

## Mini Review

# COVID-19 and Antiviral Therapies in Cancer Patients - will it Make Difference?

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## Abstract

Coronavirus Disease 2019 (COVID-19), being a community transmitted disease, is overwhelming the current health care system capacity worldwide. It was first detected in Wuhan, China in December, 2019. The systemic immunosuppressive status in cancer patients make them vulnerable and susceptible to Coronavirus Disease 2019 (COVID-19) more than any other individuals. Till now, there are no treatment guidelines for cancer patients with COVID-19. Antiviral therapies were being investigated through the past months on patients with COVID-19, however, there's a paucity of data regarding the reported incidence of COVID-19 in cancer patients compared to general population.

**Keywords:** COVID-19; Community transmitted disease; Cancer patients

## Introduction

In the early review of a Chinese national data repository, cancer patients with confirmed COVID-19 were mainly lung cancer patients [1]. The risk of fatality was suggested to be 5.6% among patients with cancer [2]. Another study suggested a 3.5 times higher risk for those patients to have a severe COVID-19 disease with higher incidence of death, or ICU admission with invasive ventilation, when compared to general population (39% vs. 8%;  $P=0.0003$ ), and a higher deterioration rate (median: 13 days vs. 43 days) [1]. Similarly, the Report of the WHO-China Joint Mission has suggested a 2-fold increase of COVID-19 risk for cancer patients than the general population [3].

## Risk Factors

Older age, with the highest fatal disease risk in patients  $\geq 65$  years, patients living in nursing homes or long-term care facilities [4], high Sequential Organ Failure Assessment (SOFA) score, or D-dimer concentration greater than  $1 \mu\text{g/ml}$ , all seem to identify patients with poor prognosis at early stage [5]. Patients with comorbid conditions such as cardiovascular disease, diabetes, hypertension, chronic respiratory disease, renal disease, and cancer patients as well, were all presented with highest risk of severe COVID-19, than general population, especially in those who are not well controlled [3,4]. Smoking was also suggested by Xia et al. [2], as a risk factor for severe disease.

There are no definitive and accurate risk factors specifically for cancer patients with COVID-19. However, unfortunately cancer

patients showed higher deteriorating conditions and poorer outcomes from the COVID-19 infection than general population [6].

Chemotherapy and cancer surgery were considered as risk factors for severe complication, even receiving the anticancer therapy in the preceding month, was associated with severe events, as reported by Linag et al. [1], (OR: 5.34,  $p<0.01$ ).

Moreover, Zhang et al. [6], had reported that anticancer therapies as chemotherapy, immunotherapy or radiation, when used within 14 days of infection, were predictors for death and severe events (hazard ratio  $>4$ ). That's why it is recommended that cancer patients receiving anticancer therapies should have vigorous screening for COVID-19 infection. This adds to the real problem of poor accessibility to the necessary medical services for those patients; either in term of getting there when needed, or the provision of normal medical care, because of COVID-19 outbreak [7].

## Action for patients on immunosuppressive therapy

Although chemotherapy was considered as a risk factor for severe events of COVID-19, till now, there's no evidence that support either withholding or replacement of chemotherapy drug. Same for targeted therapy, immunotherapy or radiation.

The possibility of cancer recurrence if therapy is delayed, discontinued or even modified must be taken in consideration before any change in regimen, thus, individualization seems to be the key. In the midst of this pandemic situation, oncologists have to weigh the risks of mortality and morbidity from COVID-19 against the magnitude of benefit of resuming and continuing the intended cancer therapies [8], consequently, it's suggested that patients may at least switch to oral drugs or home infusions, trying to limit the risk of getting infected from hospital visits [9].

On the other side, psychological support and ensuring the emotional wellbeing of cancer patients during such pandemic, will be important than ever. No doubt those cancer patients themselves must be informed about signs and symptoms of COVID-19, and should be trained in social distancing along with other hygiene practices.

## Antiviral therapies

To the moment, there's no proven benefit of using specific antiviral

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agent in treatment of COVID-19 in general population due to the difficulty of performing clinical studies in a pandemic circumstances with such a life threatening disease [10].

Antiviral therapies used in COVID-19 in the past couple of months can be summarized as follows; a clinical trial performed on a total of 199 COVID-19 confirmed patients, has showed no benefit observed in lopinavir-ritonavir treatment group (99 patients) beyond the standard care group (100 patients). Both lopinavir and ritonavir function as protease inhibitors, and both are used extensively in the management of HIV [11]. Meanwhile, adverse events as nausea, vomiting, and diarrhea were found to be higher in lopinavir-ritonavir group, while serious adverse events as respiratory failure and acute kidney disease were observed in the standard care group [12]. It is worthy to mention that, the combination of lopinavir-ritonavir seems to be most common exploratory antiviral agents which currently appear in 34 investigational studies [13].

Moreover, other studies were performed as case series or case reports. Although Chen et al. [14], in his case series study with oseltamivir on 75 patients with COVID-19 had a recovery rate of 31% and a mortality rate of 11%. Guan et al. [15], in his study on 393 patients reported that administration of oseltamivir did not decrease the intensive care unit admission rate, or the need of ventilation or death rates.

Besides, Wu et al. [16], described a multicenter retrospective study with ribavirin as an antiviral suggested agent on 80 patients with COVID-19. This study showed no critical cases, no patients used an invasive ventilator and a total of 21 cases have been discharged with an average hospital length stay of 8 days.

Regarding the use of favipiravir, an open-label study on a total of 85 patients (35 patients on favipiravir, 45 patients on control therapy), a significant higher improvement rate in chest imaging was observed in favipiravir group with better therapeutic responses in terms of disease progression and viral clearance [17].

Recently and most promising, remdesivir showed a significant, positive effect in diminishing the time to recovery, and patients on the study group was able to be discharged from the hospital within average of 11 days. This was reported by the head of the National Institutes of Allergy and Infectious Diseases; Dr. Anthony Fauci, on April, 29<sup>th</sup> 2020. This study will get published by its results within the next couple of weeks as they said. However, remdesivir is not yet approved by the Food and Drug Administration (FDA) as an effective treatment for patients with the Coronavirus.

### Treatment regimens in cancer patients

As pending further information, it's suggested that management of COVID-19 disease in cancer patients should follow the same treatment regimen as general population [9]. However, clinician should take in consideration that this category of patients is immune-compromised, that may present with fever and respiratory symptoms from a secondary opportunistic bacterial infection. Even pneumonitis can occur in after use of some cytotoxic chemo therapies [9].

### Prophylactic use of antiviral in cancer patients

The use of prophylactic antiviral has not been studied intensively to the extent to be a choice in immunosuppressed patients with COVID-19 [9]. Even in general population, the discussed trials were on patients with suspected or confirmed COVID-19 infection and not in the prophylactic setting.

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