814 CUTANEOUS IMMUNE-RELATED ADVERSE EVENTS ARE PROTECTIVE OF MORTALITY IN PATIENTS TREATED WITH ANTI-PD1 AND ANTI-PDL1 THERAPY IN A MULTI-INSTITUTIONAL COHORT STUDY

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Background Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy over the last decade. Despite the efficacy of ICIs, immune-related adverse events (irAEs) occur in over a third of treated patients and can cause lasting morbidity and mortality.[1–3] Cutaneous irAEs (cirAEs) are the most frequently reported toxicities, occurring in 20–40% of treated patients. Though recent reports have investigated the prognostic significance of irAEs on cancer outcomes, little is known about the specific impact of cirAEs and their subtypes on cancer survival.[4] In this landmark analysis, we present the first population-level study examining the influence of cirAE development following ICI therapy on the mortality of cancer patients.

Methods 7,008 patients who developed cirAEs after treatment with anti-programmed cell death receptor/ligand 1 (PD-1/PD-L1) therapy for malignant neoplasms of digestive organs, bronchus or lung, melanoma of skin, and urinary tract were identified through the TriNetX Diamond network along with 7,008 matched controls (table 1). The malignant neoplasms and cutaneous diagnoses for this study were identified from published literature and expert opinion.[5 6] Looking at cutaneous eruptions within 6 months of the first instance of ICI administration, a 6-month landmark analysis using a Cox proportional hazards model was performed to determine the impact of cirAE on overall survival.

Results Presence of any cirAE (HR=0.695, p<0.0001), non-specific rashes (HR=0.704 , p<0.0001), pruritus (HR=0.695, p<0.0001), drug eruption (HR=0.755, p=0.0013), and xerosis (HR=0.626, p=0.0013) were significantly protective of mortality using a Benjamini-Hochberg (BH) correction for multiple comparisons (table 2). Psoriasis (HR=0.703, p=0.0451) and lichen planus/lichenoid dermatitis (HR=0.511, p=0.0274) were nominally significant. Notably, though not reaching statistical significance, eczematous dermatitis (HR=0.0.612), vitiligo (HR=0.534), bullous pemphigoid (HR=0.524), and Grover's disease (HR=0.468) were associated with strong protective clinical effects. To explore the impact of landmark time on mortality, a sensitivity analysis was performed for cirAE onset within 3 months (HR=0.759, p<0.0001) and 9 months (HR=0.84, p<0.0001) of ICI initiation. A separate sensitivity analysis expanded to include all cancer types treated with ICI yielded similar results, with additional statistical significance reached for ICI-induced psoriasis (table 3).

Conclusions This is the first population-level study and largest analysis to date of the impact of cirAEs on mortality among patients with advanced cancer. With the exception of mucositis and hyperhidrosis, there was a strong clinically protective effect of cirAEs across all individual morphologies investigated. Our results demonstrate that cirAE development after ICI initiation is an important positive prognostic indicator of response to ICI therapy and patient survival.

Abstract 814 Table 1 Propensity score-matched baseline characteristics for patients treated with PD-1 or PL-L1 therapy

	ICI with cirAE		ICI without cirAE		P-value
N	7008		7008		
Age (years)	Mean	SD	Mean	SD	
Age at Index	68.2	11.2	68.3	11.1	0.7912
Gender	N	%	N	%	
Male	3972	56.7	3961	56.5	0.8513
Female	3036	43.3	3044	43.4	0.8915
Unknown	0	0	10	0.14	0.0016
Race and Ethnicity	Mean	%	Mean	%	
White Non-Hispanic	1549	22.10	1571	22.40	0.6551
Black Non-Hispanic	129	1.84	116	1.66	0.4021
Asian Non-Hispanic	17	0.24	10	0.14	0.1775
Hispanic or Latino	111	1.58	77	1.10	0.0125
Cancer Type	Mean	%	Mean	%	
Digestive organs	956	13.64	937	13.37	0.6387
Bronchus and lung	3993	56.9	3996	57.02	0.9592
Melanoma of skin	1300	18.55	1288	18.38	0.7939
Urinary tract	1306	18.64	1244	17.75	0.1746
Ill-defined, other secondary and unspecified sites	5399	77.04	5396	76.99	0.952

Abstract 814 Table 2 Association between cutaneous eruptions and surviv

Cutaneous Diagnosis‡	N	Hazard Ratio	P-value*
Hyperhidrosis	281	1.381	0.0797
Mucositis	563	1.161	0.2068
Dermatomyositis	105	0.93	0.7894
Maculopapular eruption	230	0.845	0.3625
Erythroderma	247	0.769	0.1697
Drug eruption and non-specific drug reaction	**1075**	**0.755**	**0.0013**
Hyperkeratosis	39	0.707	0.4867
Rash and other non-specific eruption	**3163**	**0.704**	**<0.0001**
Psoriasis	299	0.703	0.0451
Pruritus	**1694**	**0.695**	**<0.0001**
Xerostomia	163	0.671	0.1301
Xerosis	**441**	**0.626**	**0.0013**
Eczema and Atopic Dermatitis	72	0.612	0.1467
Vitiligo	100	0.534	0.0929
Pemphigoid	32	0.524	0.3281
Lichen Planus	97	0.511	0.0274
Grover's disease	18	0.468	0.2768
Any cutaneous diagnosis	**7008**	**0.778**	**<0.0001**

‡Cutaneous diagnoses were identified based on published literature and expert opinion.
*Benjamini-Hochberg p-value of significance = 0.0013.

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Abstract 814 Table 3 Association between cutaneous eruptions and surviva

Cutaneous Diagnosis‡	N	Hazard Ratio	P-value*
Dermatomyositis	128	1.405	0.1917
Mucositis	694	1.112	0.3398
Hyperhidrosis	322	1.063	0.697
Maculopapular eruption	264	0.951	0.7777
Lichen Planus	113	0.849	0.5988
Drug eruption and non-specific drug reaction	1194	0.83	0.028
Erythroderma	295	0.79	0.1833
Rash and other non-specific eruption	**3557**	**0.769**	**<0.0001**
Hyperkeratosis	48	0.741	0.5026
Pruritus	**1901**	**0.737**	**<0.0001**
Xerosis	**499**	**0.658**	**0.0025**
Xerostomia	228	0.63	0.0328
Eczema and Atopic Dermatitis	83	0.628	0.1633
Psoriasis	**336**	**0.581**	**0.0005**
Grover's Disease	21	0.481	0.2993
Vitiligo	103	0.458	0.0285
Pemphigoid	35	0.264	0.0207
Any cutaneous diagnosis	**7975**	**0.805**	**<0.0001**

‡Cutaneous diagnoses were identified based on published literature and expert opinion.
*Benjamini-Hochberg p-value of significance = 0.0025.

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Ethics Approval Study utilized de-identified data from a multi-institutional registry and is exempt from IRB approval.

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