REVIEW ARTICLE

Severity of Coronavirus Disease 2019 in Patients with Cancer

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ABSTRACT

The outbreak of the novel coronavirus disease 2019 (COVID-19) appears to be one of the biggest global health threats worldwide with no specific therapeutic agents identified to date. As of August 2020, over 22.4 million confirmed cases and more than 788,000 related deaths have been reported globally, and these numbers are expected to increase before the pandemic is over. Given the aggressive nature of their underlying disease, patients with cancer seem to be more vulnerable to COVID-19 and various studies have confirmed this hypothesis. In this paper, we review the current information regarding the role of cancer in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. Moreover, we discuss the effective supportive treatment options for COVID-19, including dexamethasone, tocilizumab, remdesivir, and convalescent plasma therapy (CPT), as well as discuss their efficacy in patients with cancer diagnosed with COVID-19.

Keywords: Coronavirus, COVID-19, SARS-CoV-2, Cancer, Dexamethasone, Tocilizumab, Remdesivir, Convalescent plasma therapy

1. INTRODUCTION

In December 2019, an outbreak of unexplained pneumonia cases was reported in Wuhan, China (Wuhan Municipal Health Commission. Report of Clustering Pneumonia of Unknown Etiology in Wuhan City, 2019. http://wjw.wuhan.gov.cn/front/web/showDetail/2019123108989. Accessed December 31, 2019., n.d.). A few days later, the causative microbe in this mysterious disease was recognized as a novel coronavirus (nCoV) by various independent laboratories (Lu et al., 2020; Zhou et al., 2020; Zhu et al., 2020).

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The causative virus has been, since, identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease it causes has been named coronavirus disease 2019 (COVID-19) by the World Health Organization (He et al., 2020). As of 20 August 2020, over 22.4 million confirmed cases and over 788,000 related deaths have been reported globally (https://coronavirus.jhu.edu/map.html). However, the true number is probably much higher than the official estimates based on the fact that many cases are asymptomatic carriers or go undiagnosed because of a lack of testing.

Most of the studies indicated that patients with cancer are at a higher risk of COVID-19-related complications and death when compared with the general population (Afshar et al., 2020; Mehta et al., 2020; Miyashita et al., 2020). In this context, Kuderer et al. (2020) examined the severity of COVID-19 in patients with cancer (n=1035) and obtained the following statistics: patients admitted to the

intensive care unit (ICU) = 14%; patients that required mechanical ventilation = 12%; and death ratio = 13%. By contrast, these values are much lower in patients without cancer, namely 3.2%, 2.3%, and 3.7%, respectively (Meng et al., 2020). The drivers for the increased disease severity in patients with cancer are poorly understood. One study proposed that the high rate of COVID-19-related mortality in patients with cancer are likely dependent on the comorbidities present before initiation of radiation or current anticancer therapies (Vuagnat et al., 2020). In this review, we discuss the known factors that could possibly augment the severity of COVID-19 in patients with cancer. We also review the current information about the efficiency of novel therapeutic options for COVID-19, specifically in patients with cancer.

2. FACTORS THAT CONTRIBUTE TO THE HIGH MORTALITY RISK FOR COVID-19 IN PATIENTS WITH CANCER

Recent studies have reported on retrospective case studies of COVID-19 in patients with cancer with an astonishingly high mortality rate (11.0%–28.6%) (Afshar et al., 2020; Miyashita et al., 2020; Zhang et al., 2020). Importantly, Dai et al. (2020) demonstrated that patients with hematologic cancer (leukemia, myeloma, and lymphoma), lung cancer, or metastatic cancer (stage IV) had the highest frequency of severe events, which is described as a condition that demands admission to the ICU, the use of mechanical ventilation, or can lead to death. Conversely, patients with nonmetastatic cancer experienced a similar frequency of severe conditions as patients without cancer (Dai et al., 2020). Although the investigators did not explain the rationales behind a worse COVID-19 outcome in patients with metastatic cancer, we believe that there is an increased risk in patients with metastatic cancer because these patients are mostly immune suppressed as a consequence of their treatment.

COVID-19 leads to a cytokine release syndrome and viral acute respiratory distress syndrome caused by uncontrolled severe acute inflammation (Addeo et al., 2020). Particularly with lung cancer, patients suffer from chronic pulmonary inflammation that is mainly elicited by the tumor microenvironment and the frequent underlying lung pathology (Ballaz et al., 2003; Sekine et al., 2012). Therefore, patients with lung cancer are prone to the complications of severe pathogenesis and mortality from COVID-19 (Dai et al., 2020; Rogado et al., 2020; L. Zhang et al., 2020).

Anticancer treatment is 1 of the possible driving factors that is linked to COVID-19 severity in patients with cancer, which causes a systemic immunosuppressive state (Liang et al., 2020; Patel et al., 2020; Tian et al., 2020; van de Haar et al., 2020; C. Wu et al., 2020). Yang et al. (2020) have conducted an investigation to determine if cytotoxic chemotherapy acts as a risk factor for mortality in COVID-19-infected patients with cancer. Accordingly, it was found that cytotoxic chemotherapy enhances the risk for fatal outcomes from COVID-19 (Yang et al., 2020), which is possibly caused by long-term myelosuppression and impaired immunity. Other studies obtained similar results for patients who received chemotherapy or underwent surgery in the 30 days before infection with COVID-19, according to which the patients were characterized to have a higher risk for severe events when compared with those who did not undergo chemotherapy or surgery (Al-Quteimat et al., 2020; Dai et al., 2020). In order to further confirm these data, the United Kingdom Coronavirus Cancer Monitoring Project has analyzed the mortality rate in 800 patients with cancer who were diagnosed with symptomatic COVID-19 (Lee et al., 2020). The obtained data proposed that the mortality from COVID-19 in patients with cancer was primarily driven by age, gender, and comorbidities (hypertension, cardiovascular disease, diabetes, and pulmonary disease) (Lee et al., 2020). Remarkably, they found no significant difference in the mortality from COVID-19 between patients with cancer receiving cytotoxic chemotherapy, immunotherapy, hormonal therapy, targeted therapy, or radiotherapy treatment and those not receiving active treatment (Lee et al., 2020). In agreement with these findings, Dai et al. (2020) found no difference in COVID-19 severity between patients with cancer, who underwent only radiotherapy, and patients without cancer. Thus, the effect of immunosuppression in patients with cancer on the mortality rate from COVID-19 remains controversial and requires further investigation. As yet, no evidence is available to support changing or withholding chemotherapy or immunotherapy in patients with cancer owing to a diagnosis with COVID-19. The clinical judgment is paramount in this decision, according to which the common expectation is to continue treatments, if lifesaving.

One of the major factors that most likely contribute to the high mortality risk associated with COVID-19 in patients with cancer is limited access to essential healthcare and an inability to receive the necessary medical services in a timely fashion, especially in high-risk epidemic areas, because of the high demand for medical staff and healthcare facilities (Alhalabi et al., 2020; H. Wang et al., 2020). However, the detailed contribution to COVID-19 mortality associated with this factor remains largely unknown and warrants further investigation. Taken together, various factors could increase the severity of COVID-19 in patients with cancer and the patient's inherent immunity might be a decisive factor for their prognosis after effective supportive care.

3. THE EFFECT OF COVID-19 SUPPORTIVE TREATMENTS ON THE MORTALITY RATE IN PATIENTS WITH CANCER

Since no potential cure has been reported for COVID-19 to date, the management strategies primarily focus on supportive treatment and protective measures to prevent further transmission of the virus (World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected.). Different treatment modalities are emerging for patients with COVID-19, although all the existing therapies are still being investigated. However, there is a big knowledge gap on how to tackle the crucial clinical questions about the complexities that may develop from the supportive treatments for COVID-19 in patients with cancer. Thus far, the most effective treatments for COVID-19 comprises corticosteroids (e.g., dexamethasone), tocilizumab, and remdesivir (Baden et al., 2020; Jafari et al., 2020; R. Wu et al., 2020). In addition, convalescent plasma therapy (CPT) transfusion is currently considered for the rescue of severely ill patients with COVID-19 upon hospitalization (Duan et al., 2020; Islam et al., 2020).

3.1. Corticosteroids drugs

Corticosteroids drugs including dexamethasone (Horby et al., 2020) are widely used as supportive treatment for COVID-19 (Russell et al., 2020; Villar et al., 2020). Various studies have suggested corticosteroids as a potential supportive treatment that could decrease the duration of mechanical ventilation and the overall mortality rate in patients with severe COVID-19; however, the evidence is inconsistent (Ye et al., 2020). The effect of corticosteroids on COVID-19 in patients with cancer is still unclear. Based on previous studies (Arabi et al., 2018), patients with cancer who were diagnosed with Middle East respiratory syndrome (MERS), caused by a coronavirus closely related to SARS-CoV-2 (Ragab et al., 2020), were more likely to require mechanical ventilation and vasopressors after administration of corticosteroid therapy including dexamethasone, hydrocortisone, and methylprednisolone (Arabi et al., 2018). Importantly, the authors concluded that the administration of corticosteroids did not affect the mortality rate (Arabi et al., 2018). It has been suggested that patients with cancer diagnosed with COVID-19 might, more likely, be harmed by corticosteroid treatment (Russell et al., 2020). The negative effect of corticosteroids could be driven by their function in immunosuppression (Thng et al., 2020). Dexamethasone has been shown to attenuate immune responses in patients with cancer through suppression of T cell proliferation and differentiation (Giles et al., 2018). Thus, further investigations are required to shed more light on the role of dexamethasone in the treatment of COVID-19 in patients with cancer.

3.2. Tocilizumab

Tocilizumab is a humanized monoclonal antibody that acts against both soluble and membrane-bound forms of the interleukin-6 (IL-6) receptor (Venkiteshwaran, 2009). Tocilizumab is recommended for treating severe rheumatoid arthritis (Smolen et al., 2008). Tocilizumab has also been approved as a therapy for chimeric antigen receptor T-cell-therapy-induced cytokine release syndrome (Kewan et al., 2020). Cytokine release syndrome is caused by an uncontrolled immune activation that is characterized by the occurrence of a "cytokine storm" (Lee et al., 2014), which is similar to the type seen in the most severe cases of COVID-19 (Levi, 2020). Alattar et al. (2020) reported that administration of tocilizumab in patients with severe COVID-19 is correlated with a dramatic decline in inflammatory markers, radiological improvement, and reduced ventilatory support requirements (Alattar et al., 2020). Other studies from China (Jafari et al., 2020; Wu et al., 2020) and the United States (Kewan et al., 2020) have also supported these results and confirmed that tocilizumab could induce recovery in patients with severe

cases of COVID-19 (Jafari et al., 2020; R. Wu et al., 2020). Despite being recommended as a promising treatment in COVID-19 patients with cancer (Ascierto et al., 2020; Levi, 2020), very little is known about tocilizumab's efficacy and interaction with anticancer therapeutic agents. Therefore, more studies to assess the efficacy of tocilizumab in the population with cancer are needed. Indeed, a prospective, randomized multicenter study is currently recruiting patients with advanced or metastatic cancer who have been diagnosed with COVID-19 across Europe (NCT04333914), and tocilizumab is among the agents that are proposed in this investigation.

3.3. Remdesivir

Early in 2020, the Wuhan Virus Research Institute proposed remdesivir as the fastest-acting and most powerful antiviral agent against COVID-19 in vitro (Cao et al., 2020). Remdesivir, a nucleoside analog antiviral agent that perturbs viral replication by blocking RNA polymerase, has shown the ability to inhibit replication in various types of coronaviruses including those that cause MERS and severe acute respiratory syndrome (Eastman et al., 2020; Yeoh et al., 2020). Early clinical trials of remdesivir treatment for COVID-19 were conducted in Hubei, China, between February 6, 2020, and March 12, 2020, and enrolled 237 patients (158 to remdesivir and 79 to placebo)(Y. Wang et al., 2020). Importantly, the clinical benefits of remdesivir in patients with COVID-19 were statistically insignificant (Y. Wang et al., 2020). On April 3, 2020, the European Medical Agency approved remdesivir treatment for patients with COVID-19 requiring mechanical ventilation (Singh et al., 2020). The clinical trial results showed that there may be a benefit to using remdesivir compared with the placebo in severe COVID-19 cases (Davies et al., 2020; Grein et al., 2020). Additionally, remdesivir has also been suggested as a potential inhibitor of viral infection in a human liver cancer (Huh-7) cell line (Wang et al., 2020). However, no data are available to show the effect of remdesivir treatment in patients with cancer diagnosed with COVID-19.

3.4. Convalescent Plasma Therapy Transfusion

CPT was used for the first time by von Behring and Kitasato as a rational approach to treat diphtheria in 1890 (Behring et al., 1890). Initially, convalescent plasma was obtained from individuals who recovered from the viral infection and were able to donate their antiviral immunoglobulin-containing blood; once transfused into the patient suffering from active infections, the antibodies from the convalescent plasma are thought to neutralize the virus and limit its replication and, consequently, reduce the symptoms and mortality (Behring et al., 1890; Luke et al., 2010; Rojas et al., 2020). Historical evidence demonstrated CPT to be a highly effective treatment for influenza pneumonia and what is now known as acute respiratory distress syndrome during the Spanish influenza pandemic (Bass et al., 1919; Redden, 1919; Sanborn, 1920).

The COVID-19 pandemic has placed emphasis on CPT to treat infectious diseases. Recent investigations from China demonstrated that human covalescent plasma is a potential therapeutic option that can decrease the severity and/or shorten the length of illness caused by SARS-CoV-2 (Duan et al., 2020; Shen et al., 2020; M. Ye et al., 2020; Zeng et al., 2020; B. Zhang et al., 2020). The majority of the findings suggested that CPT therapy in patients with COVID-19 appears to be safe and clinically effective in reducing mortality (Islam et al., 2020; Rajendran et al., 2020; Rojas et al., 2020; R. Wu et al., 2020). It is worth mentioning that the majority of these studies have used small sample sizes that ranged between 4 and 10 patients (Duan et al., 2020; Shen et al., 2020; M. Ye et al., 2020; Zeng et al., 2020; B. Zhang et al., 2020). However, a recent multicenter study that was conducted in the USA by Mayo Clinic researchers examined the effect of CPT on 20,000 patients hospitalized with COVID-19 across the USA between April 3, 2020, and June 2, 2020 (Joyner et al., 2020). The data support the notion that CPT is safe in hospitalized patients with COVID-19 and earlier administration of plasma within the clinical course of COVID-19 is more likely to reduce mortality. Indeed, the Food and Drug Administration has issued an emergency-use authorization for emergency use of COVID-19 convalescent plasma for the treatment of patients hospitalized with COVID-19 on August 23, 2020.(https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma).

CPT in patients with cancer diagnosed with COVID-19 has also shown high levels of efficacy. Based on the study by Hatzl et al. (2020), convalescent plasma has been used for 2 patients with COVID-19 with hematological cancer

(patient #1: diffuse large B-cell lymphoma; patient #2: follicular lymphoma) who have been on mechanical ventilation for 6 and 11 days, respectively. Impressively, both patients were off the ventilator 5 and 4 days after CP therapy, respectively (Hatzl et al., 2020). Moreover, the levels of inflammatory markers including IL-6 and serum ferritin also decreased dramatically (Hatzl et al., 2020). Although, the sample size does not allow any definitive conclusions to be drawn, these data provide continued optimism regarding the safety of COVID-19 convalescent plasma. However, we believe that using CPT in patients with cancer may provide some challenges, such as transfusion-related acute lung injury, circulatory overload, and hemolysis. Therefore, further investigation is warranted to get a more comprehensive picture.

4. CONCLUSIONS

The current review is based on the latest information available for this field at this time. The available data are insufficient to draw statistical and generalizable conclusions about the factors that might be correlated with better or worse outcomes for patients with cancer. The mortality rate of COVID-19 in patients with cancer should be interpreted with caution because of the limited information in some primary studies, for example, it is unclear if all the deaths were caused by COVID-19, cancer, or other comorbidities. Moreover, the majority of these studies analyzed small cohorts. In addition, some studies did not consider the cancer types, stages, and treatments. Furthermore, their samples comprised only hospitalized patients with cancer, whereas patients with cancer who died from COVID-19 outside the hospital setting were missed.

Based on the findings that we reviewed in this minireview, we recommend diligent preventive-care measures, as well as full supportive care for immunosuppressed patients to decrease the risk of infection. We believe that there is an urgent need for well-designed investigations to determine the management and treatment of COVID-19 in the oncology setting, as well as identify the clinical effects of continuing or withholding cancer therapy in patients with cancer diagnosed with COVID-19. Importantly, future studies should use large-scale datasets and pay attention to the detailed characteristics of infected patients with cancer, such as the cancer types and stages, chemotherapy or radiation-related variables, inflammatory profile, and care protocols that are followed during COVID-19 stages.

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REFERENCES

Addeo, A., Obeid, M. & Friedlaender, A. (2020). COVID-19 and lung cancer: risks, mechanisms and treatment interactions. *Journal for Immunotherapy of Cancer*, *8*(1), 1–7. doi: 10.1136/jitc-2020-000892.

Afshar, Z. M., Dayani, M., Naderi, M., Ghanbarveisi, F., Shiri, S. & Rajatif, F. (2020). Fatality rate of COVID-19 in patients with malignancies: a sytematic review and meta-analysis. *Journal of Infection*, *12*(30), 1–3.

Al-Quteimat, O. M. & Amer, A. M. (2020). The Impact of the COVID-19 Pandemic on Cancer Patients. *American Journal of Clinical Oncology: Cancer Clinical Trials*, *00*(00), 1–4. doi: 10.1097/COC.0000000000000712.

Alattar, R., Ibrahim, T. B. H., Shaar, S. H., Abdalla, S., Shukri, K., Daghfal, J. N., Khatib, M. Y., Aboukamar, M., Abukhattab, M., Alsoub, H. A., Almaslamani, M. A. & Omrani, A. S. (2020). Tocilizumab for the treatment of severe coronavirus disease 2019. *Journal of Medical Virology*, *April*. doi: 10.1002/jmv.25964.

Alhalabi, O. & Subbiah, V. (2020). Managing Cancer Care during the COVID-19 Pandemic and Beyond. *Trends in Cancer*, *xx*(xx), 1–3. doi: 10.1016/j.trecan.2020.04.005.

Arabi, Y. M., Mandourah, Y., Al-Hameed, F., Sindi, A. A., Almekhlafi, G. A., Hussein, M. A., Jose, J., Pinto, R., Al-Omari, A., Kharaba, A., Almotairi, A., Al Khatib, K., Alraddadi, B., Shalhoub, S., Abdulmomen, A., Qushmaq, I., Mady, A., Mady, O., Al-Aithan, A. M., … Fowler, R. A. (2018). Corticosteroid therapy for critically ill patients with middle east respiratory syndrome. *American Journal of Respiratory and Critical Care Medicine*, *197*(6), 757–767. doi: 10.1164/rccm.201706-1172OC.

Ascierto, P. A., Fox, B., Urba, W., Anderson, A. C., Atkins, M. B., Borden, E. C., Brahmer, J., Butterfield, L. H., Cesano, A., Chen, D., De Gruijl, T., Dillman, R. O., Drake, C. G., Emens, L. A., Gajewski, T. F., Gulley, J. L., Stephen Hodi, F., Hwu, P., Kaufman, D., … Weber, J. S. (2020). Insights from immuno-oncology: The Society for Immunotherapy of Cancer Statement on access to IL-6-targeting therapies for COVID-19. *Journal for ImmunoTherapy of Cancer*, *8*(1), 1–2. doi: 10.1136/jitc-2020-000878.

Baden, L. R. & Rubin, E. J. (2020). Covid-19 - The search for effective therapy. *New England Journal of Medicine*, *382*(19), 1851–1852. doi: 10.1056/NEJMe2005477

Ballaz, S. & Mulshine, J. L. (2003). The potential contributions of chronic inflammation to lung carcinogenesis. *Clinical Lung Cancer*, *5*(1), 46–62. doi: 10.3816/CLC.2003.n.021

Bass, J. & Ervin, C. (1919). Use of serum in the treatment of influenza-pneumonia. *Naval Medical Bulletin*, 71–73.

Behring, E. & Kitasato, S. (1890). Ueber das Zustandekommen der Diphtherie-Immunität und der Tetanus-Immunität bei Thieren. *Dtsch. Med. Wschr*, *16*, 1113–1114.

Cao, Y. chen, Deng, Q. xin & Dai, S. xue. (2020). Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. *Travel Medicine and Infectious Disease*, 101647. doi: 10.1016/j.tmaid.2020.101647

Dai, M., Liu, D., Liu, M., Zhou, F., Li, G., Chen, Z., You, H., Wu, M., Zheng, Q., Xiong, Y., Xiong, H., Wang, C., Chen, C., Xiong, F., Zhang, Y., Peng, Y., Ge, S., Zhen, B., Yu, T. et al. (2020). Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak. *Cancer Discovery*, *10*, 783–791. doi: 10.1158/2159-8290.CD-20-0422.

Davies, M., Osborne, V., Lane, S., Roy, D., Dhanda, S., Evans, A. & Shakir, S. (2020). Remdesivir in Treatment of COVID-19: A Systematic Benefit–Risk Assessment. *Drug Safety*, *43*(7), 645–656. doi: 10.1007/s40264-020-00952-1

Duan, K., Liu, B., Li, C., Zhang, H., Yu, T., Qu, J., Zhou, M., Chen, L., Meng, S., Hu, Y., Peng, C., Yuan, M., Huang, J., Wang, Z., Yu, J., Gao, X., Wang, D., Yu, X., Li, L., et al. (2020). Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proceedings of the National Academy of Sciences of the United States of America*, *117*(17), 9490–9496. doi: 10.1073/pnas.2004168117.

Eastman, R. T., Roth, J. S., Brimacombe, K. R., Simeonov, A., Shen, M., Patnaik, S. & Hall, M. D. (2020). Remdesivir: A Review of Its Discovery and Development Leading to Emergency Use Authorization for Treatment of COVID-19. *ACS Central Science*, *6*, 672–683. doi: 10.1021/acscentsci.0c00489.

Giles, A. J., Hutchinson, M. K. N. D., Sonnemann, H. M., Jung, J., Fecci, P. E., Ratnam, N. M., Zhang, W., Song, H., Bailey, R., Davis, D., Reid, C. M., Park, D. M. & Gilbert, M. R. (2018). Dexamethasone-induced immunosuppression: Mechanisms and implications for immunotherapy. *Journal for ImmunoTherapy of Cancer*, *6*(1), 1–13. doi: 10.1186/s40425-018-0371-5.

Grein, J., Ohmagari, N., Shin, D., Diaz, G., Asperges, E., Castagna, A., Feldt, T., Green, G., Green, M. L., Lescure, F. X., Nicastri, E., Oda, R., Yo, K., Quiros-Roldan, E., Studemeister, A., Redinski, J., Ahmed, S., Bernett, J., Chelliah, D., et al. (2020). Compassionate use of remdesivir for patients with severe Covid-19. *New England Journal of Medicine*, *382*(24), 2327–2336. doi: 10.1056/NEJMoa2007016.

Hatzl, S., Eisner, F., Schilcher, G., Kreuzer, P., Gornicec, M., Eller, P., Brodmann, M., Schlenke, P., Stradner, M. H., Krause, R., Greinix, H. & Schulz, E. (2020). Response to "COVID-19 in persons with haematological cancers." *Leukemia*, *Table 1*. doi: 10.1038/s41375-020-0914-x.

He, F., Deng, Y. & Li, W. (2020). Coronavirus disease 2019: What we know? *Journal of Medical Virology*, *92*(7), 719–725. doi: 10.1002/jmv.25766.

Horby, P., Lim, W., Emberson, J., Mafham, M., Bell, J., Linsell, L., Staplin, N., Brightling, C., Ustianowski, A., Elmahi, E., Prudon, B., Green, C., Felton, T., Chadwick, D., Rege, K., Fegan, C., Chappell, L. C., Faust, S. N., Jaki, T., et al. (2020). Effect of Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report. *MedRxiv*, 1–20. doi: https://doi.org/10.1101/2020.06.22.20137273.

Islam, A., Rafiq, S., Karim, S., Laher, I. & Rashid, H. (2020). Convalescent plasma therapy in the treatment of COVID-19: Practical considerations: Correspondence. *International Journal of Surgery*, *79*, 204–205. doi: 10.1016/j.ijsu.2020.05.079.

Jafari, A., Dadkhahfar, S. & Perseh, S. (2020). Considerations for interactions of drugs used for the treatment of COVID-19 with anti-cancer treatments. *Critical Reviews in Oncology/Hematology*, *151*, 102982. doi: 10.1016/j.critrevonc.2020.102982.

Joyner, M. J., Bruno, K. A., Klassen, S. A., Kunze, K. L., Johnson, P. W., Lesser, E. R., Wiggins, C. C. & Senefeld, J. W. (2020). Safety Update: COVID-19 Convalescent Plasma in 20,000 Hospitalized Patients. *Mayo Clinic Proceeding*, *95*, 1–15. doi: 10.1016/j.semerg.2020.05.002.

Kewan, T., Covut, F., Al, M. J., Jaghbeer, À., Rose, L., Gopalakrishna, K. V. & Akbik, B. (2020). Tocilizumab for treatment of patients with severe COVID À 19 : A retrospective cohort study. *EClinicalMedicine*, 100418. doi: 10.1016/j.eclinm.2020.100418.

Kuderer, N. M., Choueiri, T. K., Shah, D. P., Shyr, Y., Rubinstein, S. M., Rivera, D. R., Shete, S., Hsu, C. Y., Desai, A., de Lima Lopes, G., Grivas, P., Painter, C. A., Peters, S., Thompson, M. A., Bakouny, Z., Batist, G., Bekaii-Saab, T., Bilen, M. A., Bouganim, N., et al. (2020). Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *The Lancet*, 1907–1918. doi: 10.1016/S0140-6736(20)31187-9.

Lee, D. W., Gardner, R., Porter, D. L., Louis, C. U., Ahmed, N., Jensen, M., Grupp, S. A. & Mackall, C. L. (2014). Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*, *124*(2), 188–196. doi: 10.1182/blood-2014-05-552729.current.

Lee, L. Y. W., Cazier, J. B., Starkey, T., Turnbull, C. D., Kerr, R. & Middleton, G. (2020). COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *The Lancet*, *395*(10241), 1919–1926. doi: 10.1016/S0140-6736(20)31173-9

Levi, M. (2020). Tocilizumab for severe COVID-19: A promising intervention affecting inflammation and coagulation. *European Journal of Internal Medicine*, *76*, 21–22. doi: 10.1016/j.ejim.2020.05.018.

Liang, W., Guan, W., Chen, R., Wang, W., Li, J., Xu, K., Li, C., Ai, Q., Lu, W., Liang, H., Li, S. & He, J. (2020). Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet Oncology*, *21*(3), 335–337. doi: 10.1016/S1470-2045(20)30096-6.

Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., Bi, Y., Ma, X., Zhan, F., Wang, L., Hu, T., Zhou, H., Hu, Z., Zhou, W., Zhao, L., et al. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet*, *395*(10224), 565–574. doi: 10.1016/S0140-6736(20)30251-8

Luke, T. C., Casadevall, A., Watowich, S. J., Hoffman, S. L., Beigel, J. H. & Burgess, T. H. (2010). Hark back: Passive immunotherapy for influenza and other serious infections. *Critical Care Medicine*, *38*(SUPPL. 4). doi: 10.1097/CCM.0b013e3181d44c1e

Mehta, V., Goel, S., Kabarriti, R., Cole, D., Goldfinger, M., Acuna-Villaorduna, A., Pradhan, K., Thota, R., Reissman, S., Sparano, J. A., Gartrell, B. A., Smith, R. V., Ohri, N., Garg, M., Racine, A. D., Kalnicki, S., Perez-Soler, R., Halmos, B. & Verma, A. (2020). Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System. *Cancer Discovery*. doi: 10.1158/2159-8290.cd-20-0516.

Meng, L., Qiu, H., Wan, L., Ai, Y., Xue, Z., Guo, Q., Deshpande, R. & Zhang, L. (2020). Intubation and Ventilation amid the COVID-19

outbreak. *Anesthesiology*, *132*, 1317–1332. doi: 10.1097/ALN.0000000000003296

Miyashita, H., Mikami, T., Chopra, N., Yamada, T., Chernyavsky, S., Rizk, D. & Cruz, C. (2020). Do patients with cancer have a poorer prognosis of COVID-19? An experience in New York City. *Annals of Oncology*, *xxx*, 2019–2020. doi: 10.1016/j.annonc.2020.04.006

Patel, R., Park, J., Shah, A. & Saif, M. W. (2020). COVID-19 and Cancer Patients. *Cancer Medicine*, *3*(1), 40–48. doi: 10.1038/s41395-018-0061-4.

Ragab, D., Eldin, H. S., Taeimah, M. & Khattab, R. (2020). The COVID-19 Cytokine Storm ; What We Know So Far. *Frontiers in Immunology*, *11*(June), 1–4. doi: 10.3389/fimmu.2020.01446.

Rajendran, K., Narayanasamy, K., Rangarajan, J., Rathinam, J., Natarajan, M. & Ramachandran, A. (2020). Convalescent plasma transfusion for the treatment of COVID-19: Systematic review. *Journal of Medical Virology*, *April*, 1–9. doi: 10.1002/jmv.25961.

Redden, W. (1919). Treatment of Influenza-Pneumonia by Use of Convalescent Human Serum. *Boston Medical and Surgical Journal*, *161*, 688–691.

Rogado, J., Pangua, C., Serrano-montero, G., Obispo, B., Martín, A., Pérez-pérez, M., López-alfonso, A., Gullón, P. & Ángel, M. (2020). Covid-19 and lung cancer: A greater fatality rate? *Lung Cancer*, *146*, 19–22.

Rojas, M., Rodríguez, Y., Monsalve, D. M., Acosta-Ampudia, Y., Camacho, B., Gallo, J. E., Rojas-Villarraga, A., Ramírez-Santana, C., Díaz-Coronado, J. C., Manrique, R., Mantilla, R. D., Shoenfeld, Y. & Anaya, J. M. (2020). Convalescent plasma in Covid-19: Possible mechanisms of action. *Autoimmunity Reviews*, *April*, 102554. doi: 10.1016/j.autrev.2020.102554.

Russell, C. D., Millar, J. E., & Baillie, J. K. (2020). Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *The Lancet*, *395*(10223), 473–475. doi: 10.1016/S0140-6736(20)30317-2.

Sanborn, G. P. (1920). The Use of the Serum of Convalescents in the Treatment of Influenza Pneumonia: A Summary of the Results in a Series of One Hundred and One Cases. *Boston Medical and Surgical Journal*, *183*, 171–177.

Sekine, Y., Katsura, H., Koh, E., Hiroshima, K. & Fujisawa, T. (2012). Early detection of COPD is important for lung cancer surveillance. *European Respiratory Journal*, *39*(5), 1230–1240. doi: 10.1183/09031936.00126011.

Shen, C., Wang, Z., Zhao, F., Yang, Y., Li, J., Yuan, J., Wang, F., Li, D., Yang, M., Xing, L., Wei, J., Xiao, H., Yang, Y., Qu, J., Qing, L., Chen, L., Xu, Z., Peng, L., Li, Y., et al. (2020). Treatment of 5 Critically Ill Patients with COVID-19 with Convalescent Plasma. *JAMA - Journal of the American Medical Association*, *323*(16), 1582–1589. doi: doi:10.1001/jama.2020.4783.

Singh, A. K., Singh, A., Singh, R. & Misra, A. (2020). Remdesivir in COVID-19: A critical review of pharmacology, pre-clinical and clinical studies. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*, *14*(4), 641–648. doi: 10.1016/j.dsx.2020.05.018.

Smolen, J. S., Beaulieu, A., Rubbert-Roth, A., Ramos-Remus, C., Rovensky, J., Alecock, E., Woodworth, T. & Alten, R. (2008). Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomised trial. *The Lancet*, *371*(9617), 987–997. doi: 10.1016/S0140-6736(08)60453-5.

Thng, Z. X., De Smet, M. D., Lee, C. S., Gupta, V., Smith, J. R., McCluskey, P. J., McCluskey, P. J., Thorne, J. E., Kempen, J. H., Kempen, J. H., Zierhut, M., Nguyen, Q. D., Pavesio, C., Agrawal, R. & Agrawal, R. (2020). COVID-19 and immunosuppression: A review of current clinical experiences and implications for ophthalmology patients taking immunosuppressive drugs. *British Journal of Ophthalmology*, 1–5. doi: 10.1136/bjophthalmol-2020-316586.

Tian, J., Yuan, X., Xiao, J., Zhong, Q., Yang, C., Liu, B., Cai, Y., Lu, Z., Wang, J., Wang, Y., Liu, S., Cheng, B., Wang, J., Zhang, M., Wang, L., Niu, S., Yao, Z., Deng, X., Zhou, F., et al. (2020). Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study. *The Lancet Oncology*, *2045*(20), 1–11. doi: 10.1016/S1470-2045(20)30309-0.

Van de Haar, J., Hoes, L. R., Coles, C. E., Seamon, K., Fröhling, S., Jäger, D., Valenza, F., de Braud, F., De Petris, L., Bergh, J., Ernberg, I., Besse, B., Barlesi, F., Garralda, E., Piris-Giménez, A., Baumann, M., Apolone, G., Soria, J. C., Tabernero, J., et al. (2020). Caring for patients with cancer in the COVID-19 era. *Nature Medicine*, *26*(5), 665–671. doi: 10.1038/s41591-020-0874-8

Venkiteshwaran, A. (2009). *Tocilizumab*. *1*(5), 432–438.

Villar, J., Ferrando, C., Martínez, D., Ambrós, A., Muñoz, T., Soler, J. A., Aguilar, G., Alba, F., González-Higueras, E., Conesa, L. A., Martín-Rodríguez, C., Díaz-Domínguez, F. J., Serna-Grande, P., Rivas, R., Ferreres, J., Belda, J., Capilla, L., Tallet, A., Añón, J. M., et al. (2020). Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. *The Lancet Respiratory Medicine*, *8*(3), 267–276. doi: 10.1016/S2213-2600(19)30417-5.

Vuagnat, P., Frelaut, M., Ratohul, T., Basse, C., Diakite, S., Noret, A. & Bellesoeur, A. (2020). COVID-19 in breast cancer patients: a cohort at the Institut Curie hospitals in Paris area. *Breast Cancer Research*, *22*(55), 1–10. doi: 10.1186/s13058-020-01293-8.

Wang, H. & Zhang, L. (2020). Risk of COVID-19 for patients with cancer. *Lancet Oncology*, *21*(4), e181. doi: doi: 10.1016/S1470-2045(20)30149-2

Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., Shi, Z., Hu, Z., Zhong, W. & Xiao, G. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Research*, *30*(3), 269–271. doi: 10.1038/s41422-020-0282-0.

Wang, Y., Zhang, D., Du, G., Du, R., Zhao, J., Jin, Y., Fu, S., Gao, L., Cheng, Z., Lu, Q., Hu, Y., Luo, G., Wang, K., Lu, Y., Li, H., Wang, S., Ruan, S., Yang, C., Mei, C., et al. (2020). Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *The Lancet*, *395*(10236), 1569–1578. doi: 10.1016/S0140-6736(20)31022-9.

World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. WHO 2020. (n.d.).

Wu, C., Chen, X., Cai, Y., Xia, J., Zhou, X., Xu, S., Huang, H., Zhang, L., Zhou, X., Du, C., Zhang, Y., Song, J., Wang, S., Chao, Y., Yang, Z., Xu, J., Zhou, X., Chen, D., Xiong, W., et al. (2020). Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Internal Medicine*, 1–10. doi: 10.1001/jamainternmed.2020.0994

Wu, R., Wang, L., Kuo, H. C. D., Shannar, A., Peter, R., Chou, P. J., Li, S., Hudlikar, R., Liu, X., Liu, Z., Poiani, G. J., Amorosa, L., Brunetti, L. & Kong, A. N. (2020). An Update on Current Therapeutic Drugs Treating COVID-19. *Current Pharmacology Reports*, 1–15. doi: 10.1007/s40495-020-00216-7

Wuhan Municipal Health Commission. Report of Clustering Pneumonia of Unknown Etiology in Wuhan City. 2019. http://wjw.wuhan.gov.cn/ front/web/showDetail/2019123108989. *Accessed December 31, 2019.* (n.d.).

Yang, K., Sheng, Y., Huang, C., Jin, Y., Xiong, N., Jiang, K., Lu, H., Liu, J., Yang, J., Dong, Y., Pan, D., Shu, C., Li, J., Wei, J., Huang, Y., Peng, L., Wu, M., Zhang, R., Wu, B., et al. (2020). Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: a multicentre, retrospective, cohort study. *The Lancet Oncology*, *2045*(20), 1–10. doi: 10.1016/S1470-2045(20)30310-7.

Ye, M., Fu, D., Ren, Y., Wang, F., Wang, D., Zhang, F., Xia, X. & Lv, T. (2020). Treatment with convalescent plasma for COVID-19 patients in Wuhan, China. *Journal of Medical Virology*. doi: 10.1002/jmv.25882.

Ye, Z., Wang, Y., Colunga-Lozano, L. E., Prasad, M., Tangamornsuksan, W., Rochwerg, B., Yao, L., Motaghi, S., Couban, R. J., Ghadimi, M., Bala, M. M., Gomaa, H., Fang, F., Xia, Y. & Guyat, G. H. (2020). Efficacy and safety of corticosteroids in COVID-19 based on evidence for COVID-19, other coronavirus infections, influenza, community-acquired pneumonia and acute respiratory distress syndrome: a systematic review and meta-analysis. *Canadian Medical Association Journal*, 1–12.

Yeoh, C. B., Lee, K. J., Rieth, E. F., Mapes, R., Tchoudovskaia, A. V., Fischer, G. W. & Tollinche, L. E. (2020). COVID-19 in the Cancer Patient. *Anesthesia & Analgesia*, *131*(1), 16–23. doi: 10.1213/ane.0000000000004884.

Zeng, Q.-L., Yu, Z.-J., Gou, J.-J., Li, G.-M., Ma, S.-H., Zhang, G.-F., Xu, J.-H., Lin, W.-B., Cui, G.-L., Zhang, M.-M., Li, C., Wang, Z.-S., Zhang, Z.-H. & Liu, Z.-S. (2020). Effect of Convalescent Plasma Therapy on Viral Shedding and Survival in Patients With Coronavirus Disease 2019. *The Journal of Infectious Diseases*, *222*, 38–43. doi: https://doi.org/10.1093/infdis/jiaa228.

Zhang, B., Liu, S., Tan, T., Huang, W., Dong, Y., Chen, L., Chen, Q., Zhang, L., Zhong, Q., Zhang, X., Zou, Y. & Zhang, S. (2020). Treatment With Convalescent Plasma for Critically Ill Patients With Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *Chest*, e1-5. doi: 10.1016/j.chest.2020.03.039.

Zhang, L., Zhu, F., Xie, L., Wang, C., Wang, J., Chen, R., Jia, P., Guan, H. Q., Peng, L., Chen, Y., Peng, P., Zhang, P., Chu, Q., Shen, Q., Wang, Y., Xu, S. Y., Zhao, J. P. & Zhou, M. (2020). Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Annals of Oncology*, *31*(7). doi: 10.1016/j.annonc.2020.03.296.

Zhou, P., Yang, X. Lou, Wang, X. G., Hu, B., Zhang, L., Zhang, W., Si, H. R., Zhu, Y., Li, B., Huang, C. L., Chen, H. D., Chen, J., Luo, Y., Guo, H., Jiang, R. Di, Liu, M. Q., Chen, Y., Shen, X. R., Wang, X., et al. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, *579*(7798), 270–273. doi: 10.1038/s41586-020-2012-7.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G. F. & Tan, W. (2020). A novel coronavirus from patients with pneumonia in China, 2019. *New England Journal of Medicine*, *382*(8), 727–733. doi: 10.1056/NEJMoa2001017.