Immune-related (IR)-Pneumonitis during the COVID-19 Pandemic: Multidisciplinary Recommendations for Diagnosis and Management


Keywords: Pneumonitis, Immunotherapy, COVID-19, immune-related adverse event, anti-IL6, corticosteroids

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Abstract

Immunotherapy-related (IR)-pneumonitis is a rare and potentially fatal toxicity of anti-PD(L)1 immunotherapy. Expert guidelines for the diagnosis and management of IR-pneumonitis include multi-disciplinary input from medical oncology, pulmonary medicine, infectious disease, and radiology specialists. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a recently recognized respiratory virus that is responsible for causing the Coronavirus Disease 2019 (COVID-19) global pandemic. Symptoms and imaging findings from IR-pneumonitis and COVID-19 pneumonia can be similar, and early COVID-19 viral testing may yield false negative results, complicating the diagnosis and management of both entities. There is thus an emerging need for the adaptation of expert guidelines for IR-pneumonitis in the setting of the global COVID-19 pandemic. Herein, we present a set of multidisciplinary consensus recommendations for the diagnosis and management of IR-pneumonitis in the setting of COVID-19 including: (1) Isolation procedures, (2) Recommended imaging and interpretation, (3) Adaptations to invasive testing, (4) Adaptations to the management of IR-pneumonitis, (5) Immunosuppression for steroid-refractory IR-pneumonitis, and (6) Management of suspected concurrent IR-pneumonitis and COVID-19 infection.

Background

Immunotherapy-related (IR)-pneumonitis is a uncommon but potentially fatal toxicity that occurs in 5-10% of patients treated with anti-PD(L)1 immunotherapy, and is defined as a focal or diffuse inflammation of the lung parenchyma [1]. Patients with IR-pneumonitis most commonly present clinically with non-productive cough and shortness of breath, and less commonly with fever and chest pain [2]. The diagnosis of IR-pneumonitis is one of exclusion, and involves completion of a standard institutional evaluation to rule out respiratory infection inclusive of laboratory testing, chest CT imaging, and in select symptomatic cases, bronchoscopy with bronchoalveolar lavage (BAL), with the goal of ruling out alternative diagnoses such as infection and malignant lung infiltration [3-5].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a newly recognized respiratory virus responsible for the Coronavirus Disease 2019 (COVID-19) global pandemic. Since its declaration as a global pandemic by the World Health Organization (WHO) on March 11, 2020, over 5 million cases of documented COVID-19 have been diagnosed worldwide, resulting in over 330,000 deaths [6]. Importantly, patients with co-morbidities such as cancer appear to have higher case-fatality rates from
COVID-19 [7-9]. Retrospective studies suggest patients with hematologic malignancies, lung cancer, and metastatic cancer are at particularly high risk of severe disease [10]. Interestingly, receipt of PD-1 pathway blockade does not appear to impact the severity of COVID-19 in cancer patients [11]. That said, the diagnosis and management of toxicities related to immune checkpoint blockade in the era of COVID-19 poses several challenges. Similar to patients who develop IR-pneumonitis, those with COVID-19 infection tend to present clinically with fever, cough, myalgia, fatigue, and shortness of breath [12-14]. Unlike IR-pneumonitis, however, COVID-19 is a viral illness transmissible via droplet, human contact, and possibly airborne transmission, and thus requires infection prevention measures to limit transmission. Across the world, testing and triage algorithms have been developed in order to identify patients most suitable for COVID-19 testing via viral polymerase chain reaction (PCR) assay of nasopharyngeal samples. In general, patients who develop fever, respiratory changes, or other symptoms consistent with COVID-19 are considered for testing. Although widespread testing of asymptomatic individuals is not currently recommended, institutions may opt to test select asymptomatic populations such as residents of long-term care facilities or patients undergoing operative interventions. For symptomatic patients, diagnostic evaluation with chest imaging (chest x-ray, CT) and other laboratory tests (ferritin, ESR, CRP, LDH, D-dimer, IL-6) is completed according to institutional algorithms to assist in identifying cases that may clinically worsen [15], but have yet to be validated for their associations with clinical outcome.

Since patients with cancer have a COVID-19-related fatality rate of up to 25% [7], the timely diagnosis and management of this infection has rapidly risen to a level of equal importance as the management of these patients’ underlying cancers, and the complications of their treatment. Thus, the ability to effectively discern and appropriately manage IR-pneumonitis in the context of COVID-19 is a question of increasing clinical relevance in cancer patients, since anti-PD-(L) immunotherapy is approved in 15 different cancer indications, with over 40% of patients with cancer in the United States are now eligible to receive immunotherapy in a standard of care setting [16].

Methods

Recommendations: Group Representation and Input

In response to the need for clear and concise recommendations for the management of IR-pneumonitis in the setting of the global COVID-19 pandemic, these recommendations were drafted with multidisciplinary cross-institutional input from medical oncology, infectious diseases including hospital epidemiology and infection control, pulmonary medicine and radiology subspecialists with expertise in
IR-Pneumonitis and COVID-19. The most pressing clinically relevant questions and recommendations were discussed using an iterative, modified Delphi methodology.

**Recommendation Objectives**

The primary objectives of this position paper are to outline diagnostic evaluation and management principles for IR-pneumonitis in the setting of COVID-19. This includes emerging issues related to appropriate: (1) isolation procedures, (2) imaging and interpretation, (3) adaptations to invasive testing for IR-pneumonitis, (4) adaptations to current medical management of IR-pneumonitis, (5) immunosuppressive therapy for steroid-refractory IR-pneumonitis, and (6) management of suspected concurrent IR-pneumonitis and COVID-19 infection.

**Strengths and Limitations of Recommendations**

The recommendations in this clinical guidance document represent expert opinion that is based on limited and primarily retrospective data. Recommendations are subject to change as new data becomes available.

**Clinical Considerations and Recommendations**

Previous to the COVID-19 pandemic, published consensus guidelines for the diagnosis and management of IR-pneumonitis had been developed by multiple oncologic societies [3, 4, 17, 18]. We propose that selected recommendations within these guidelines be adapted in the context of COVID-19, and outline these changes in Table 1. These recommendations provide overall guidance in common clinical scenarios, however specific management decisions should be made on a case-by-case basis, weighing individual risks/benefits in the context of patient goals, co-morbidities, disease status, and provider safety. In addition, wherever possible, multi-specialty input should be sought [19].

**Isolation procedures**

The WHO and other groups have established guidelines for the appropriate screening and triage of patients with suspected COVID-19 [20-22]. When possible, routine patient visits and monitoring of otherwise clinically asymptomatic individuals receiving cancer treatments should be conducted via telemedicine [21, 22]. If in-person clinical evaluation is required, we recommend screening for the new onset of symptoms concerning for COVID-19 by phone prior to the scheduled visit, and again at in-
For patients who screen positive for symptoms concerning for IR-pneumonitis and/or COVID-19 when in the oncology clinic, the patient should be isolated in a separate dedicated COVID-19 screening/testing area to limit exposure to other patients and healthcare workers. Specifically, this includes ensuring that the patient immediately dons a face mask, and is placed in a private room (ideally with negative-pressure capabilities) with the door closed. Staff assessing these patients should be trained on optimal infection prevention practices including appropriate donning and safe doffing of personal protective equipment (PPE) which may include a fit-tested N95 or other respirator, protective eyewear, gown and gloves. Due to nationwide PPE shortages we recognize many facilities may not have sufficient respirators for all healthcare workers evaluating patients with COVID-19, and may preserve respirators for those undergoing aerosol generating procedures. Upon vacating the clinic room, it is vital to clean, disinfect, and await adequate air exchange, as directed by institutional guidance from infection control specialists. These measures are important in order to prevent potential onward transmission from a patient with suspected IR-pneumonitis and/or COVID-19 to ensure patients are seen in a setting where appropriate infection prevention practices can be instituted, such as a dedicated COVID-19 assessment area including mobile drive-through testing.

**Imaging of IR-pneumonitis and COVID-19**

The most common appearances of IR-pneumonitis and COVID-19 infection on chest x-ray and chest CT imaging are depicted in Figure 1. Since interstitial lung changes are poorly appreciated on chest x-ray, diagnostic chest CT is the recommended imaging modality for the evaluation of IR-pneumonitis [4]. The spectrum of imaging findings of IR-pneumonitis on chest CT are described using radiographic patterns according to American Thoracic Society (ATS) and European Respiratory Society (ERS) classifications of interstitial pneumonias and related conditions including 1) acute interstitial pneumonia (AIP)/acute respiratory distress syndrome (ARDS) pattern; 2) cryptogenic organizing pneumonia (COP) pattern; 3) non-specific interstitial pneumonia (NSIP) pattern; and 4) hypersensitivity pneumonitis (HP) pattern [1, 23-27]. Among these, the most common pattern is the COP pattern, characterized by multifocal bilateral parenchymal consolidations and ground glass opacities (GGOs) in a peripheral and lower lung distribution on chest CT [23]. In addition, many patients frequently have diffuse bilateral lung involvement and the distribution is often independent from that of tumor involvement of the lung [2].
Similar to IR-pneumonitis, chest x-ray appears to be less sensitive in detecting lung pathology for COVID-19 compared to CT imaging. In the largest single retrospective compilation of patient data from 1099 patients from 552 hospitals in 30 municipalities in mainland China, 59% of patients with COVID-19 had abnormal chest radiograph findings, whereas 86% had abnormal chest CT findings [28]. The imaging manifestations of COVID-19 pneumonia are also variable, and have a wide spectrum ranging from normal chest CT in PCR-positive patients to fulminant and extensive bilateral interstitial opacities [29-37] (Figure 1). Evolving knowledge indicates that the typical CT imaging features of COVID-19 pneumonia include peripheral, bilateral GGOs or multifocal rounded GGOs that are noted with or without consolidation, or other findings suggestive of organizing pneumonia [38]. Therefore, the radiographic pattern of typical COVID-19 pneumonia certainly overlaps with a COP pattern of IR-pneumonitis, which is the most frequently observed pattern. Similarly, the most fulminant cases from both entities result in the manifestations of ARDS characterized by diffuse or multifocal extensive GGOs and consolidations on imaging. In both entities, imaging manifestations reflect the lung’s response to injury, and the lung’s response patterns are often limited to several types as previously described [26]. Thus, overlap is inevitable, making it difficult to distinguish between entities based on imaging alone.

Further complicating the diagnosis, abnormalities on chest CT may precede positive COVID-19 testing in some patients [32, 35]. Several studies have shown that completely asymptomatic infection may have imaging abnormalities (which tend to be less severe than in symptomatic patients) [35]. Conversely, a substantial percentage of patients with confirmed COVID-19 may initially present with normal CT imaging [30]. The optimal approach to the longitudinal management of these patients has not been elucidated. Relevant to these cases, the WHO recommends symptomatic treatment and self-isolation only for patients with mild symptoms not requiring hospitalization [20, 39]. Therefore, in patients in whom grade 1 IR-pneumonitis is suspected, asymptomatic COVID-19 should now be considered in the differential diagnosis. Specific management recommendations for grade 1 IR-pneumonitis are outlined in the management section below.

**Invasive diagnostic testing for IR-pneumonitis**

The standard evaluation for IR-pneumonitis involves completion of a broad assessment of common respiratory pathogens via laboratory and non-invasive testing including but not limited to a respiratory viral panel, testing for atypical lung infections (e.g. mycoplasma, aspergillus, pneumocystis jiroveci),
sputum culture and blood culture. In addition, a contrast-enhanced chest CT scan is recommended to assess lung tumor progression, and may require CT angiography technique if pulmonary embolism is suspected. Other common pulmonary co-morbidities, particularly in patients with lung cancers, such as exacerbations of chronic obstructive pulmonary disease or congestive heart failure, should also be considered. Evaluation in symptomatic and critically ill cases may also include bronchoscopy with BAL +/- lung biopsy in order to assess for respiratory pathogens that may have been missed on non-invasive testing, as well as for malignant lung infiltration.

However, performing a bronchoscopy to diagnose suspected IR-pneumonitis may increase viral transmission risk of COVID-19 through aerosolization and may precipitate respiratory failure in patients with tenuous clinical status. Precautions to minimize coughing and aerosolization, such as elective intubation, and the use of disposable bronchoscopes (if available) should be considered. Overall, we recommend that bronchoscopy for suspected IR-pneumonitis should be avoided or only completed in selected cases in which appropriate airborne precautions have been taken, and in consultation with both pulmonary medicine and infectious disease specialists. In selected cases in which this is needed, this procedure should ideally be performed in a negative pressure room with full COVID-19 precautions including appropriate donning of PPE. These recommendations align with those laid out by the Surviving Sepsis Campaign guidelines on the management of critically ill adults with COVID-19 [40].

**Management of IR-pneumonitis in the setting of COVID-19:**

**Grade 1 IR-pneumonitis**

The management of patients who develop grade 1 IR-pneumonitis (radiographic abnormalities but otherwise asymptomatic) is a contentious area in clinical practice. Published guidelines recommend either holding immunotherapy, or cautiously continuing treatment [3, 4, 17, 18]. While imaging findings consistent with COVID-19 may appear in otherwise asymptomatic individuals, the decision to pursue COVID-19 testing for these patients is controversial, and likely will be affected by the availability of tests and region-specific risks of COVID-19. Thus, testing for COVID-19 in the setting of suspected grade 1 pneumonitis should be made on a case-by-case basis in consultation with institutional infectious disease and infection control specialists. Given this, we recommend that those with suspected grade 1 IR-pneumonitis continue to be monitored at 3-7 days after initial diagnosis in order to assess for potential development of either symptomatic pneumonitis or COVID-19. In addition, because radiographic
changes of COVID-19 may appear before symptoms develop or PCR testing is warranted, we recommend withholding of anti-PD(L)1 immunotherapy in this scenario (Table 1). The duration of ICI withholding should be made on a case-by-case basis, depending on subsequent development of symptoms, and further clinical assessments.

**Grade 2 and higher IR-pneumonitis**

High-dose corticosteroid therapy is the cornerstone of treatment for patients who develop symptomatic (grade ≥2) IR-pneumonitis. Due to the potential fatality risk from this immune-related adverse event (irAE), and guided by its severity by Common Toxicity Criteria for Adverse Events (CTCAE) [41], corticosteroids are often commenced prior to completion of a full diagnostic evaluation, and may be co-prescribed with empiric antimicrobials.

The role for corticosteroids in the management of COVID-19 infection is controversial. Several retrospective studies suggest a potential role for corticosteroids in the management of severe COVID-19 infection with ARDS. In a single-center retrospective analysis from Wuhan Jinyintan Hospital in China, methylprednisolone use in COVID-19 patients with ARDS was associated with a reduced risk of death (HR, 0.38; 95% CI, 0.20-0.73) [42]. In a separate published but not peer-reviewed single-center study, methylprednisolone given at a dose of 1-2mg/kg/d for five to seven days in patients hospitalized for severe COVID-19 pneumonia was associated with a shorter duration of supplemental oxygen use [43]. Other studies have shown that a greater percentage of patients requiring ICU admission have received corticosteroids than those not needing ICU-level care [13], and demonstrated that more non-survivors of severe COVID-19 infection received corticosteroids compared with survivors [44, 45]. However, these data are likely to represent confounding by indication in the setting of critical illness.

In other viral ARDS syndromes, data has been mixed on the utility of corticosteroids. Large-scale meta-analyses suggest corticosteroid use may be associated with increased risk of mortality and hospital-acquired infection in influenza patients [46]. However, the quality of this data was poor and a subsequent analysis found no association between corticosteroid use and risk of death [47]. In critically-ill patients infected with MERS-CoV or SARS-CoV, corticosteroid treatment was not associated with increased mortality, but was associated with a delay in viral RNA clearance [48, 49]. In the treatment of ARDS as a whole, corticosteroid use has been shown to be associated with a reduced duration of mechanical ventilation, but its effect on all-cause mortality is uncertain [50, 51].
Taking the above data into account, the surviving sepsis guidelines on the management of critically ill adults with COVID-19 makes a weak recommendation against the routine use of systemic corticosteroids in mechanically ventilated adults with COVID-19 without ARDS. However, they make a weak recommendation for systemic corticosteroid use in mechanically ventilated COVID-19 patients with ARDS [40]. Other guidelines similarly recommend prudent corticosteroid use for selected critically ill patients with COVID-19 only [52], or routine avoidance of corticosteroids unless indicated for another reason [39]. Multiple clinical trials (NCT04244591, NCT04323592, NCT04273321) are currently ongoing to clarify the role for corticosteroids in critically-ill COVID-19 patients.

Based on the clear benefit for corticosteroids in IR-pneumonitis, and the conflicting evidence for corticosteroids in COVID-19 with limited evidence in non-critically ill patients, we recommend confirmation of COVID-19 status before proceeding with corticosteroid therapy in patients with suspected grade 2 IR-pneumonitis.

For patients with grade 3 or higher IR-pneumonitis, in whom expedited treatment is critical, we recommend empiric corticosteroids while awaiting results of COVID-19 testing (Table 1). Steroids can then be discontinued in the setting of a positive COVID-19 PCR test result. In the setting of a negative COVID-19 PCR with ongoing high level of clinical suspicion for COVID-19, it is reasonable to reassess for concurrent COVID-19 infection with repeat PCR testing within 5-7 days of corticosteroid initiation.

**Immunosuppression for steroid-refractory IR-pneumonitis in the context of COVID-19**

While the majority of cases of IR-pneumonitis will improve with high-dose corticosteroids, steroid-refractory pneumonitis is not uncommon [2]. In the event of IR-pneumonitis that does not clinically improve after ≥ 48 hours of high-dose steroids, multiple guidelines recommend consideration of alternative immunomodulating agents including infliximab, cyclophosphamide, mycophenolate mofetil, or intravenous immunoglobulin (IVIG) [3, 4, 17, 18]. However, prospective data in support of these strategies is lacking, and is based largely on case series and case reports [53, 54].

One attractive potential treatment for steroid-refractory IR-pneumonitis is anti-IL6 therapy. IL6 is a prominent cytokine implicated in acute inflammation, particularly in phenomena such as cytokine release syndrome (CRS) secondary to chimeric antigen receptor (CAR)-T cell therapy [55]. Anti-IL6
agents such as tocilizumab and sarilumab are standard-of-care treatments for CRS from CAR-T [18]. This treatment may also be an effective strategy for irAEs. In a single-center retrospective study of 34 patients with steroid-refractory irAEs, including 12 with IR-pneumonitis, 79.4% of patients demonstrated clinical improvement following tocilizumab treatment [56]. A prospective study of tocilizumab for the treatment of GI and rheumatologic irAEs is ongoing (NCT03601611), but additional prospective studies are warranted to further evaluate the efficacy of anti-IL6 therapy in the treatment of IR-pneumonitis.

Cytokine release and severe systemic inflammation also appear to play a prominent role in severe ARDS secondary to COVID-19 infection. Multiple retrospective studies suggest COVID-19 infected patients requiring ICU-level care have higher levels of markers of systemic inflammation including D-dimer, multiple interleukins and TNFα [12, 13]. Furthermore, higher levels of inflammatory markers including CRP, ferritin, IL6 and D-dimer have been observed in non-survivors compared to survivors of COVID-19 [42, 44, 45, 57]. Thus anti-inflammatory treatments, such as anti-IL6 therapy, are mechanistically appealing for the treatment of COVID-19. Early data has been encouraging, with multiple case reports supporting the efficacy of tocilizumab in the treatment of severe COVID-19 infection [58-60]. In addition, a prospective Chinese trial showed improved oxygenation in patients treated with tocilizumab [61], resulting in the approval of this therapy for the treatment of severe COVID-19 in China. These encouraging data have led to the development of multiple ongoing prospective clinical trials for anti-IL6 therapy in patients with severe COVID-19, of which there are >40 enrolling worldwide at the time of this publication. Furthermore, the Society for Immunotherapy of Cancer (SITC) recently published a consensus statement on IL6 targeted therapies for COVID-19, advocating for maximal expeditious effort to make available anti-IL6 agents for compassionate use, as well as suggesting monitoring of FiO2, PaO2/FiO2, CRP, and IL6 in COVID-19 patients receiving anti-IL6 agents [62].

**Concurrent IR-pneumonitis and COVID-19 infection**

Since there are published data in support of the potential benefit of anti-IL6 therapy for both steroid-refractory IR-pneumonitis and severe COVID-19 infection, anti-IL6 may be a reasonable treatment option for immunotherapy-treated patients with steroid-refractory IR-pneumonitis in the era of COVID-19 infection, as well as in the setting of possible concurrent IR-pneumonitis and COVID-19 infection. Anti-IL6 therapy should not, however, replace initial management with corticosteroids in these patients. Rather, early implementation (≤48hr of high-dose steroids if no clinical improvement or sooner if further
deterioration) of anti-IL6 therapy should be considered in an effort to limit prolonged exposure to high-dose corticosteroids.

Conclusions
With the escalation of the COVID-19 crisis, there is a critical need for guidelines outlining management strategies for cancer patients. With FDA-approvals in over 15 different cancer indications for anti-PD(L)1 immunotherapy, immunotherapy-treated cancer patients represent a distinct subset of patients who may experience IR-pneumonitis, a challenging clinical situation to manage during the COVID-19 crisis. The multidisciplinary recommendations provided herein are intended to serve as a starting point for addressing the critical issues for diagnosis and management of IR-pneumonitis in the setting of COVID-19. We highlight the requirement for isolation procedures while COVID-19 rule out is conducted in those with IR-pneumonitis, the need to forgo bronchoscopy except in selected or exceptional cases, adaptation of corticosteroid treatment in the context of COVID-19, and recommendations for additional immunosuppressive options such as anti-IL6 in steroid-refractory IR-pneumonitis or when concurrent COVID-19 infection is suspected. Crucially, these preliminary recommendations are made in light of the current immediate need for guidance, but should be refined as prospective data emerge.

Acknowledgements
Patients with cancers, those who are suffering from COVID-19, frontline healthcare workers caring for patients with COVID-19, and the many researchers who have gone to great lengths to publish vital data on this global crisis.

Authors' contributions

Funding
None

Availability of data and materials
Not applicable
Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

JN: Research funding: Merck, AstraZeneca; Consulting/Advisory Board: Bristol-Myers Squibb, AstraZeneca, Roche/Genentech; Honoraria: Bristol-Myers Squibb, Merck, AstraZeneca
DBJ: Advisory Boards/Consulting: Array Biopharma, BMS, Jansen, Merck, Novartis; Research Funding: BMS, Incyte.
JRB: Advisory Boards/Consulting: Amgen, BMS, Genentech/Roche, Eli Lilly, GlaxoSmithKline, Merck, Sanofi; Research Funding: AstraZeneca, BMS, Genentech/Roche, Merck, RAPT Therapeutics Inc., Revolution Medicines; Data and Safety Monitoring Board/Committees: GlaxoSmithKline, Sanofi.
MN: Advisory Boards/Consulting: Daiichi Sankyo, AstraZeneca; Research Funding: Merck, Canon Medical Systems, AstraZeneca, Daiichi Sankyo; Honorarium: Roche.
PMF: Advisory Boards/Consulting: Abbvie, AstraZeneca, BMS; Research Funding: AstraZeneca, BMS, Kyowa, Novartis, Corvus.
JER, KS, DFK, CR, SMS: None

References


Table 1: Pneumonitis diagnostic evaluation and management considerations in setting of COVID-19.

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<tr>
<th>Pneumonitis Grading (G)</th>
<th>Diagnostic Evaluation, Safety Procedures &amp; Management</th>
<th>Treatment</th>
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| G1*: Clinically asymptomatic with radiographic changes ONLY | - Assess oxygenation at baseline & with ambulation  
- Testing for respiratory pathogens including COVID-19 should be made on case-by-case basis | - Hold immunotherapy  
- Follow-up with treating oncologist in 3-7 days  
- If develops symptoms in follow-up, treat as G2 | COVID-19 Negative  
COVID-19 Positive |
| G2: Clinically symptomatic, restricting instrumental activities of daily living | - Screening at COVID-19 testing facility (if possible)  
- If screen positive in clinic, provide patient mask and place in private room with negative pressure (if available)  
- COVID-19 testing +/- RVP as appropriate  
- Pulmonary medicine/infectious disease consultation, as appropriate  
- Hold immunotherapy | - Hospitalization not required  
- Commence oral prednisone 1 mg/kg/day (or equivalent)  
- Consider empiric antimicrobials (as appropriate)  
- Follow-up with treating oncologist in 48-72 hours:  
  - If clinical improvement, follow-up in 1-2 weeks with clinic visit +/- chest imaging  
  - If no improvement, treat according to G3 | - Consult relevant institutional infection control representative  
- Hospitalization unlikely required  
- Counsel on infection prevention measures  
- Counsel on concerning signs/symptoms that warrant presentation to hospital or emergency room  
- COVID-19 directed therapy per individualized institutional management guidelines in consultation with infectious disease and infection control specialists  
- Consider discontinuing corticosteroids (where appropriate) | |
| G3: Severe symptoms limiting activities of daily living, oxygen indicated  
G4: Life-threatening respiratory compromise | - As above for G2  
- Prioritize expedited hospitalization  
- Commence empiric pneumonitis treatment with IV methylprednisolone 1-2 mg/kg/d (or equivalent)  
- Consider empiric antimicrobials | - Permanently discontinue immunotherapy  
- Continue IV corticosteroids  
- If no improvement after 48-72 hours consider:  
  - Repeat COVID-19 testing +/- RVP  
  - Additional immunosuppressive therapy such as infliximab 5 mg/kg x1 (can repeat after 14 days if needed), mycophenolate mofetil 1-1.5g twice per day, IVIG 2 g/kg in divided doses  
  - If clinical suspicion for COVID-19 remains, consult infectious disease and consider COVID-19 directed therapy where appropriate (e.g. anti-IL6) | - Discontinue corticosteroids  
- Consult infectious disease  
- Implement COVID-19-directed therapy per individualized institutional management guidelines in consultation with infectious disease and infection control specialists (e.g. anti-IL6) | |

Grade by Common Terminology Criteria for Adverse Events (CTCAE) criteria version 4.03. *For G1 pneumonitis, a chest CT with contrast should be obtained if not already performed. Guidelines also suggest obtaining pulmonary function testing (PFTs) but in the setting of COVID-19 and risk of virus transmission with PFTs, we do not recommend obtaining routine PFTs if there is any suspicion for COVID-19. **Follow-up preferable by virtual telemedicine visit or telephone. Practitioner should wear contact personal protective equipment with eye protection (PAPR or N95 with face shield/goggles), gown, and gloves G: grade; IV: intravenous; IVIG: intravenous immunoglobulin, RVP: respiratory viral panel