

In the format provided by the authors and unedited.

Determinants of COVID-19 disease severity in patients with cancer

Elizabeth V. Robilotti^{1,2,3}, N. Esther Babady^{1,4}, Peter A. Mead^{1,3}, Thierry Rolling¹, Rocio Perez-Johnston⁵, Marilia Bernardes¹, Yael Bogler¹, Mario Caldararo¹, Cesar J. Figueroa^{1,3}, Michael S. Glickman^{1,3}, Alexa Joanow¹, Anna Kaltsas^{1,3}, Yeon Joo Lee^{1,3}, Anabella Lucca^{1,6}, Amanda Mariano¹, Sejal Morjaria^{1,3}, Tamara Nawar¹, Genovefa A. Papanicolaou^{1,3}, Jacqueline Predmore¹, Gil Redelman-Sidi^{1,3}, Elizabeth Schmidt¹, Susan K. Seo^{1,3}, Kent Sepkowitz^{1,3}, Monika K. Shah^{1,3}, Jedd D. Wolchok^{3,7}, Tobias M. Hohl^{1,3}, Ying Taur^{1,3,8} and Mini Kamboj^{1,2,3,8} ✉

¹Infectious Diseases, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA. ²Infection Control, Memorial Sloan Kettering Cancer Center, New York, NY, USA. ³Department of Medicine, Joan and Sanford Weill Medical College of Cornell University, New York, NY, USA. ⁴Clinical Microbiology Service, Department of Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA. ⁵Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA. ⁶Employee Health and Wellness Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA. ⁷Human Oncology and Pathogenesis Program, Department of Medicine, Ludwig Center and Parker Institute for Cancer Immunotherapy at Memorial Sloan Kettering Cancer Center, New York, NY, USA. ⁸These authors contributed equally: Ying Taur, Mini Kamboj. ✉e-mail: kambojm@mskcc.org

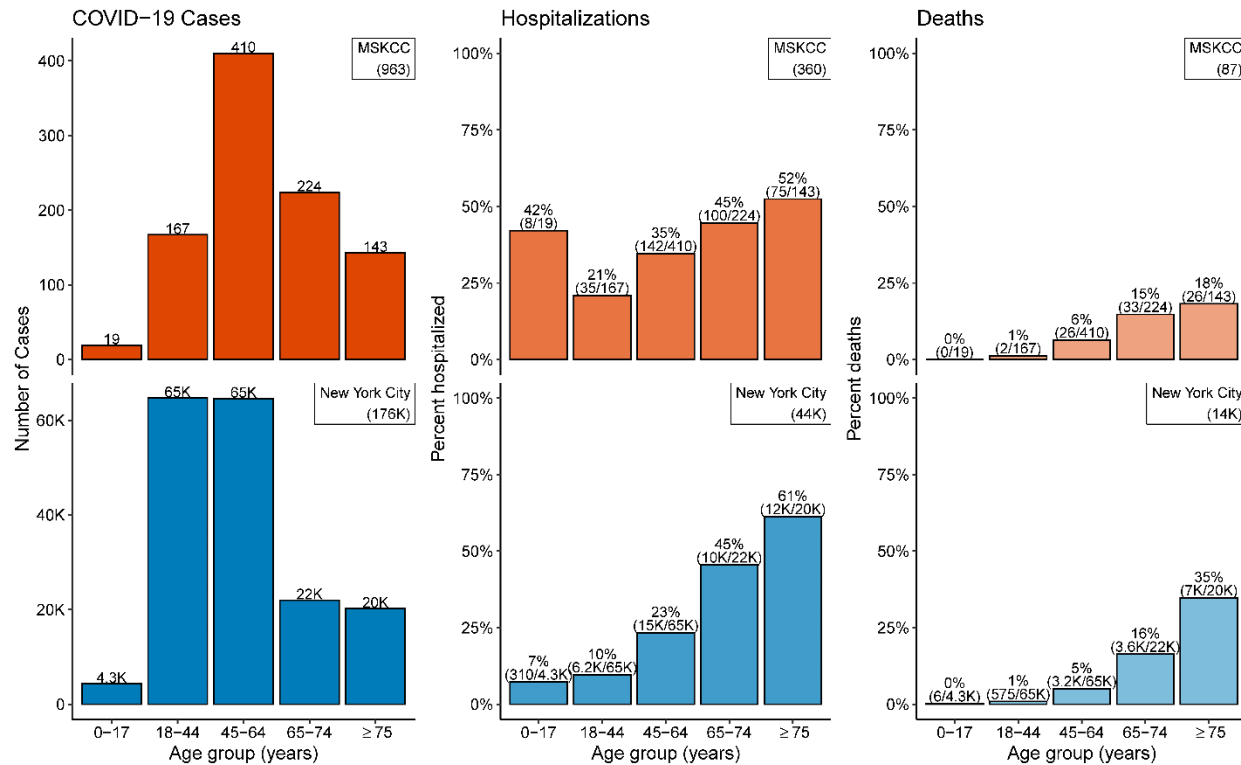
Supplementary Information for:

Determinants of Severity in Cancer Patients with COVID-19 Illness

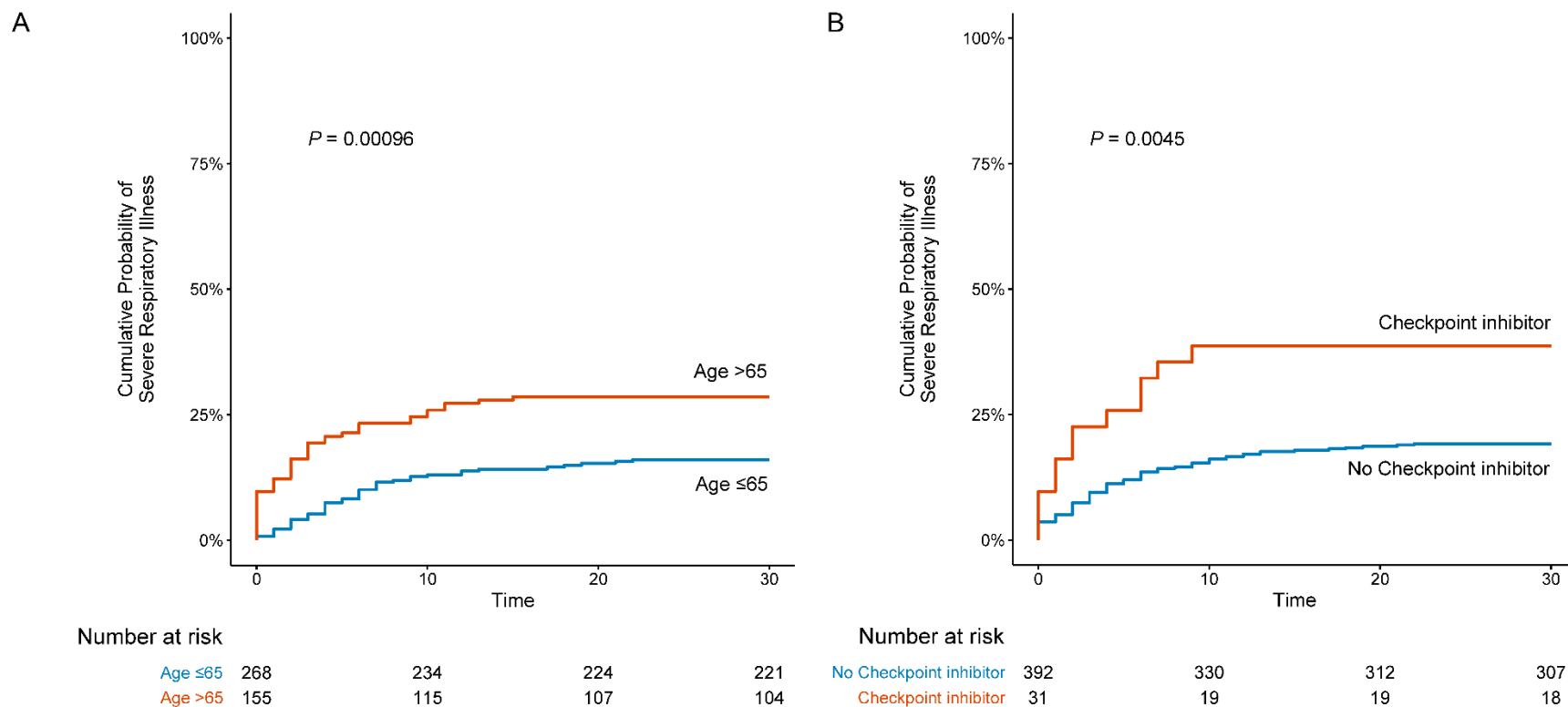
Elizabeth V. Robilotti, M.D. M.P.H, N. Esther Babady, Ph.D., Peter A. Mead, M.D., Thierry Rolling M.D., Rocio Perez-Johnston M.D., Marilia Bernardes, M.D., Yael Bogler, M.D., Mario Caldararo, M.D., Cesar J. Figueroa Ortiz, M.D., Michael S. Glickman, M.D., Alexa Joanow, M.S., Anna Kaltsas, M.D., Yeon Joo Lee, M.D., Anabella Lucca Bianchi, M.D., Amanda Mariano, M.S., Sejal Morjaria, M.D., Tamara Nawar, M.D., Genovefa A. Papanicolaou, M.D., Jacqueline Predmore, M.S., Gil Redelman-Sidi, M.D., Elizabeth Schmidt, M.S., Susan K. Seo, M.D., Kent Sepkowitz, M.D., Monika K. Shah, M.D., Jedd D. Wolchok, M.D. PhD., Tobias M. Hohl, M.D. PhD, *Ying Taur, M.D. MPH, *Mini Kamboj, M.D.

*These authors contributed equally: Ying Taur, Mini Kamboj

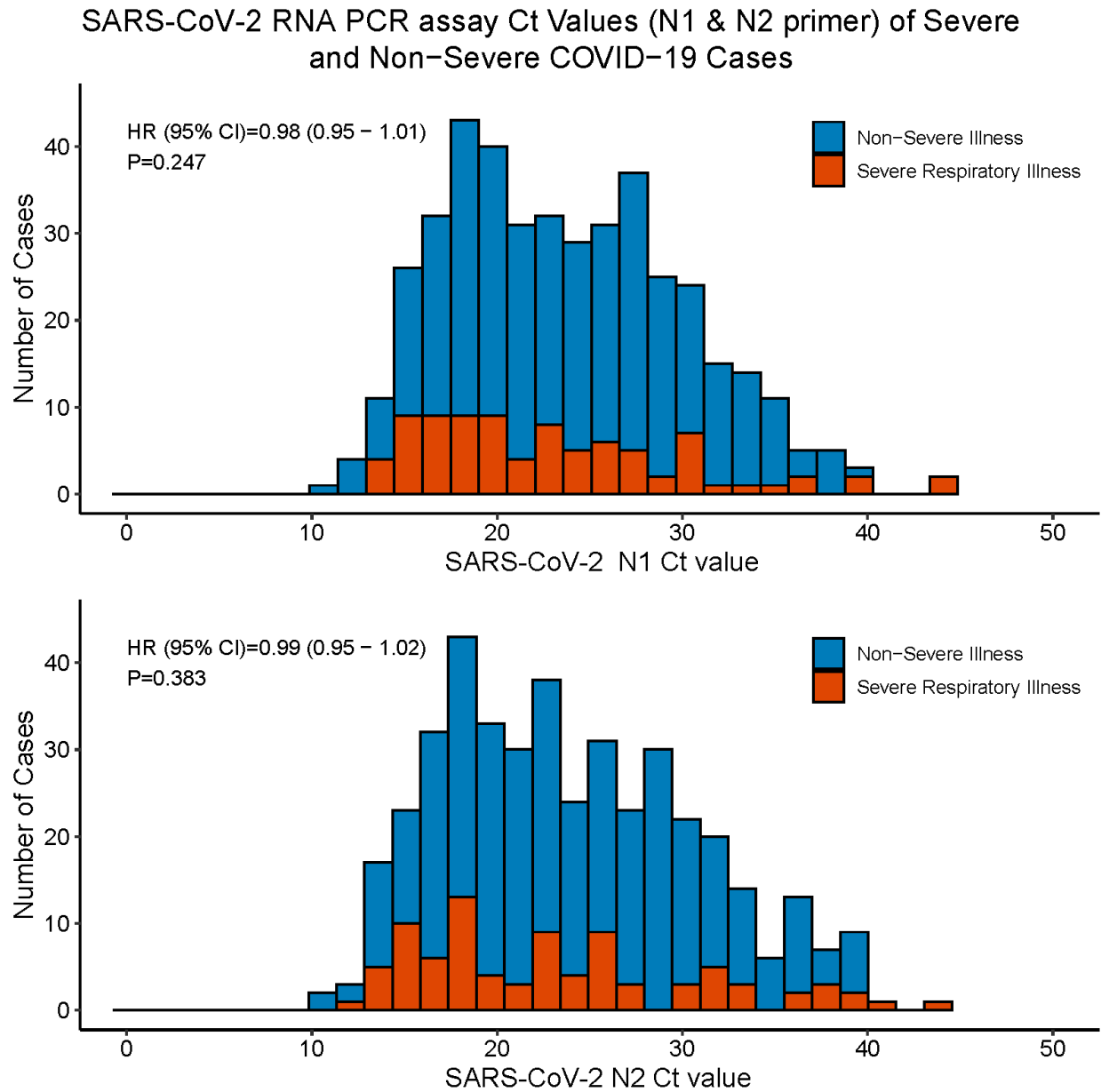
Supplemental Figure 1: Age-specific comparison of COVID-19 cases, hospitalizations, and deaths at MSKCC (top panels, N=946 cases) and across New York City (bottom panels, N=176,086). Data include the time period from March 10 to May 7, 2020. New York City case data is collected from NYC Department of Health: <https://www1.nyc.gov/site/doh/covid/covid-19-data.page>



Supplemental Figure 2: Cumulative probability of severe respiratory illness during COVID-19 illness, using Kaplan-Meier estimation. Severe respiratory illness was defined as requiring high-flow oxygen or mechanical ventilation within 30 days of diagnosis. The following risk factors are shown: (A) age >65 years, and (B) treatment with immune checkpoint inhibitor. P-values from a two-sided Mantel-Cox log-rank test are shown.



Supplemental Figure 3: Ct values of SARS-CoV-2 PCR assay and risk of severe respiratory illness. Ct value distributions are shown for SARS-CoV-2 N1 and N2 primers. The Cox proportional hazard ratio shows increase in risk of severe respiratory illness for each unit increase in Ct value is shown, along with two-sided 95% confidence interval and P-value.



Supplemental Table 1: Chest Radiographic and Computed Tomography (CT) Findings in COVID-19 cases

Chest radiograph (X-ray) findings	No. (%)
Normal	58 (28)
Abnormal	149 (72)
Total performed	207 (100)

Computed tomography (CT) chest findings	No. (%)
Normal	4 (10)
Abnormal	35 (90)
Unilateral	12 (31)
Bilateral	23 (59)
Peripheral involvement	30 (77)
Ground-glass infiltrates	30 (77)
Focal consolidation	13 (33)
“Crazy paving” finding	2 (5)
Pleural effusion	5 (13)
Adenopathy	1 (3)
Total performed	39 (100)

Note: 207 X-rays and 39 CTs were obtained from 423 study subjects

Supplemental Table 2: COVID-19 Treatments administered

<u>Medication</u>	<u>Total patients (percent)</u>
<i>Remdesivir</i>	4 (1)
<i>Azithromycin</i>	138 (33)
<i>Tocilizumab</i>	6 (1)
<i>Hydroxychloroquine</i>	150 (35)
<i>Convalescent plasma</i>	9 (2)
<i>Systemic corticosteroids</i>	117 (28)

Note: Treatments are listed for 423 study subjects.

Supplemental Table 3: Multivariate Cox Model of Severe Respiratory Illness in ICI treatable cancers^a, with inclusion of lung cancer as predictor

Hospitalization, by logistic regression (N=268)

<i>Predictor^b</i>	<i>Univariate</i>		<i>Multivariate</i>	
	<i>OR (95% CI)</i>	<i>P-value</i>	<i>OR (95% CI)</i>	<i>P-value</i>
<i>Age (>65y)</i>	1.36 (0.74 - 2.46)	0.315	1.18 (0.62 - 2.22)	0.606
<i>Lung Cancer</i>	3.54 (1.66 - 7.46)	0.001	3.89 (1.67 - 8.96)	0.002
<i>Hematologic malignancy</i>	2.00 (0.98 - 3.97)	0.057	2.38 (1.00 - 5.70)	0.051
<i>Metastatic disease</i>	0.71 (0.40 - 1.30)	0.265	0.64 (0.29 - 1.44)	0.280
<i>Immune checkpoint inhibitor</i>	2.79 (1.24 - 6.11)	0.014	2.66 (1.05 - 6.54)	0.039

Severe respiratory illness, by Cox proportional hazard (N=275)

<i>Predictor^b</i>	<i>Univariate</i>		<i>Multivariate</i>	
	<i>HR (95% CI)</i>	<i>P-value</i>	<i>HR (95% CI)</i>	<i>P-value</i>
<i>Age (>65y)</i>	1.42 (0.84 - 2.39)	0.195	1.25 (0.73 - 2.14)	0.414
<i>Lung Cancer</i>	3.19 (1.77 - 5.76)	<0.001	3.31 (1.68 - 6.52)	<0.001
<i>Hematologic malignancy</i>	1.67 (0.93 - 3.01)	0.089	2.03 (0.94 - 4.37)	0.072
<i>Metastatic disease</i>	0.76 (0.45 - 1.27)	0.294	0.70 (0.34 - 1.43)	0.331
<i>Immune checkpoint inhibitor</i>	2.46 (1.30 - 4.65)	0.006	2.22 (1.06 - 4.65)	0.034

^a Includes 275 patients with the following malignancies, where ICI was given as therapy: breast, colorectal, genitourinary, gynecologic, lymphoma, neurologic, skin.

^b Model covariates were selected as pertinent to lung cancer and immune checkpoint blockade.

Supplemental Table 4: Presenting symptoms as predictors of subsequent hospitalization and severe respiratory illness for patients with COVID-19

Hospitalization, by logistic regression (N=411)

<i>Predictor</i>	<i>Univariate</i>		<i>Multivariate</i>	
	<i>OR (95% CI)</i>	<i>P-value</i>	<i>OR (95% CI)</i>	<i>P-value</i>
<i>Fever</i>	1.79 (1.10 - 2.98)	0.020	1.44 (0.86 - 2.48)	0.170
<i>Cough</i>	2.13 (1.25 - 3.78)	0.005	1.54 (0.86 - 2.82)	0.149
<i>Shortness of breath</i>	3.58 (2.39 - 5.41)	<0.001	3.05 (2.00 - 4.68)	<0.001
<i>Diarrhea</i>	2.66 (1.70 - 4.17)	<0.001	2.32 (1.45 - 3.73)	<0.001

Severe respiratory illness, by Cox proportional hazard (N=423)

<i>Predictor</i>	<i>Univariate</i>		<i>Multivariate</i>	
	<i>HR (95% CI)</i>	<i>P-value</i>	<i>HR (95% CI)</i>	<i>P-value</i>
<i>Fever</i>	1.53 (0.85 - 2.76)	0.159	1.17 (0.64 - 2.13)	0.613
<i>Cough</i>	1.71 (0.88 - 3.31)	0.112	1.11 (0.56 - 2.19)	0.766
<i>Shortness of breath</i>	4.88 (2.95 - 8.07)	<0.001	4.42 (2.64 - 7.41)	<0.001
<i>Diarrhea</i>	2.27 (1.47 - 3.51)	<0.001	1.89 (1.22 - 2.94)	0.004

Supplemental Table 5: Laboratory Biomarkers as predictors of subsequent severe respiratory illness for patients with COVID-19

Severe respiratory illness, by Cox proportional hazard with (N=423)

<i>Predictor (time dependent)</i>	<i>Univariate</i>		<i>Multivariate</i>	
	<i>HR (95% CI)</i>	<i>P-value</i>	<i>HR (95% CI)</i>	<i>P-value</i>
<i>Procalcitonin (>0.5 ng/mL)</i>	6.15 (3.82 - 9.90)	<0.001	3.04 (1.79 - 5.16)	<0.001
<i>Lymphopenia (<0.5 K/mcL)</i>	4.08 (2.55 - 6.52)	<0.001	2.26 (1.39 - 3.69)	0.001
<i>Interleukin-6 (>100 pg/mL)</i>	12.52 (7.47 - 20.98)	<0.001	4.90 (2.84 - 8.46)	<0.001
<i>D-Dimer (>1 mcg/mL)</i>	5.39 (3.17 - 9.16)	<0.001	1.67 (0.92 - 3.03)	0.090
<i>Lactate dehydrogenase (250 U/L)</i>	7.08 (4.38 - 11.43)	<0.001	2.59 (1.52 - 4.42)	<0.001

Note:

All predictors were coded as time-dependent predictors.

Except for lymphopenia, these biomarkers were obtained with varying frequency, at the discretion of providers; therefore, interpretation may be limited.