COVID-19 in ONCOLOGY PATIENTS

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Hematology/Oncology Fellow PGY-4
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IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide
WHAT ARE WE IN FOR?

› Part I – Important background data
› Part II – Focus on relevant papers
› Part III – Discussion of any available guidelines
› Part IV – Discussion of treatments and areas of investigation
› Part VI – Questions and Discussion
PART I – BACKGROUND
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

Source: Johns Hopkins CSSE • Get the data • Created with Datavizapper
WHAT IS THE SARS-COV-2?

› Member of the Coronaviridae family
HOW IS IT SPREAD?

- Spread through respiratory tract by droplets, respiratory secretions, and direct contact
  - Viable in aerosols for 3+ hours
  - Stable on plastics and stainless steel for up to 72 hours
- Virus RNA has been identified in samples from stool, GI tract, saliva, tears, and urine
- Median incubation period is reported to be 3-5 days (1-14 days)
- 95% experience symptoms by day 12.5 of contact

HOW DO PATIENTS PRESENT?

› Clinical presentations can range from asymptomatic to severe respiratory failure
  › In China
    › 81% mild
    › 14% severe
    › 05% critical
    › Case fatality rate 2.3% (China)
      › Cases aged 70-79 8.0%
      › Case older than 80 14.8%
    › Case fatality rate 7.2% (Italy)
      › 20% had active cancer

› Primary symptoms
  › Fever, fatigue, dry cough, myalgia, dyspnea

› Uncommon symptoms
  › Sputum production, headache, hemoptysis, diarrhea, pleuritic chest pain

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Table 2 Clinical Symptoms associated with COVID-19.

<table>
<thead>
<tr>
<th>Clinical types</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild type</td>
<td>nonpneumonia or mild pneumonia</td>
</tr>
<tr>
<td>Severe type</td>
<td>dyspnea, respiratory frequency ≥ 30/min, blood oxygen saturation ≤ 93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio &lt; 300, and/or lung infiltrates &gt;50% within 24 to 48 hours</td>
</tr>
<tr>
<td>Critical type</td>
<td>respiratory failure, septic shock, and/or multiple organ dysfunction or failure</td>
</tr>
</tbody>
</table>
HOW IS IT DIAGNOSED?

› Current standard is nucleic acid detection via samples from nasopharyngeal swabs by real time PCR or full genome sequencing
  › RT-PCR of throat swabs only 60% positive in early stages of the disease even for patients with severe disease
  › Sputum samples > Nasal swabs > throat swabs

› 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

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% Ill defined margins
- 35% Smooth or irregular interlobular septal thickening
- 47% Air bronchograms
- 10% Crazy-paving pattern
- 32% thickening of adjacent pleura


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

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).
DIAGNOSTIC CHALLENGES IN ONCOLOGY PATIENTS

- 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 on 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


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).
PART II – JOURNAL ARTICLES
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., et al., for the China Medical Treatment Expert Group for Covid-19
WHO ARE THE PATIENTS?

› 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
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
Comment | Volume 21, Issue 3, P339–337, 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 | Check for updates
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

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

*, 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

*Please see supplemental document
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

*Please see supplemental document
WHAT ARE THE AUTHORS RECOMMENDATIONS?

1. An intentional postponing of adjuvant chemotherapy or elective surgery for stable cancer patients in endemic areas.

2. Stronger personal protective provisions should be made for patients with cancer or cancer survivors.

3. 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.

Liang et al, Lancet Oncology, February 2020
Analysis of Epidemiological and Clinical features in older patients with Corona Virus Disease 2019 (COVID-19) out of Wuhan

Jiangshan Lian, Xi Jin, Shaorui Hao, Huan Cai, Shanyan Zhang, Lin Zheng, Hongyu Jia, Jianhua Hu, Jianguo Gao, Yimin Zhang... Show more
WHO ARE THESE PATIENTS?

- 788 patients - 136 patients greater than 60, 652 younger than 60
- No significant difference in smoking history
- Higher frequency of older patients were women (57.3% vs. 46.4%)
- Higher frequency of co-morbidity in older patients (55.1% vs. 21.9%)
  - 3/652 (0.46%) of young patients and 3/136 (2.21%) of older patients had cancer

Lian et al, Clinical Infectious Diseases, March 2020

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Age &lt;60 (n=652)</th>
<th>Age ≥60 (n=136)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>41.13±11.38</td>
<td>68.28±7.314</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>303/652 (46.47%)</td>
<td>78/136 (57.35%)</td>
<td>0.021</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>46/652 (7.06%)</td>
<td>8/136 (5.88%)</td>
<td>0.622</td>
</tr>
<tr>
<td>Coexisting Condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>143/652 (21.93%)</td>
<td>75/136 (55.15%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>73/652 (11.20%)</td>
<td>53/136 (38.97%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>33/652 (5.06%)</td>
<td>24/136 (17.65%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>25/652 (3.83%)</td>
<td>6/136 (4.41%)</td>
<td>0.753</td>
</tr>
<tr>
<td>Cancer</td>
<td>3/652 (0.46%)</td>
<td>3/136 (2.21%)</td>
<td>0.067</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>5/652 (0.77%)</td>
<td>2/136 (1.47%)</td>
<td>0.347</td>
</tr>
<tr>
<td>Heart disease</td>
<td>5/652 (0.77%)</td>
<td>6/136 (4.41%)</td>
<td>0.005</td>
</tr>
<tr>
<td>COPD</td>
<td>0/652 (0%)</td>
<td>3/136 (2.21%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>0/652 (0%)</td>
<td>1/136 (0.74%)</td>
<td>0.173</td>
</tr>
</tbody>
</table>
HOW DID THEY PRESENT?

- Median incubation time was 5 days for both groups
- Older patients more likely to be diagnosed with severe (16.1% vs. 5.98%) or critical (8.82% vs. 0.77%) disease
- No significant difference in percentages of fever, cough, sputum production, GI symptoms, myalgias, and headache between two groups
  - Older patients tend to present with higher fevers (>38°C)
- Older patients were more likely to present with SOB (12.5% vs. 3.07%) and were less likely to have congestion (1.47% vs. 6.90%)
- Older patients had more severe laboratory derangements
  - Lymphocytopenia, anemia, transaminitis, elevated creatinine kinase, elevated LDH, elevated CRP
- Older patients more commonly presented with multiple mottling and ground glass opacities on CT imaging

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age &lt;60 (n=652)</th>
<th>Age ≥ (n=136)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute respiratory distress</td>
<td>35/652 (5.37%)</td>
<td>23/136 (16.91%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>1/652 (0.15%)</td>
<td>1/136 (0.74%)</td>
<td>0.316</td>
</tr>
<tr>
<td>Liver function abnormality</td>
<td>72/652 (11.04%)</td>
<td>10/136 (7.35%)</td>
<td>0.200</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>10/652 (1.53%)</td>
<td>3/136 (2.21%)</td>
<td>0.478</td>
</tr>
</tbody>
</table>

Lian et al, Clinical Infectious Diseases, March 2020
HOW WERE THEY MANAGED?

- 86% of older patients and 85.5% of younger patients were treated with antiviral therapy within 3 days of symptom onset.
- Median treatment duration was 11 days for both groups.
- No difference regarding the antiviral regimen between two groups.
  - Interferon alpha + lopinavir/ritonavir + arbidol, interferon alpha + lopinavir/ritonavir, lopinavir/ritonavir + arbidol, interferon alpha + arbidol
- 9.36% of young patients vs 26.68% of older patients were treated with steroids.
- 5.83% of young patients vs 17.65% of older patients were treated with IVIG.
- 1.38% of young patients vs 9.56% of older patients required ICU care.
- 1.38% of young patients vs 6.62% of older patients required ventilation.
  - Non-invasive 0.61% vs 2.21%
  - Invasive 0.77% vs. 4.41%
- All patients survived by the end point (February 12, 2020) and 44.6% of young patients vs. 22.8% of older patients had been discharged.
Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China

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
OUTLINE REPORTS

Outcome of Oncology Patients Infected With Coronavirus

*Abdul-Rahman Jazieh*, MD, MPH; *Thamer H. Alenazi*, MD; *Ayman Alhejazi*, MD; *Faisal Al Safi*, MD; and *Ashwag Al Olayan*, MD
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% ARDS, 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>
<thead>
<tr>
<th>TABLE 4.</th>
<th>Patient Outcomes (N = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>No.</td>
</tr>
<tr>
<td>Survival</td>
<td></td>
</tr>
<tr>
<td>Dead</td>
<td>16</td>
</tr>
<tr>
<td>Alive</td>
<td>3</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
</tr>
<tr>
<td>Multi-organ failure</td>
<td>6</td>
</tr>
<tr>
<td>Septic shock</td>
<td>4</td>
</tr>
<tr>
<td>Cancer related</td>
<td>4</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>2</td>
</tr>
<tr>
<td>ARDS</td>
<td>2</td>
</tr>
<tr>
<td>Othera</td>
<td>3</td>
</tr>
<tr>
<td>Median No. of days from hospital admission to death (min-max)</td>
<td>23 (10-79)</td>
</tr>
<tr>
<td>Median No. of days from hospital admission to ICU admission (min-max)</td>
<td>12 (1.76)</td>
</tr>
<tr>
<td>Median No. of days from ICU admission to death (min-max)</td>
<td>10 (1.25)</td>
</tr>
</tbody>
</table>

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit; min, minimum; max, maximum.
*aSevere metabolic acidosis, no code (kidney injury), severe community acquired pneumonia.
Research Letter

March 25, 2020

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

Jing Yu, MD1,2,3; Wen Ouyang, MD1,2,3; Melvin L. K. Chua, MBBS, PhD1,4,5; et al

Author Affiliations  |  Article Information

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 COVID-19

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 with 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 of a patient with CLL

Case report from China published in The Lancet Hematology

39 M with hx of NHL previously treated with R-CHOP and CLL on oral chlorambucil (10mg/m2) per day which he had stopped taking in 12/2019 due to cost

2/16/2020 presented with fever
- Wbc 9.1 (96% lymphs), hgb 8, plt 79, plasma concentration of immunoglobulins were globally reduced
- CT chest with bilateral GGO
- SARS-COV-2 PCR positive

Treated with Chlorambucil 2mg BID to control his CLL

Treated with interferon alpha bid, IVIG 20g daily, IV methylprednisolone 40mg BID for 9 days
- Continued to have fever and require non-invasive mechanical ventilation

Day 8 dyspnea resolved, and he was able to be weaned from mechanical ventilation

Treatment day 10-14 transitioned to IV methylprednisolone 40mg BID with oral chlorambucil 2mg twice per day

CT Chest 3/1/2020 with significant improvement observed for 7 more days and discharged
PART III – AVAILABLE GUIDELINES
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
They do not offer their own set of guidelines, but refer the CDC’s guidelines.

No current guidelines about what practices should do if a patient seen is later found to have been infected.

All patients seen in clinic should be screened for potential exposures or symptoms.

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.

There is no evidence for prophylactic antiviral therapy for immunosuppressed patients.
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)

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
High risk patients (exposures or symptoms) should be tested for SARS-CoV-2 via the CDC recommended PCR test as well as for all other high-risk respiratory viruses.

Chest imaging should be highly considered

Treatment
  - Normal chest imaging + no symptoms -> no therapy
  - Normal chest imaging + mild symptoms -> no therapy
  - Abnormal chest imaging +/- lower respiratory tract symptom -> ID consult
    - To consider compassionate use of remdesivir or hydroxychloroquine with ID guidance
  - Positive BAL -> consult ID

Deferring transplant/CAR T when possible
  - EBMT recommends 14 days of isolation with RT PCR testing for all patients prior to clearance
  - EBMT recommends deferring treatment for 3 months after diagnosis of COVID19 or at least until the patient is asymptomatic and has had 2 RT PCR negative tests 1 week apart
  - EBMT recommends that patients with exposures should wait 21 days prior to considering treatment
  - Donors cannot have traveled or had known exposures for 28 days
  - Donors cannot donate for 3 months after known disease if urgent and donor is well they need to test negative by RT PCR
WHO SHOULD WE BE TESTING?

**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 signs/symptoms of lower respiratory tract infection.

- **Tier 3:** Patients in outpatient setting who meet the criteria for influenza 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?

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.
1. Close contact is defined by being within 6 ft of a patient for a prolonged period or having direct contact with infectious secretions.

2. Patients with confirmed COVID-19 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.
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
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

<table>
<thead>
<tr>
<th>Priority level</th>
<th>Categorisation based on treatment intent and risk/benefit ratio of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Curative treatment with a high (more than 50%) chance of success</td>
</tr>
<tr>
<td>2</td>
<td>Curative treatment with an intermediate (15% to 50%) chance of success</td>
</tr>
<tr>
<td>3</td>
<td>Non-curative treatment with a high (more than 50%) chance of more than 1 year extension to life</td>
</tr>
<tr>
<td>4</td>
<td>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</td>
</tr>
<tr>
<td>5</td>
<td>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</td>
</tr>
<tr>
<td>6</td>
<td>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</td>
</tr>
</tbody>
</table>
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
Specific drug and treatment priorities for medical, surgical and radiation oncologists

- Emphasis on curative intent and non-immunosuppressive regimens.
- Broken down by priority level addressing chemotherapy, endocrine therapy, antiHER2, CDK4/5 inhibitors
- Please see supplement for specific guidelines

<table>
<thead>
<tr>
<th>Table 1. Priorities for Breast Disease Focused Outpatient Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Priority A</strong></td>
</tr>
<tr>
<td>Potentially unstable (e.g. hematoma, infection)</td>
</tr>
<tr>
<td>New diagnosis of invasive cancer-may convert to telemedicine visit</td>
</tr>
<tr>
<td>Established patients with new problems or symptoms from treatment-convert as many visits to telemedicine visits</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Priorities for Breast Disease Focused Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Priority A</strong></td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>Biopsies for abnormal mammograms or breast symptoms</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Hypothetical Triage Decision Tree for Presentation of Patient with Positive COVID-19 Testing

- Patient with positive test for SARS-CoV-2 referred for treatment
  - Ensure all personnel with possible patient exposure have appropriate PPE
  - Confirm appropriate isolation/quarantine measures with hospital team are in place
  - Assess acuity of referral & importance of starting & completing RT

  - Timely initiation of RT important but not critical to patient survival
    - If possible, delay treatment until after infectious period has passed
    - If non-elective, consider additional delay until CDC recommended social-distancing policies are lifted
    - Use the most hyperfractionated regimen that is clinically reasonable

  - Treatment start can reasonably be delayed
    - Delay treatment at MINIMUM to after patient's infectious period has passed
    - Strongly consider additional delay until CDC recommended social-distancing policies are lifted
    - If elective, delay as long as clinically reasonable in context of evolving environmental infectiousness concerns

  - Timely initiation of RT critical to patient care
    - Begin simulation & tx process with all involved wearing appropriate PPE (patient & staff)
    - Observe all hospital/CDC recommendations regarding patient handling & quarantine
    - Appropriately sterilize/sanitize/discard anything infected-patient comes into contact with
    - Use the most hypofractionated regimen that is clinically reasonable

---

Figure 1 – A hypothetical decision tree for the triage of a patient with COVID-19 referred for radiation therapy

- **\( ^a \)** cord compression, significant hemorrhage, very high \( \alpha/\beta \) intact cancers (locally adv gyn, H&N, lung)
- **\( ^b \)** adjuvant RT after R0 or microscopically positive margins in grossly resected cancers, medium \( \alpha/\beta \) intact cancers
- **\( ^c \)** elective cases (blatomatomies, BNI & IV TGN), low \( \alpha/\beta \) intact cancers (GG2-3 prostate ca, longstanding LGM 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
Editorial

- 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

Lancet Oncology, April 2020
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 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
### Table 1: Practical suggestions to treat patients with lung cancer during the SARS-CoV-2 pandemic

<table>
<thead>
<tr>
<th>Non-small cell lung cancer</th>
<th>Small cell lung cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Should be started when possible</strong>†</td>
<td>NACHT for locally advanced resectable disease</td>
</tr>
<tr>
<td></td>
<td>Sequential/concurrent CHT/RT§§ for stage III disease</td>
</tr>
<tr>
<td></td>
<td>First-line treatment for metastatic disease</td>
</tr>
<tr>
<td></td>
<td>Palliative or ablative radiotherapy (SBRT) outside the lung**</td>
</tr>
<tr>
<td><strong>2. Should not be stopped without justification</strong></td>
<td>NACHT for locally advanced resectable disease</td>
</tr>
<tr>
<td></td>
<td>Sequential/concurrent CHT/RT§§ for stage III disease</td>
</tr>
<tr>
<td></td>
<td>First-line treatment for metastatic disease</td>
</tr>
<tr>
<td></td>
<td>Maintenance ICIT</td>
</tr>
<tr>
<td><strong>3. Can be given preferentially</strong></td>
<td>CT/RT for stage III disease</td>
</tr>
<tr>
<td></td>
<td>Oral chemotherapy for ECOG PS 2 and elderly patients (instead of intravenous)</td>
</tr>
<tr>
<td><strong>4. Can be withheld or delayed after careful consideration</strong> ‡</td>
<td>Withhold ACHT in patients at significant COVID-19-related risk‡‡</td>
</tr>
<tr>
<td></td>
<td>Delay ICIT (within 42 days) for stage III disease after CHT/RT</td>
</tr>
<tr>
<td></td>
<td>Withhold maintenance pemetrexed</td>
</tr>
<tr>
<td></td>
<td>Prolong intervals of ICIT</td>
</tr>
<tr>
<td><strong>5. Should not be started without justification</strong></td>
<td>Third and beyond lines of chemotherapy in patients at significant COVID-19-related risk‡‡</td>
</tr>
<tr>
<td></td>
<td>PCI (favouring MRI surveillance)</td>
</tr>
<tr>
<td></td>
<td>Thoracic consolidation radiotherapy for extensive stage</td>
</tr>
<tr>
<td></td>
<td>Third and beyond lines of chemotherapy in patients at significant COVID-19-related risk‡‡</td>
</tr>
</tbody>
</table>

*Regimens with longer interval (including ICIT; 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 cases 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 distant 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; ICIT, 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.
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 patient experienced fever, SOB, breathlessness or cough?
     - Has the patient, or household contacts, participated in high risk travel?
     - Has the patient, 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 established (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 patients should be physically separated from COVID-19 patients
- Anticipate limitations in available blood supply
- Adequately address patient distress
PART IV – TREATMENTS AND AREAS OF INVESTIGATION
## ARE THERE TREATMENTS OUT THERE? – NONE YET

### Treatments with potential clinical effect

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir</td>
<td>• investigational monophosphoramidate prodrug of an adenosine analog</td>
<td>• In multiple clinical trials</td>
</tr>
<tr>
<td></td>
<td>• Binds to the RNA dependent RNA polymerase and acts as a RNA chain terminator</td>
<td>• Decreased virus lung titers in animal models</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Promising in-vitro data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Case reports of potential clinical benefit</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Available through compassionate use request from gilead</td>
</tr>
<tr>
<td>Chloroquine and Hydroxychloroquine</td>
<td>• Antimalarial agents with anti-inflammatory and immunomodulatory activities</td>
<td>• In multiple clinical trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Promising in-vitro data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Promising case reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Non-blinding non-randomized study of 36 patients showed increased viral clearance with hydroxychloroquine (6 pts received azithromycin in addition with heightened viral clearance)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Recent RCT of hydroxychloroquine with 30 pts showed no benefit</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No safety or efficacy data to drive dosing</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>• HIV-1 protease inhibitor</td>
<td>• Promising in-vitro activity against SARS-CoV-1 and MERS</td>
</tr>
<tr>
<td></td>
<td>• Potent CYP3A4 inhibitor which acts as a booster</td>
<td>• Promising case reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bin et al, recently published a negative RCT in NEJM</td>
</tr>
<tr>
<td>Convalescent plasma</td>
<td>• Passive immunity from recovered patients</td>
<td>• US FDA announced on 03/24/2020 that it can be collected and used in emergent settings</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• For not time sensitive requests (4-8 hours), complete form 3926 and email <a href="mailto:CBER_eIND_Covid-19@FDA.HHS.gov">CBER_eIND_Covid-19@FDA.HHS.gov</a>, call 1-866-300-4374 for emergencies</td>
</tr>
</tbody>
</table>
ARE THERE TREATMENTS OUT THERE? – NONE YET

› Potential Adjuncts
  › Tocilizumab is undergoing a phase III trial for patients with severe disease
  › Other anti-inflammatory drugs are also being evaluated in severe disease such as sarilumab, corticosteroids (very mixed data at this time)

› When risks outweigh the benefits
  › Ribavirin +/- interferon
  › Oseltamivir and baloxavir

› Additional agents under investigation
  › Anakinra, abidol, baricitinib, bevacizumab, brilacidin, convalescent plasma (see below), darunavir/cobicistat, disulfiram, eculizumab, favipiravir, galidesivir, griffithsin, IVIG, nelfinavir, niclosamide, REGN3048, sarilumab, sofosbuvir, TZLS-501, Vit C, XueBijing

› Passive immunity with convalescent sera or from genetically engineered animal hosts
  › There is evidence from SARS-CoV-1 that convalescent sera contain neutralizing antibodies related to the virus

Letter to the Editor

Tocilizumab, an anti-IL6 receptor antibody, to treat Covid-19-related respiratory failure: a case report
Role of Tocilizumab

- The pathogenesis of severe acute respiratory syndrome related to coronavirus involves a cytokine storm with high serum levels of pro-inflammatory cytokines and chemokines.
- IL-6 appears as one of the key cytokines promoting the cytokine storm.
- Case report of a pt with newly diagnosed metastatic sarcomatoid clear cell renal cell carcinoma who after 8 days of COVID-19 illness txt with lopinavir-ritonavir became suddenly dyspneic with a rising O2 requirement.
  - Txt with 2 doses of tocilizumab 8mg/kg IV 8 hours apart followed by clinical improvement without apparent toxicity.
ANYTHING WE SHOULD AVOID?

› There is evidence from SARS/MERS cases that corticosteroids can delay viral clearance without any survival benefit and therefore should be avoided if possible unless indicated for another reason
   › Research ongoing

› Theoretical concern of increased ACE2 receptor expression in the setting of NSAID or ACEi/ARB use
   › Research ongoing
   › No current recommendations to stop these medications

Questions or Comments?

Source: xkcd.com
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