oral chemotherapy for ECOG PS 2 and elderly patients (instead of intravenous) 	 Oral rather than intravenous chemotherapy 	
4. Can be withheld or delayed after careful consideration ^{††}	 Withhold ACHT in patients at significant COVID- 19-related risk‡‡ Delay ICI (within 42 days) for stage III disease after CHT/RT Withhold maintenance pemetrexed Prolong intervals of ICI* 	 Prolong intervals of ICI* 	
5. Should not be started without justification	Third and beyond lines of chemotherapy in patients at significant COVID-19-related risk‡‡	 PCI (favouring MRI surveillance) Thoracic consolidation radiotherapy extensive stage Third and beyond lines of chemotherapy in patients at significant COVID-19-related risk‡‡ 	

*Regimens with longer interval (including ICI; ie, nivolumab 480 mg every 4 weeks or pembrolizumab 400 mg every 6 weeks) should be preferred.

†Shorter duration of chemotherapy (ie, four cycles of chemotherapy instead of six) should be discussed with patients and use of prophylactic G-CSF should be considered.

‡NACHT could be helpful to bridge time to surgery in case where surgery is not possible.

§In patients with adequate respiratory function.

Try to start RT on day 1 of chemotherapy, only two cycles will be needed, three cycles if starting RT with cycle 2, or sequential. "Exception: indicated if compression of airways or bleeding. Fractions of SBRT could be reduced if organ at risk constraints (from eight fractions to five or three) and palliative RT single or in two fractions (8–10 Gy or 17 Gy, respectively) should be used where possible. ††Patients with family members or caregivers who tested positive for COVID-19 should be tested before or during any cancer treatment, whenever. If a patient results positive and is asymptomatic 28 days of delay should be considered before (re)starting the treatment. In the case of SARS-CoV-2, two negative tests at 1-week interval should be performed before (re)starting the treatment.

‡‡Patients at significant COVID-19-related risk: aged ≥70, with ischaemic cardiac disease, atrial fibrillation, uncontrolled hypertension or diabetes, chronic kidney disease.

ACHT, adjuvant chemotherapy; CHT, chemotherapy; COVID-19, coronavirus disease; ECOG PS, Eastern Cooperative Oncology Group Performance Status; G-CSF, granulocyte colony-stimulating factor; ICI, immune checkpoint inhibitor; NACHT, neoadjuvant chemotherapy; PCI, prophylactic cranial irradiation; RT, radiotherapy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SBRT, stereotactic body radiotherapy.

⁸³ Banna et al, ESMO open, April 2020

Conquering Thoracic Cancers Worldwide

IASIC

Home care for cancer patients



- Letter describing the strategies employed by the Tuscany Tumor Association during the COVID-19 pandemic
- > Two triage approach to protect patients and providers from infection
 - > 1) Phone triage 48 hours prior
 - > Has the pt experienced fever, SOB, breathlessness or cough?
 - > Has the pt, or household contacts, participated in high risk travel?
 - Has the pt, or household contacts, had any direct contact with people infected with COVID-19?
 - > Has the patient, or household contacts, had direct contact with people currently in quarantine?
 - > 2) If first screen negative the patient will undergo a second telephone interview in order to schedule home accesses, avoiding unnecessary contacts. Patients are assessed score symptom severity with the PERSONS score and life expectancy with the palliative prognostic score.
 - Based on these scores' patients are given a color green, yellow, or red based on severity and care is triaged based on clinical need

Cancer Management



- > Focus an appropriate resource allocation to allow for ongoing cancer care
- Clear communication and transparency between stakeholders, suppliers, and health organizations about treatment supply lines
- Cancer diagnosis should still be a priority and strategies for safe diagnostic procedures need to be establishes (i.e. endoscopy in negative pressure rooms)
- > Minimize unnecessary foot traffic in clinics
- > Screen all patients and providers for symptoms/exposures
- > Chemo delays, switching to oral regimens, prolonging regimens on a case by case basis
- > Hospitalized cancer pts should be physically separated from COVID-19 pts
- > Anticipate limitations in available blood supply
- > Adequately address patient distress

Cancer guidelines during the COVID-19 pandemic 🦇



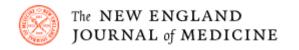
- > Some additional guidelines not discussed above
 - The Society of Surgical Oncology website includes disease site specific resources to help guide decisions
 - European Society of Surgical Oncology (ESSO) advised against seeing patients older than 70 in clinic unless urgent
 - > American Society for Radiation Oncology contains a large section on COVID19
 - > US FDA, US NCI and EMA have issued guidance on managing clinical trials
 - Global Radiation Oncology Target Response is a paper with 121 contributors with specific advice to guide radiotherapy treatments (i.e. what can be omitted)

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Framework for prioritizing use of radiotherapy and IASLC systemic therapy during COVID-19

This prioritization Lower Priority **Higher Priority** scheme still Imminent risk of early mortality Acute leukaemias, aggressive lymphomas, metastatic germ cell tumours requires Potential high morbidity and/or impaired quality of life Radiotherapy for spinal cord compression or opioid-refractory pain Consideration of crisis owing to bone metastases **Definitive curative treatments** resources Concurrent chemoradiotherapy for head and neck, cervical, or anal cancers Patient specific risk > Neoadjuvant or adjuvant indications with substantial benefit Adjuvant chemotherapy for stage III colon cancer, chemotherapy factors and goals and/or radiotherapy for high-risk breast cancer Neoadjuvant or adjuvant indications with modest survival benefit Ability of staff to Neoadjuvant or adjuvant chemotherapy for bladder cancer, or adjuvant chemotherapy for NSCLC safely deliver Palliative indications with substantial survival benefit Immunotherapy for melanoma, systemic therapy for metastatic breast cancer treatment or metastatic colorectal cancer Palliative indications with modest survival benefit and/or major symptom control > How long a patient Palliative chemotherapy for upper gastrointestinal cancers, radiotherapy for bone metastasis unresponsive to other treatments has been waiting Palliative indications without benefits in terms of overall survival or major symptom control for care Second-line and third-line palliative chemotherapy for many solid tumours Alternative treatments exist or delay does not affect outcomes Bone metastases manageable with medications, prostate cancer appropriate for active surveillance

Conquering Thoracic Cancers Worldwide



Perspective



Between Scylla and Charybdis — Oncologic Decision Making in the Time of Covid-19

Mark A. Lewis, M.D.

- > Perspective piece
- Discusses challenges about weighing risks/benefits of cancer treatment during the pandemic
- Concern for a bimodal peak of caner deaths- the immediate spike in those dying form COVID followed by a latent toll of those whose treatments were de-intensified, delayed, or canceled all together



> Editorial

- > Due to the fact lung cancer patients are at higher risk for severe COVID 19 due to age, co-morbidities, structural lung disease, likely prior smoking history, as well as their cancer and its treatment, baseline SARS-COV-2 testing for all patients affected by lung cancer should be recommended
- Also recommends considering bronchoscopy to increase testing sensitivity in the s/o negative RT-PCR and a concerning CT chest w/ or w/o symptoms

Caring for our cancer patients in the wake of COVID-10



> Limit exposure

- > Virtual outpatient visits
- Virtual assessments of any possible symptoms prior to scheduled chemotherapy, with delayed treatment for those who have possible COVID-19 symptoms
- > Encouraging hand washing and social distancing
- > Restrict visiting on inpatient wards

Rationalize treatment

- > Prioritize systemic treatment to those who will have most benefit (i.e. curative)
- > Consider treatment delays, especially in high risk patients
- > Prioritization and rationalization of surgeries based on urgency, symptoms, and possibly cure

> Limit morbidity

- > More liberal use of growth factor
- Early identification of infection with on the door triage/assessments in those w/ fevers or symptoms
- > Delaying all treatments in COVID-positive or query patients
- > Ensure that patients are fully vaccinating
- > Provision of oncological support in decision making for admitted COVID-19 cancer patients

Taking care of older patients with cancer in the context of COVID-19 pandemic



> Letter

- Treatment decisions need to take into consideration cancer type, disease extent, prognosis, and treatment opportunities irrespective of a patients age
 - > *while acknowledging the risks associated with viral infection
- > Evaluation of life expectancy should be part of treatment decision making
- Alternatives to standard therapy that have few side effects on the immune system (i.e. endocrine therapy) should be favored and are preferred to no treatment
- Consider using committees, including ethics, to make treatment decisions

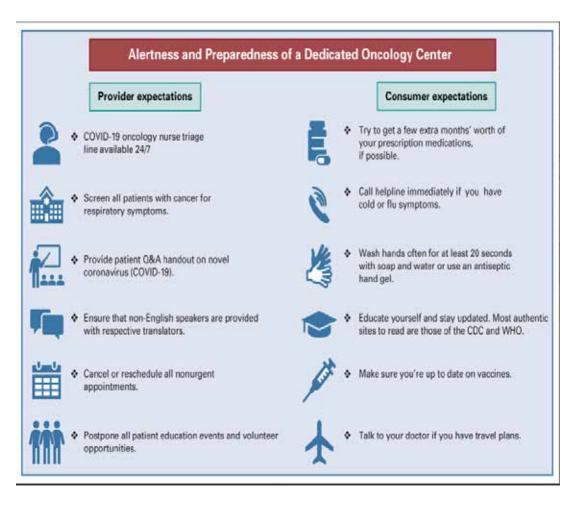
Mourey et al, Lancet Oncology, April 2020

Managing COVID-19 in patients with cancer: a double blow for oncologists



> Editorial

- Cancer patients likely are higher risk for severe COVI-19 as well as higher risk for exposure to the virus
- > Multiple practical challenges
 - > How to interpret imaging
 - Knowing drug-drug interactions with upcoming COVID-19 treatments
 - Practically considering how to deliver care



How to guarantee the best care to pts with cancer during IASLC the COVID-19 epidemic: the Italian experience

- > Had to establish an adapted risk communication with updates of statistics related to infected cases and an adjusted level of alert of patients/providers
- > PPE and rigorous infection prevention/control measures in clinics
- Three cancer comprehensive cancer center were identified to delivery cancer care in a hub-spoke model
- > Widespread patient education about the virus and how to protect themselves
- > Telemedicine was widely used
- > Checkpoint areas for COVID-19 screening were set up prior to access to one of the cancer hospitals
 - > Patients of concern were tested and transferred to COVID-19 hospitals
- Continued clinical trials as able, working closely with sponsors to allow for flexibility and elimination of any burdensome procedures/visits with continued close monitoring

How to guarantee the best of care to patients with cancer IASLC during the COVID-19 epidemic: the Italian experience

Table 1. National strategy to guarantee access to care of patients with cancer

Setting	Strategy	Measures
Patients "off treatment"	Prevention Symptom-oriented follow-up Implement telemedicine follow-up	Education on COVID-19 symptoms to increase patient awareness Phone contact with all patients in the epidemic areas to implement social isolation measures Suggestion for protection supplies in case of suspect contacts
Patients "on treatment" with curative intent	Prevention Implement cancer care within a hub-and-spoke network Guarantee a "COVID-19–free" clinical pathway in the hub hospital	All measures listed above Guarantee the best of care Reduce access to hospital for relatives and vendors Cancer team using PPE Establish checkpoint in the hub to avoid access of infected patients Intensify safety monitoring for patients receiving active treatment using telemedicine
Patients "on treatment" in the metastatic setting	Prevention Implement cancer care within a hub-and-spoke network Guarantee a COVID-19–free clinical pathway in the hub hospital	All measures listed above Prioritize treatment according to magnitude of clinical benefit that qualifies patient for a specific treatment (e.g., significant overall survival gain and/or substantial improvement in QoL) When chemotherapy is recommended, prefer oral treatments to reduce access to hospital All patients must be assured of the best home-based supportive care and enhanced symptoms control via telemedicine

Abbreviations: PPE, personal protection equipment; QoL, quality of life.

How to guarantee the best of care to patients with cancer IASLC during the COVID-19 epidemic: the Italian experience

Table 2. Examples of prioritizing cancer treatment: European Society for Medical Oncology model for early breast cancer medical treatment

High priority	Medium priority	Low priority
Neoadjuvant and adjuvant chemotherapy for patients with triple-negative breast cancer	Prefer endocrine therapy and delay surgery for postmenopausal women with stage I cancers, low-intermediate grade tumors, lobular breast cancers, low-risk genomic signatures	Follow-up imaging, restaging studies, echocardiograms, electrocardiograms, and bone density scans can be delayed if patient is clinically asymptomatic or there are clinical signs of response in the neoadjuvant setting
Neoadjuvant and adjuvant chemotherapy in combination with targeted therapy for patients with HER2+ breast cancer		
Neoadjuvant and adjuvant endocrine therapy \pm chemotherapy for estrogen receptor+/HER2– breast cancer		
Completion of neoadjuvant chemotherapy (with or without anti-HER2 therapy) that has already been initiated		
Continuation of standard adjuvant endocrine therapy in pre- and postmenopausal setting Use telemedicine to manage potential toxicity reported by patients		
Continuation of treatment in the context of a clinical trial, provided patient benefits outweigh risks, with possible adaptation of procedures without affecting patient safety and study conduct		

Safety at the Time of the COVID-19 pandemic: how to keep our oncology patients and healthcare workers safe



- Caregivers who are exhibiting concerning symptoms should be isolated
- No clear guidelines exist regarding when a cancer pt who has tested positive for COVID-19 can resume therapy
 - > CDC recommends a two test approach each >/=24 hours apart in the s/o symptom and fever resolution
 - If no testing at least 7 days from initial symptoms and 3 days from last fever
- > Anticipate PPE shortages
- Self-care and stress management

Table 1. Recommendations for Oncology Practices
During COVID-19

Patient Safety

Prescreen and screen for COVID-19 symptoms and exposure history via telephone calls or digital platforms

Develop screening clinics to allow for patients with symptoms to be evaluated and tested in a dedicated unit with dedicated staff

Convert in-person visits to telemedicine visits when possible

Limited or no visitor policy

Limit surgeries and procedures to only essential, urgent, or emergent cases

Consideration of alternative dosing schedule to allow for fewer in-person visits to the cancer center and/or the infusion center

Switch therapy to oral oncolytics if equivalent formulation of infusional therapy is available

Transition outpatient care to care at home whenever possible (eg, pump disconnection, administration of growth factors, hormone therapy)

Increase interval between scans or use biochemical markers in lieu of scans

Provide resources for wellness and stress management for patients

Healthcare Worker Safety

Assure appropriate personal protective equipment (PPE) per guidelines

Create a centralized resource or website to communicate the recommendations to the healthcare workers as guidelines around PPE and workflows change

Implement daily screening tools and/or temperature checks

Telecommute when possible, with limited onsite staff participating in rotations on a daily basis

Establish clear stay-at-home and return-to-work guidelines

Provide resources for wellness and stress management for healthcare workers

Recommendations of individualized medical Tx and common IASLC AEs for lung ca pts during the outbreak of COVID-19 epidemic

- > Focus on infection prevention
- > New treatment starts should be made considering tumor burden and the clinical condition of the patient
- For patients with low tumor burden, stable disease, or undergoing post operative chemo or maintenance t/c delaying treatment or switching to oral options where available
- > For patients on immunotherapy potential immune related AEs (i.e. pneumonitis) should be considered
 - > For patients with stable disease treatment can be postponed or suspended
- > Extend restaging exams/scans in patients w/o symptoms
- Patients should be encouraged to monitor their respiratory symptoms as well as report any fevers
- Patients should be encouraged to sleep, eat a health diet, exercise, and participate in wellness exercises

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