COVID Awareness Issue

# A Short Note on Multiple Myeloma and COVID 19

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**Received Date:** January 19, 2021
**Publication Date:** January 21, 2021

## ABSTRACT

*Multiple Myeloma (MM) is characterized by the excess amount of monoclonal plasma cells in the bone marrow. Hematological Malignancies have a similar rate of infection rates but the severity and mortality are respectively higher than normal. Patients with MM are more likely susceptible to viral and bacterial illness. MM and its treatments lead to immune-deficiency, hypogammaglobulinemia and impaired B cell response so by default they are more susceptible to SARS-Cov2 infection. COVID 19 screening should be done in all patients before providing the anti-cancer therapies. High levels of granulocyte-macrophage colony-stimulating factors and Interleukins 6 (IL6) are activated in severe COVID 19. In this short note, we will discuss the effect of COVID 19 on MM patients and its treatment aspects.*

## Introduction

He et al stated the outcomes of COVID 19 in the patients with hematological disease. **(**1**)** The Management of COVID 19 patients with cancer is challenging. Hospitalized patients with hematological cancers have similar infection rates but more severe disease and case fatality rates. Few reports before this reported the outcomes of COVID-19 patients with cancer. **(**2**)** Patients with MM are peculiar in that they are with a ~7-10-fold susceptible to viral and bacterial diseases with a higher chance of getting contaminated **(**3**)** MM patients need more attention during this pandemic and treatment of choice is very challenging sometimes. The quality of care for these patients has been affected during this pandemic. **(**4**)**.

The mean age of diagnosis with myeloma is about 65 and comorbidities involving the immune system are more likely to arise in elderly patients. Diagnostic lymphopenia is a well-known risk factor for infection. **(**5,6,7**)** Functional immunoglobulin deficiency found in most patients with myeloma can also lead to an elevated risk of infection. Elevated infections are also associated with decreased CD+4 T-cell count at diagnosis. **(**8,9**)**. Immunomodulatory drugs (IMiDs) cause neutropenia, which increases the infection risk. Steroids are well known to increase the risk of infections (including pneumocystis and fungus) and the combination with IMiDs and PIs increases this further. The infection risk is highest during the first 3–4 months of therapy. **(**4**)** Prophylactic levofloxacin for 12 weeks in newly diagnosed myeloma has been shown to reduce deaths significantly **(**10**)** All of the previous factors make MM patients more susceptible to the serious adverse events that could arise with COVID-19 infection.

## Methodology

The Database used is Pubmed, Pubmed Central and Google Scholar. The papers are reviewed from these databases. After reviewing a couple of papers, this short note is prepared.

## Reviewing 5 Papers

**Malin Hultcrantz et al.(**11**):** Owing to both cancer and treatment, multiple myeloma patients have a compromised immune system; in this largest disease-related cohort to date with multiple myeloma and COVID-19 patients, we found risk factors for adverse effects to be shared relative to the general population, and mortality rates to be within the higher spectrum of officially reported mortality rates.

**Evangelos Terpos et al. (**12**):** Patients with MM and symptomatic COVID-19 disease should interrupt anti-myeloma treatment until recovery. For patients with positive PCR test for SARS-CoV-2, but with no symptoms for COVID-19, a 14-day quarantine should be considered if myeloma-related events allow the delay of treatment. The need for surveillance for drug interactions due to polypharmacy is highlighted.

**Al Saleh et al (**4**):** Screening for COVID-19 should be done in all patients before therapy. For standard-risk patients, we recommend the following: ixazomib, lenalidomide, and dexamethasone (IRd) (preferred), cyclophosphamide lenalidomide and dexamethasone (CRd), daratumumab lenalidomide and dexamethasone (DRd), lenalidomide, bortezomib, and dexamethasone (RVd), or cyclophosphamide, bortezomib, and dexamethasone (CyBorD). For high-risk patients, we recommend carfilzomib, lenalidomide, and dexamethasone (KRd) (preferred) or RVd. Decreasing the dose of dexamethasone to 20 mg and giving bortezomib subcutaneously once a week is recommended. We recommend delaying autologous stem cell transplant (ASCT), unless the patient has a high-risk disease that is not responding

well, or if the patient has plasma cell leukemia (PCL). Testing for COVID-19 should be done before ASCT

**Bo Wang et al: (**13**)** Drug exposure and MM disease status at the time of contracting COVID-19 had no bearing on mortality. Mounting a severe inflammatory response to SARS-CoV-2 and severe hypogammaglobulinemia was associated with higher mortality. The majority of patients mounted an antibody response to SARS-CoV-2. These findings pave a path to the identification of vulnerable MM patients who need early intervention to improve outcomes in future outbreaks of COVID-19.

**CARDAMON Trial: (**14**)** 15 patients stopped carfilzomib maintenance completely after a median of 15 cycles (range 5–18), six of whom completed < 12 (median seven cycles; range 5–8); 14 carried on uninterrupted and 41 patients restarted after a median treatment pause of 12 weeks (range 8–19·6). These protocol amendments allowed 55 patients who would otherwise have stopped trial treatment to stay on carfilzomib maintenance on the CARDAMON study (Fig 1). Of 25 outstanding MRD BM assessments, 20 were delayed by a median of two months (range 1–3), with investigations resuming when restrictions eased in June. As of 5 August 2020, eight of the delayed BM assessments have been performed, while three patients declined. PET-CT scans were delayed in 6/9 patients, of which two have been performed.

## Discussion

From a nationwide analysis in China, 18 (1%) out of 1,590 COVID-19 cases had a history of cancer **(**15**)**. Treatment of these patients is challenging. Although in my personal experience, Cancer is co-morbid to COVID 19 or not, it's controversial. Here I want to state the genetic theory. I believe that a specific gene pool is getting affected by this virus. In a tertiary care center in eastern India, we have seen that cancer patients with COVID 19 are mostly asymptomatic and didn't experience any COVID 19 related symptoms. So more gene-level study is needed in this sector.

For standard-risk MM patients ixazomib+Lenalinomide+dexamethasone is preferred. For high-risk patients, Carfilzomib+Lenalidomide+Dexamethasone is preferred. Before the treatment, RT PCR of the COVID 19 test was needed. If possible, delaying the autologous stem cell transplant is important.

Recommendations for the management of patients with multiple myeloma during the COVID-19 pandemic **(**16**)**

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| Autologous hematopoietic cell transplantation | Pursue induction regimens of up to six cycles in all patients to postpone the transplant procedure. In standard-risk multiple myeloma, consider doing additional cycles of induction, and delaying transplant until first relapse Patients with high-risk cytogenetics (especially those with deletion of chromosome 17p) should still receive high-dose melphalan and AHCT as first-line treatments whenever possible Test patients for SARS-CoV-2 infection before transplant |
| Use of steroids | Consider reducing steroid doses, as done in older patients, and to possibly interrupt steroids in patients already in complete remission while receiving continuous treatment |
| Management of outpatient visits | To reduce unnecessary visits to the hospital, consider doing the following: Use teleconsultation Pharmacists should be able to provide prescription doses for 2–3 months of treatment at a time Favor home hospitalization or home care Change the treatment administration schedule to one with a lower frequency Change the administration of daratumumab to every 4 weeks instead of every 2 weeks after the initial 8-week weekly administration, in patients with very good partial response Switch from an intravenous or subcutaneous treatment to a fully oral treatment combination For bisphosphonate intravenous home administration, switch from an intravenous to an oral bisphosphonate or transient interruption |
| Clinical trials and clinical research activities | For patients already enrolled in clinical trials, their participation should, in principle, continue with the following recommendations: Outpatient visits should be replaced by teleconsultation Clinical research organizations should allow home delivery of the medication under investigation to avoid hospital visits Hospital pharmacies should be authorized to deliver 2–3 months' worth of medication For patients who are likely to benefit substantially from inclusion in a clinical trial, test them for SARS-CoV-2 infection before enrolment For inclusion of new patients in a clinical trial, each team must carefully weigh the advantages and disadvantages of each inclusion |

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**Volume 1 Issue 1 January 2021**