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Insights from immuno-oncology: the Society for Immunotherapy of Cancer Statement on access to IL-6-targeting therapies for COVID-19

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Thehypoxia and profound inflammatory response associated with the pneumonitisobserved with the SARS-CoV-2 virus responsible for the recent COVID-19 pandemic has overwhelmed intensive care facilities in the epicenters of infection including Wuhan, China, Northern Italy and in the USA, the Seattle and New York City areas. The Society for Immunotherapy of Cancer (SITC) stands along with and supports our colleagues in emergency departments, intensive care units (ICUs) and inpatient wards in the global effort to overcome this unprecedented pandemic. It is becoming apparent that the 'ground glass' infiltrative appearance seen on CT scans from patients with COVID-19 with pneumonitis is reminiscent of imaging from patients with immune checkpoint inhibitor (ICI)-induced pneumonitis.[1 2] Additionally, elevated interleukin-6 (IL-6) is a hallmark inflammatory signature seen in serum of patients with severe COVID-19 acute respiratory distress.[3] Many of us have experience with the administration of immune-modulatory agents, which is why the cancer immunotherapy community is poised to contribute to the current fight against COVID-19.

One possibility is to encourage the use of IL-6 or IL-6-receptor (IL-6R) blocking antibodies like tocilizumab (Actemra™, Roche-Genentech), sarilumab (Kevzara™, Regeneron) and siltuximab (Sylvant™, EUSA Pharma) that are Food and Drug Administration (FDA) approved for various conditions, including rheumatological disease and the lymphoproliferative disorder Castleman's syndrome. These agents could be used on easily and immediately available compassionate use protocols that could be approved on an emergency basis by all institutional review boards (IRBs) around the world for critically ill patients with COVID-19-induced hypoxia. Tocilizumab also is already FDA approved to manage cytokine release syndrome (CRS) in patients receiving chimeric antigen receptor T cell therapy.[4 5] In addition, tocilizumab has been shown to reduce toxicity in patients treated with ICIs who were steroid refractory,[6] and has been added to the ICI agents ipilimumab and nivolumab in an ongoing US phase II study (NCT03999749) to ameliorate immune-related toxicity. In Castleman's disease, a lymphoproliferative disorder caused by Kaposi's Sarcoma Herpesvirus, a pathogen that produces viral IL-6, tocilizumab has been shown to reduce viral loads.[7] Tocilizumab is also being explored as a potential supportive care measure for the management of CRS in patients with cancer treated with a number of CD3-based bispecific molecules. Now, data from the frontlines of the pandemic indicates that the agent may offer lifesaving benefit for COVID-19 patients with respiratory distress.

Emerging evidence suggests that high levels of C reactive protein (CRP) and IL-6 are observed in patients infected with COVID-19.[1 8] Anecdotal experience on the use of tocilizumab at doses comparable to those used for the management of CRS from investigators in Italy[9] and from China[10] has reported rapid improvement in both intubated and non-intubated patients. In these reports, expeditious administration of anti-IL-6R therapy for patients in acute respiratory distress has been critical. A recent study protocol to evaluate the efficacy of tocilizumab in COVID-19-induced pneumonitis accrued over 300 patients worldwide in less than 24 hours. Additionally, Genentech will also provide 10 000 vials of tocilizumab to the US Strategic National Stockpile.[11] Tocilizumab was also approved in China in March 2020, for the treatment of patients with COVID-19 with serious lung damage and elevated IL-6. Sponsors, investigators and regulators have moved with unprecedented speed and collaboration to initiate protocols to formally study the safety and efficacy of antiviral agents and vaccines, as well as various anti-IL-6 antibodies in patients with COVID-19. In the USA, a trial of sarilumab in the COVID-19 setting is ongoing.[12]

Although randomized data definitively showing that IL-6R blockade benefits patients with COVID-19-induced pneumonitis are currently lacking, we propose that an effort should be made to maximize the availability of anti-IL-6 agents, includingtocilizumab and sarilumab for use on a compassionate basis to critically illhospitalized SARS-CoV-2-infected patients during this extraordinary situation. In addition, consideration should be given to focus efforts on rapidly expanding the ability of clinicians and clinical investigators to access investigational anti-IL-6 agents, in particular for those agents where phase 1 and/or phase 2 studies have been completed, and acceptable safety has been demonstrated. Even if the primary impact of a single dose of these drugs is to accelerate recovery and get patients off ventilator support and out of the ICU more rapidly, this could significantly decompress our severely overburdened healthcare systems. We suggest that straightforward parameters including complete blood counts and differentials, serum lactate dehydrogenase (LDH), ferritin, CRP and IL-6 be recorded in treated patients, that serum be retained for future analyses, and simple clinical parameters be assessed including time in ICU, days of hospitalization and pulmonary parameters, including forced expiratory volume in 1 s (for non-intubated patients), fractional inspired oxygen (FiO_2), arterial oxygen tension/FiO_2 ratio and type of oxygen supplementation need be recorded pre-anti-IL-6R and post-anti-IL-6R therapy. A simple compassionate use protocol could be assembled from existing templates, and all efforts should be made for emergency approval of the use of IL-6R blocking antibodies by local IRBs within 24 hours of the request being made. Additionally, consideration should be given by pharma and biotech to redirect the use of facilities and increase personnel involved in drug manufacturing and those serving as liaisons to the frontlines to facilitate drug availability. Extraordinary times call for extraordinary measures, and SITC calls on all involved, including pharmaceutical sponsors, health authorities and IRBs, to continue to move swiftly and creatively to remove barriers and increase access to agents like anti-IL-6R drugs that may improve our care for COVID-19 pneumonitis.

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Correction notice Since the online publication of this article, the authors have noticed errors in author names, affiliations, the competing interests section and also the main text.

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