SARS-CoV-2 Specific Monoclonal Antibody for the Treatment of Mild-to-Moderate COVID-19 in Cancer Patients: A Single-center Experience

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Dear Editor:

We read with interest the article by Ganesh et al. regarding monoclonal antibody (mAb) therapy for COVID-19 in high-risk patients [1]. mAb against SARS-CoV-2 is a promising therapy for non-hospitalized patients with mild to moderate COVID-19 illness who are at high-risk for severe disease or hospitalization. In the general population, mAb decreased the risk of hospitalization and death by 60%, as reported by Bariola et al. [2]. However, its efficacy and safety in cancer patients is not well described. We aimed to assess the impact of mAb in non-hospitalized patients with mild to moderate COVID-19 undergoing treatment for solid organ cancer, hematologic malignancies (HM), recipients of hematopoietic stem cell transplant (HCT) and chimeric antigen receptor T-cell (CAR-T) therapy at City of Hope Medical Center.

We retrospectively reviewed the medical records of patients who received mAb from 12/31/2020 to 3/9/2021 at our medical center. Institutional eligibility guidelines for mAb therapy during the study period were based on the availability and supply of mAb from the local county health department. In general, our eligibility criteria for mAb therapy were more stringent than the U.S. Food and Drug Administration (FDA) emergency use authorization (EUA) guidelines [3]. We extracted baseline demographics, clinical, and cancer-related data. Outcomes included hospitalization, ICU admission, and 30-day mortality. Baseline characteristics were described using frequencies and percentages for categorical variables, and median and interquartile range (IQR) for continuous variables. Patient characteristics between hospitalized and nonhospitalized groups were compared using *t* test for continuous variables and Fisher's exact test for categorical variables. This study was approved by City of Hope's Institutional Review Board.

Forty-two patients received mAb. Thirty-five (83%) had bamlanivimab and 7 (17%) casirivimab-imdevimab. Twenty-one (50%) were female, primarily Hispanic (45%), and with a median age of 52 years. Thirty-two (76%) patients had HM, and 10 (24%) had a solid organ cancer. Of the 32 patients with HM, 16 (38%) had an allogenic HCT, 5 (12%) an autologous HCT, and 3 (7%) CAR-T therapy. Median time from HCT and CAR-T therapy to COVID-19 diagnosis was 439 and 985 days, respectively. Overall, the median time to mAb infusion was 5 days from symptoms onset and 3 days from molecular diagnosis of COVID-19. All patients had 30-day follow-up data. Five (12%) patients were hospitalized due to COVID-19, with a median length of stay of 6 days, and all recipients of bamlanivimab. Hospitalization was significantly associated with prior CAR-T therapy (p=0.03) and older age; 62 years for hospitalized vs 50 years for non-hospitalized patients (p=0.04). Only 1 (3%) patient, a CAR-T therapy recipient for diffuse large B cell lymphoma, treated with bamlanivimab for mild COVID-19 progressed to severe disease requiring ICU care. This patient died at day +79 of CAR-T, and 29 days after bamlanivimab infusion. The four remaining hospitalized patients included one with leiomyosarcoma in remission, one with acute myeloid leukemia receiving bi-specific T-cell engagers, one with chronic lymphocytic leukemia (CLL) in remission at day +1,053 post CAR-T, and another CLL on cirmtuzumab and ibrutinib. There were no mAb attributable adverse effects in our cohort. Additional patient characteristics are shown in Table 1.

Our experience in this single-center observational study provides added support both for safety and a therapeutic role of mAb in the management of outpatient COVID-19 in immunocompromised cancer patients. Notably, all hospital admissions in our cohort occurred after bamlanivimab infusion. This may have coincided with the emergence of SARS-CoV-2 variants resistant to bamlanivimab monotherapy, such as the Epsilon variant (B.1.429/B.1.427) first detected in California, which prompted a revised recommendation against the use of bamlanivimab alone [4]. More recently, the FDA announced a pause in

the distribution of bamlanivimab-etesevimab on a national basis and recommended to use mAb's that retain activity against circulating strains of SARS-CoV-2 [5]. Now, as the highly transmissible and virulent Delta variant (B.1.617.2) has become the dominant strain, there is a need for further assessment in larger studies on the efficacy of mAb against SARS-CoV-2 variants and the clinical settings theycan be used in to establish the magnitude of benefit in this vulnerable population. This includes prophylactic approaches in cancer patients with a known exposure to SARS-Cov2 who are at high risk for severe disease, non-hospitalized patients with COVID-19, or those who have prolonged viral shedding [6].

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Author Contributions:

Drs Puing, Ho and Dadwal had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to data collection.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Puing, Ho, Taplitz, Dadwal.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Puing, Frankel.

Text

	Total	Hospitalized	Nonhospitalized	*P*
	(n = 42)	(n = 5)	(n = 37)	*value*

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Sex				
Female, No. (%)	21 (50.0)	1 (20.0)	20 (54.1)	0.34
Age				
Age, median (IQR), y	51.5 (37.75-62)	62 (60-67)	50 (35-61)	**0.04**
Age $\geq$ 65, No. (%)	8 (19.0)	2 (40.0)	6 (16.2)	0.24
Ethnicity				
Hispanic, No. (%)	19 (45.2)	3 (60.0)	16 (43.2)	0.64
Other, No. (%)	23 (54.8)	2 (40.0)	21 (56.8)	
BMI				
BMI, median (IQR), kg/m^2	26 (23.05-31.075)	25 (24.3-30)	26 (23-31.1)	0.48
BMI $\geq$ 35, No. (%)	9 (21.4)	1 (20.0)	8 (21.6)	1
Co-Morbidity				
Hypertension, No. (%)	12 (28.6)	1 (20.0)	11 (29.7)	1
Diabetes, No. (%)	7 (16.7)	1 (20.0)	6 (16.2)	1
Pulmonary, No. (%)	4 (9.5)	-	4 (10.8)	1
Former smoker, No. (%)	12 (28.6)	2 (40.0)	10 (27.0)	0.61
Malignancy				
Solid organ cancer, No. (%)	10 (23.8)	1 (20.0)	9 (24.3)	1
Hematologic malignancy, No. (%)	32 (76.2)	4 (80.0)	28 (75.7)	1
Allogeneic HCT, No. (%)	16 (38.1)	-	16 (43.2)	0.14
Autologous HCT, No. (%)	5 (11.9)	-	5 (13.5)	1
CAR-T, No. (%)	3 (7.1)	2 (40.0)	1 (2.7)	**0.03**
COVID-19 severity				
Mild, No. (%)	32 (76.2)	2 (40.0)	30 (81.1)	0.08

Moderate, No. (%)	10 (23.8)	3 (60.0)	7 (18.9)	0.08
Time to mAb infusion from symptoms onset, median (IQR), d	5 (3-7)	3 (2-4)	5 (3-7)	0.06
Time to mAb infusion from COVID-19 diagnosis, median (IQR), d	3 (1.25-4)	2 (1-2)	4 (2-4)	0.09
mAb therapy				
Bamlanivimab, No. (%)	35 (83.3)	5 (100.0)	30 (81.1)	0.57
Casirivimab-Imdevimab, No. (%)	7 (16.7)	-	7 (18.9)	0.57

Table 1. Patient characteristics

Abbreviations: BMI, body mass index; CAR-T, chimeric antigen receptor T-cell; d, days; HCT, hematopoietic stem cell transplant; IQR, interquartile range; mAb, monoclonal antibody; y, years.