1270 PREDICTING RISK FACTORS FOR SEVERE IMMUNE-RELATED ADVERSE EVENTS REQUIRING HOSPITALIZATION FROM CHECKPOINT INHIBITORS

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Background As immune checkpoint inhibitors (CPI) are increasingly approved for the treatment of multiple cancer types, hospitalizations related to severe immune-related adverse events (irAE) will increase in tandem. Here, we identify risk factors that predict hospitalization from an irAE to help guide clinical decision-making for future patients on CPI therapy.

Methods This retrospective case-control study included patients exposed to CPIs who were hospitalized from 1/2012 to 12/2020 at our tertiary care hospital by computationally extracting data from the electronic health record. We then performed manual chart review to include only confirmed irAE-related hospitalizations. Controls were patients who had received CPI therapy without an irAE hospitalization matched by gender, age and cancer type to the cases. Controls were manually chart reviewed for data abstraction and to confirm there was not an irAE hospitalization. We assessed association of hospitalization with variables of interest using student t and fisher exact as appropriate. We included variables in the multivariate logistic regression analysis that had $p < 0.10$ in the univariate analysis.

Results Of 3137 patients treated with CPIs, 114 (3.6%) were hospitalized for irAEs, resulting in 124 hospitalizations. In this preliminary analysis, 158 controls were reviewed. Patients who were hospitalized did not have significant differences in age, gender, race, cancer type, body mass index, Eastern Cooperative Oncology Group (ECOG) performance status, smoking and alcohol history, and Charlson Comorbidity Index (table 1). The hospitalized group had more patients treated with combination therapy (PD-1/L1 and CTLA-4) (33.3% vs 13.3%) and less PD-1/L1 monotherapy (60.5% vs 82.9%) ($p=0.001$). The hospitalized group also had less prior CPI therapy (12.9% vs 31.0%, $p=0.001$). Patients hospitalized for an irAE had more pre-existing autoimmune conditions although not statistically significant (13.7% vs 6.9%, $p=0.065$). After multivariate logistic regression, pre-existing autoimmune condition (OR 2.41, 95% CI: 1.01–5.75 $p=0.048$) and combination immunotherapy (4.02, 2.13–7.59 $p<0.001$) was associated with increased odds of hospitalization, while prior CPI therapy was associated with decreased odds (0.32, 0.16–0.65 $p=0.001$) (table 2).

Conclusions This real-world data suggest patients who have a pre-existing autoimmune condition or are being treated with combination immunotherapy had higher odds of an irAE hospitalization, while tolerating prior CPI therapy decreased odds of hospitalization. Understanding who is at risk for these events is critical both for weighing the risks and benefits of therapy, monitoring for toxicities, as well as eventually developing treatments that can prevent, modify or treat irAEs.

Ethics Approval This study was approved by the UCSF Human Research Protection Program [#17–22987].

Abstract 1270 Table 1 Baseline demographics and univariate of cases vs matched controls. *Comparing white to other races/ethnicities, **comparing ever used alcohol (prior or current) to never, ***comparing autoimmune condition to no autoimmune condition, comparing all cancers to melanoma

	Cases Hospitalized for an irAE (n=114)	*Matched Controls* CPI therapy without an irAE hospitalization (n=158)	p-value
Age (yrs) mean (range)	61.5 (22-91)	60.8 (15-94)	0.67
BMI mean (range)	26.4 (15.4-45.7)	26.3 (13.2-52.1)	0.82
Gender (%)			
Male	66 (57.8)	88 (55.7)	0.86
Female	47 (41.2)	69 (43.7)	
Other/Nonbinary/not answered	1 (0.9)	1 (0.6)	
Race/ethnicity (%)			
White	85 (74.6)	108 (68.4)	0.28*
Hispanic	13 (11.4)	8 (5.1)	
African American	3 (2.6)	10 (6.3)	
Asian	12 (10.5)	26 (16.5)	
American Indian/ Alaska Native	4 (3.5)	1 (0.6)	
Unknown	1(0.8)	3 (1.8)	
ECOG at first CPI			
0-1	101 (88.6)	139 (88.0)	0.97
≥ 2 or unknown	13 (11.4)	19 (12.0)	
Alcohol status			
Current consumer	48 (42.1)	87 (55.1)	0.45**
Prior consumer	46 (39.6)	37 (23.4)	
Never consumer	20 (17.5)	32 (20.3)	
Unknown	0 (0)	2 (1.2)	
Smoking status			
Current smoker	5 (4.3)	10 (6.3)	0.90
Prior smoker	52 (45.6)	70 (44.3)	
Never smoker	57 (50.0)	76 (48.1)	
Unknown	0 (0)	2 (1.2)	
Autoimmune condition			
Present, on immunomodulatory therapy	4 (3.5)	1 (0.6)	0.065***
Present, not on immunomodulatory Therapy	12 (10.5)	10 (6.3)	
Absent	98 (85.9)	147 (93.0)	
Charlson Comorbidity Index (%)			
≤4	11 (9.6)	17 (10.8)	0.40
5 – 8	59 (51.7)	89 (56.3)	
≥9	44 (38.6)	51 (32.3)	
Type of cancer (%)			
Melanoma	39 (34.2)	62 (39.2)	0.370
Lung	14 (12.3)	19 (12.0)	
Head and Neck	8 (7.0)	12 (8.2)	
RCC	11 (9.6)	15 (9.5)	
Bladder	2 (1.8)	4 (2.5)	
Gastric	5 (4.4)	4 (2.5)	
MSI+colon	2 (1.8)	1 (0.6)	
Breast	5 (4.4)	9 (5.7)	
Skin SCC	3 (2.6)	1 (0.6)	
HCC	4 (3.5)	6 (3.8)	
Ovarian	2 (1.8)	0 (0)	
Prostate	3 (2.6)	3 (1.8)	
Cholangiocarcinoma	3 (2.6)	2 (1.3)	
Anal SCC	0 (0)	3 (1.8)	
Endometrial	0 (0)	2 (1.2)	
Other	13 (11.4)	13 (8.2)	
CPI combination type			
Combination CPI	38 (33.3)	21 (13.3)	0.001
CPI Monotherapy	55 (48.2)	107 (67.7)	
CPI plus Chemo	12 (0.5)	13 (8.2)	
CPI plus other immunomodulator	9 (7.9)	17 (10.8)	
CPI type			
Combination CPI	39 (34.2)	21 (13.3)	<0.001
PD-1 or PD-L1 Monotherapy	69 (60.5)	131 (82.9)	
CTLA-4 Monotherapy	6 (5.2)	6 (3.8)	
CPI drug			
Ipilimumab	6 (5.2)	6 (3.8)	<0.001
Nivolumab	23 (20.2)	60 (38.0)	
Ipi/Nivo	35 (30.7)	19 (12.0)	
Pembrolizumab	39 (34.2)	63 (39.8)	
Durvalumab	2 (1.7)	2 (1.3)	
Atezolizumab	3 (2.6)	4 (2.5)	
Cemiplimab	2 (1.7)	1 (0.6)	
Ipi/Pembro	3 (2.6)	1 (0.6)	
Spartalizumab	0 (0)	1 (0.6)	
Tremelimumab/Durva	1 (0.9)	1 (0.6)	
Part of a clinical trial			
Yes	29 (25.4)	46 (29.1)	0.58
No	85 (74.5)	112 (70.9)	
Prior CPI therapy			
Yes	15 (12.9)	49 (31.0)	0.001
No	99 (85.3)	108 (68.3)	
Prior radiation therapy within 90 days of CPI initiation			0.37
Yes	18 (15.8)	32 (20.3)	
No	96 (84.2)	122 (77.2)	
Prior surgery within 90 days of CPI initiation			1.00
Yes	18 (15.8)	25 (15.8)	
No	96 (84.2)	131 (82.9)	
Metastatic or unresectable at CPI initiation			0.36
Yes	103 (90.4)	146 (92.4)	
No	11 (9.5)	10 (6.3)	
Stage (%)			
Stage I	3 (2.6)	4 (2.5)	0.75
Stage II	6 (5.2)	5 (3.2)	
Stage III	14 (12.2)	24 (15.2)	
Stage IV	90 (78.9)	125 (79.1)	
Unknown	1 (0.9)	0 (0)	
History of an irAE			
Yes	114 (100.0)	74 (46.8)	NA
No	0 (0)	84 (53.1)	

Abstract 1270 Table 2 Multivariate logistic regression analysis to predict hospitalization from an irAE

Multivariate Analysis		
Predictor	**Odds ratio (95% CI)**	**p-value**
Autoimmune condition		
No	1.00	
Yes	2.41 (1.01-5.75)	0.048
CPI type		
PD-1/PD-L1	1.00	
CTLA-4	1.86 (0.54-6.42)	0.33
PD-1/L1 and CTLA-4 combination	4.02 (2.13-7.59)	<0.001
Prior CPI therapy		
No	1.00	
Yes	0.32 (0.16-0.63)	0.001

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1270