

Supplementary Material: Contribution of the Skin–Gut Axis to Immune-Related Adverse Events with Multi-System Involvement

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Table S1. Search strategy Cohort 1.

DataLine Search Criteria for Cohort 1
L12.0 - BULLOUS PEMPHIGOID L13.9 - BULLOUS DISORDER, UNSPECIFIED L20.9 - ATOPIC DERMATITIS, UNSPECIFIED L27.0 - Generalized skin eruption due to drugs and medicaments taken internally L29.9 - PRURITUS, UNSPECIFIED L50.8 - Other urticaria L50.9 - URTICARIA, UNSPECIFIED L80 - Vitiligo L81.6 - Other disorders of diminished melanin formation L81.8 - Other specified disorders of pigmentation L81.9 - DISORDER OF PIGMENTATION, UNSPECIFIED
Criteria
1) Patients who have had any of the following ICD-10 codes, effective the last 3 years: L12.0 - BULLOUS PEMPHIGOID L13.9 - BULLOUS DISORDER, UNSPECIFIED L20.9 - ATOPIC DERMATITIS, UNSPECIFIED L27.0 - Generalized skin eruption due to drugs and medicaments taken internally L29.9 - PRURITUS, UNSPECIFIED L50.8 - Other urticaria L50.9 - URTICARIA, UNSPECIFIED L80 - Vitiligo L81.6 - Other disorders of diminished melanin formation L81.8 - Other specified disorders of pigmentation L81.9 - DISORDER OF PIGMENTATION, UNSPECIFIED
OR Patients with a ClinDoc in the last 3 years with the term 'rash'
2) The patients were treated with immunotherapy in the 3 months before criteria 1.: include patients on active ICB between 09/28/2017 and 09/28/2020 Use DataLine list or include the following: CEMIPLIMAB DURVALUMAB IPILIMUMAB ATEZOLIZUMAB AVELUMAB NIVOLUMAB CEMIPLIMAB PEMBROLIZUMAB NIVOLUMAB AVELUMAB ATEZOLIZUMAB PEMBROLIZUMAB DURVALUMAB MEDI0680 (AMP-514) NIVOLUMAB IPILIMUMAB PDR001 SPARTALIZUMAB
3) The patients have not had a liquid primary tumor diagnosis: SEER Category1 in ('Lymphoma','Myeloma','Leukemia')

Table S2. Sub-cohort analysis by cancer type.

Cohort 1									
Variable	Melanoma (<i>n</i> = 25)		GU (<i>n</i> = 47)		Lung (<i>n</i> =30)		Other (<i>n</i> = 50)		<i>p</i> -value
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
ircAE Only	21	84%	36	77%	24	80%	45	90%	<i>P</i> = 0.348
ircAE + irColitis	4	16%	11	23%	6	20%	5	10%	
ircAE before irColitis	3	75%	9	82%	3	50%	3	60%	<i>P</i> = 0.547
irColitis before ircAE	1	25%	2	18%	3	50%	2	40%	
Cohort 2									
Variable	Melanoma (<i>n</i> = 76)		GU (<i>n</i> = 39)		Lung (<i>n</i> = 46)		Other (<i>n</i> = 85)		<i>p</i> -value
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Colitis Only	66	87%	28	72%	44	96%	73	86%	<i>P</i> = 0.019
ircAE + irColitis	10	13%	11	28%	2	4%	12	14%	
ircAE before irColitis	6	60%	8	73%	2	100%	10	83%	<i>P</i> = 0.515
irColitis before ircAE	4	40%	3	27%	0	0%	2	17%	

GU= genitourinary, ircAE=immune-related cutaneous adverse event, irColitis=immune-related colitis.