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Letter

Impact of COVID-19 on case fatality rate of patients with cancer during the Omicron wave

Matthew Lee,^{1,11} Ryann Quinn,^{1,11} Kith Pradhan,^{2,11} Kateryna Fedorov,¹ David Levitz,¹ Ariel Fromowitz,¹ Astha Thakkar,¹ Lauren C. Shapiro,¹ Rafi Kabarriti,^{3,4} Rafael E. Ruiz,⁵ Erin M. Andrews,⁵ Raja Thota,⁵ Edward Chu,^{1,4} Shalom Kalnicki,^{3,4} Yitz Goldstein,⁶ David Loeb,⁷ Andrew Racine,⁷ Balazs Halmos,^{1,4,*} Vikas Mehta,^{8,9,*} and Amit Verma^{1,10,*}

¹Department of Oncology, Montefiore Medical Center, Montefiore Einstein Cancer Center (MECC), Albert Einstein College of Medicine, Bronx, NY, USA

²Department of Epidemiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

³Department of Radiation Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

⁴MECC Cancer Therapeutics Program, Montefiore Einstein Cancer Center (MECC), Albert Einstein College of Medicine, Bronx, NY, USA

⁵Department of Network Performance Group, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

⁶Department of Pathology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

⁷Department of Pediatrics, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

⁸Department of Otolaryngology and Head and Neck Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

⁹MECC Cancer Epidemiology Prevention and Control Program, Montefiore Einstein Cancer Center (MECC), Albert Einstein College of Medicine, Bronx, NY, USA

¹⁰MECC Stem Cell Cancer Biology Program Montefiore Einstein Cancer Center (MECC), Albert Einstein College of Medicine, Bronx, NY, USA

¹¹These authors contributed equally

*Correspondence: bahalmos@montefiore.org (B.H.), vikameht@montefiore.org (V.M.), amit.verma@einsteinmed.edu (A.V.)

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The SARS-CoV-2 Omicron (B.1.1.529) variant has emerged as the dominant variant in the USA. To assess the case fatality rate (CFR) in patients with cancer during this wave of the pandemic, we performed a retrospective analysis of COVID-19 cases seen in a New York hospital system between December 1, 2021 and January 17, 2022. A total of 285 patients with COVID-19 and cancer were identified: 223 with solid tumors and 62 with hematologic malignancies. A CFR of 14/285 (4.9%) was identified, and mortality was associated with increased age, metastatic involvement, and increased co-morbidities. Mortality in the cancer cohort was higher when compared to a control cohort (odds ratio [OR] 2.57 [95% confidence interval (CI): 1.35–4.56, $p = 0.0022$]) after adjusting for age, gender, and vaccine status. These results highlight increased mortality in patients with cancer during the recent COVID-19 wave, although mortality was significantly lower than with the initial variant, likely due to vaccination, better therapeutics, and possibly decreased virulence. Mortality among patients with cancer was associated with identifiable risk factors and comorbidities.

The SARS-CoV-2 Omicron (B.1.1.529) variant has been shown to possess extensive, albeit incomplete, ability to evade the immune system in previously infected or vaccinated individuals. A large number of mutations in the receptor binding

domain of the Spike protein allow the Omicron variant to spread quickly through communities in the USA (Cele et al., 2021). We and others have previously demonstrated an elevated CFR for cancer patients infected with SARS-CoV-2 (Liu et al., 2021; Mehta et al., 2020; Zhang et al., 2021). To determine the CFR during this present Omicron wave of the pandemic, a total of 285 patients with cancer and COVID-19 were identified in the Montefiore Health System (New York) from December 1, 2021 to January 17, 2022. Of this patient cohort, 270 (95%) patients tested positive for COVID-19 after December 19, 2021. Even though we did not genotype viral isolates, more than 90% of viral isolates in December starting December 19, 2021, and 95%–100% starting January, were Omicron variants in both the Montefiore Health System and NYC; this shows that our cohort consisted predominantly of patients infected with the Omicron variant (<https://www1.nyc.gov/assets/doh/downloads/pdf/covid/omicron-variant-report-jan-13-22.pdf>).

Our cancer cohort was comprised of 134 (47%) males and 151 (53%) females, and it included a diverse ethnic population consisting of 110 (39%) Hispanic, 95 (33%) African American, and 41 (14%) Caucasian patients. The median age of patients was 61 years old (range 2–96 years old) with a majority being adult (>18 years old) patients ($n = 272$, 95%).

The cohort included 223 (78%) patients with solid tumors and 62 (22%) patients with hematologic malignancies (Table S1A). In patients with solid malignancies, 25% had metastatic disease, and they were older than patients with hematologic malignancies, with 94 patients (42%) >65 years old in the solid tumor group, compared with 18 patients (29%) in the hematologic malignancy group. Of the 13 patients who were younger than 18 years old, 10 had hematologic malignancies (77%) and 3 (23%) had solid tumors. A total of 138 patients (48%) were on active cancer treatment within 90 days of COVID-19 infection: 77 (27%) on chemotherapy and 17 (6%) on immunotherapy. 10 (3.5%) patients had previously received anti-CD20 therapy, and 12 patients (4%) had previously undergone stem cell transplants.

Of the cancer cohort, 205 (72%) patients were fully vaccinated (this includes both patients who received the primary vaccine series and those with a booster), 56 (19.5%) patients were unvaccinated, and 9 (3.5%) patients were partially vaccinated (defined as having received one dose of the BNT162b2 or mRNA-1273 vaccine). 37 out of the 62 hematologic malignancy patients (60%) were fully vaccinated, and 8 (13%) had received boosters, in contrast with solid malignancy patients, of whom 169 out of the 223 (76%) were fully vaccinated and 52 (23%) had received boosters. Further



analysis of the unvaccinated subgroup revealed a median age of 52 and median Charlson score of 5; 10 (18%) of the unvaccinated patients were younger than 18 years old. The vaccinated subgroup was older (median age 64), had a higher median Charlson score (6), and included only 1 (0.5%) vaccinated patient younger than 18 years old (Table S1A).

14 oncology patients had died from COVID-19 disease at the time of analysis (January 27, 2022), with a CFR of 4.9% (Table S1B). There was a significant difference in mortality for admitted patients compared to those seen only in the emergency room or outpatient setting (OR 10.26 [95% CI: 2.25–46.78, $p = 1.54E-4$]) (Table S1A). Furthermore, there were significantly increased odds of inpatient admission for unvaccinated cancer patients (OR 2.01 [95% CI: 1.10–3.67, $p = 0.022$]). However, there were no significant differences in mortality between solid and liquid tumors, or among different racial groups. There was also no difference in mortality between vaccinated and unvaccinated cancer patients (Table S1A). 80 patients (28%) had asymptomatic COVID-19 infections.

We observed significantly higher mortality ($p = 0.02$) for cancer patients with concomitant COVID-19 in patients aged >65 years old. Solid tumor patients with metastatic disease also had higher mortality when compared to patients with early and/or localized disease ($p = 0.001$). Patients with more comorbidities as measured by the Charlson score had strikingly higher mortality ($p = 2.85E-7$).

To further understand the specific reasons for the higher mortality among oncology patients, we performed a detailed chart review of each patient who had passed away (Table S1B). We observed that several patients had advanced stages of cancer with antecedent complications at the time of COVID-19 diagnosis. In several cases, patients acquired COVID-19 while admitted to an inpatient facility. The absence of respiratory symptoms and/or findings of hypoxia in several patients suggested that these patients had incidental COVID-19 infections but died from their underlying cancer diagnoses (5 of 14). Of note, all the patients from this cohort who had received booster

vaccinations appeared to have died from other underlying causes with incidental COVID-19 infection. Second, a cohort of patients had readily identifiable immune predispositions for a poor outcome with COVID-19 with either: (1) a lack of immunization, poor and/or partial immunization status ($n = 3$; Ad26.CoV2.S only or mRNAx1) or (2) underlying severe immune suppression ($n = 3$; one with advanced AIDS and two patients with a documented poor or non-response by anti-Spike antibody testing to COVID-19 vaccination). Overall, these findings further highlight the importance of vaccinations, especially booster vaccinations, in order to prevent COVID-19-related deaths.

To determine whether mortality was elevated in the cancer cohort, we assessed a control group of 10,996 individuals who had a positive polymerase chain reaction (PCR) test result for COVID-19 in the Montefiore Health System during the same time frame. The median age of control patients was 38 years old (range 0–102), compared with a median age of 61 in the cancer cohort. A total of 5,802 (53%) control individuals were fully vaccinated (with or without a booster), compared to 72% of cancer patients. We first evaluated the association between cancer and mortality by using multivariable logistic regression between the entire cancer cohort and the entire control cohort while adjusting for vaccine status, age, and gender as confounders. The results showed a significantly higher mortality rate in the cancer cohort when compared to the control cohort (OR 2.57 [95% CI: 1.35–4.56, $p = 0.0022$]) (Table S1C). Older patients were also shown to have significantly higher mortality (OR 1.09 [95% CI: 1.08–1.10, $p = 7.66E-46$]), and those who were fully vaccinated had a statistically significantly lower mortality (OR 0.46 [95% CI: 0.31–0.67, $p = 6.63E-05$]). Furthermore, within the fully vaccinated cohort, we observed significantly lower odds of mortality in patients who had received the booster (OR 0.206 [95% CI: 0.062–0.514, $p = 0.002746$]) compared to those who were vaccinated but did not receive the booster.

In addition, to account for the higher percentage of vaccinated patients in the cancer cohort and the likely benefit of

vaccination in limiting mortality, we compared vaccinated cancer patients ($n = 206$) with vaccinated control individuals ($n = 5802$). We performed a 5-1 nearest neighbor pairing of controls to cancer patients by propensity score (Figure S1) based on age and gender by using a Fisher's exact test on the 2×2 mortality by cancer contingency table. Using this method, we observed higher mortality in the cancer cohort (OR 3.91 [95% CI: 1.66–8.97, $p = 8.54E-4$]) (Table S1D).

When we compared the cancer cohort with our control cohort, we found that those who were fully vaccinated had a statistically significantly lower mortality in the control cohort (Table S1C). Although this observation was not clearly seen within the cancer cohort, the discrepancy is likely related to a number of confounding factors, which included a small number of patients in the unvaccinated cancer cohort, along with the unvaccinated cancer cohort being overall younger (median age 52 versus 64 years old) and a larger fraction of that group being pediatric patients (18% of unvaccinated patients were <18). In addition, 27/206 (13%) of the vaccinated patients in our cancer cohort had received the Ad26.CoV2.S vaccine, with 21 (10%) having received just one dose. One dose of the Ad26.CoV2.S vaccine is now considered an inferior vaccination strategy due to waning immunity (Lin et al., 2022), and this has also been demonstrated in our study with lower IgG titers specifically in cancer patients compared with mRNA-based vaccines (Thakkar et al., 2021). The time elapsed after last vaccination (mean of 185 days) may also have contributed to lessening the protective effect of the immunization within the smaller cancer cohort.

Overall, our findings show that even though the CFR is less than in previous waves, where it was as high as 28% (Mehta et al., 2020), the adverse impact of the current Omicron COVID-19 wave on cancer patients with advanced age, advanced tumors, and increased comorbidities continues to be demonstrated. Mortality among patients during the Omicron wave appears associated with clearly identifiable and potentially actionable risk factors related to disease status, immune suppression, and vaccination status.

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.ccell.2022.02.012>.

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tion. The other authors declare no competing interests.

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