Supplementary Tables

Supplementary Table S1. Real-world (literature-reported) cases of immune checkpoint inhibitor–associated immunobullous dermatoses (BP, PV, LABD, MMP, PNP, DH, and LPP): clinical presentation, diagnostic workup, management, and outcomes.

Disorder Category	Study (Year)	Study Type	N (Cases)	Age	Sex	Cancer Type	ICI Agent(s)	Onset Time	Key Clinical / Diagnostic Features	Treatment	Outcome
Bullous Pemphigoid (BP)	Asdourian et al. (2022)	Systematic review	127	Median 71 (IQR 64-77)	78.7% male	Melanoma (most common), NSCLC, others	PD-1, PD-L1, CTLA-4	Variable; up to months after cessation	Prodromal pruritus (~50%); tense bullae	Topical/systemic steroids; steroid-sparing agents	ICI discontinued in most; biologics effective in refractory cases
	Kawsar et al. (2022)	Multicentre observational	22 (16 BP)	Median 76	Male predominant	Melanoma (73%); 81% BRAF wildtype	PD-1/PD-L1 (mono or combo)	Median 12 mo (mono); 7 mo (combo)	27% mucosal involvement; 25% non-bullous at presentation	≥1 line therapy required in 91%	ICI stopped in 55%; 50% reflare on rechallenge
	Saffuri et al. (2025)	Cohort study	16	Older vs controls ($p<0.05$)	Male predominant ($p=0.0066$)	Cutaneous SCC (43.8%), others	PD-1/PD-L1	Mean 61.3 weeks	Anti-BP180 NC16A positive (81.8%); no epitope spreading	Higher prednisone doses vs classic BP	66.6% permanently discontinued ICI
	Schauer et al. (2022)	Retrospective monocentric	8	Range 26 - 73 years	87.5% male	Mostly melanoma	Various ICIs	Median 10 months	75% palmar/plantar; BPDAI >57 in 50%	Topical/systemic steroids; rituximab	Persistent disease; rituximab required
	Merli et al. (2023)	Italian multicenter	45	74 (46-90)	91.1% male	Various	ICIs	Variable	BP-like eruption predominant	Immunosuppression; ICI interruption	Variable
	Nykaza et al. (2025)	Retrospective case series	17	Mean 72.7	59% male	Various	Pembrolizumab, nivolumab, dostarlimab, cemiplimab	Not specified	Active BP requiring therapy	Dupilumab	CR 75%, PR 12%; median response 19.5 days
	Guan et al. (2022)	Case report	1	69	Male	Lung SCC	Pembrolizumab	3 weeks	Grade 3 BP; steroid-refractory; ↑ anti-BP180, IL-6, IL-10	IVIG effective after steroid failure	Tumor response maintained
	Cui et al. (2025)	Case report	1	77	Male	Lung SCC	Sintilimab	12 mo prodrome; 16 mo bullae	Photodistributed pruritic eczema → bullae	IV methylprednisolone → taper	No recurrence at 19 mo
	Lopez-Geskin (2018)	Case report + review	1	72	Female	Cutaneous SCC	Nivolumab	Variable	Refractory pruritus	Topical/systemic steroids	Variable

Pemphigus Vulgaris (PV)	Buquicchio et al. (2021)	Case report	1	95	Male	Cutaneous SCC	Cemiplimab	~21 weeks	Mucocutaneous PV; anti-Dsg1 positive	Oral prednisone; ICI stopped	Complete PV resolution; cancer CR
	Krammer et al. (2019)	Case report	1	85	Male	NSCLC	Nivolumab	Not specified	Flare of pre-existing PV	Betamethasone/triclosan cream + topical prednisolone + systemic therapy with prednisolone + methotrexate (MTX) + folic acid substitution.	The gradual reduction of the prednisolone dose to the initial one of 5mg daily and simultaneously administration of an increased dose of MTX (up to 10mg once per week) followed.
	Nakamura et al. (2023)	Case report	1	73	Male	Esophageal SCC	Ipilimumab + nivolumab	During combo	PV during therapy	Ipilimumab stopped; topical steroids	PV controlled; cancer PR
	Garje et al. (2018)	Case report	1	64	Male	Urothelial carcinoma	Pembrolizumab	After initiation	Flare of quiescent bullous disease	Systemic and topical corticosteroids, Pembrolizumab discontinued due to flaring of his bullous pemphigoid	After several months of therapy, the skin lesions resolved. For the bladder cancer, he was started on paclitaxel and his bullous pemphigoid remained quiescent on low-dose prednisone and topical therapy.
Linear IgA Bullous Dermatosis (LABD)	Siegel et al. (2018)	Retrospective cohort	9/853	Mean 67.4	55.5%	Various	Anti-PD-1/PD-L1 + vancomycin	During therapy	LABD triggered by vancomycin	Steroids; ICI interruption	Maintenance required
	Jonna et al. (2019)	Case report	1	73	Male	NSCLC	Nivolumab	After 1 year	Gingival LABD	Systemic steroids	Durable response
	Haymete et al. (2025)	Case report	1	41	Female	Breast carcinoma	Pembrolizumab + chemo	After vancomycin	SJS/TEN-like LABD	Vancomycin stopped	Resolution

	Nadelmann et al. (2022)	Systematic review (case reported included)	1/56	Not specified	Not specified	Not specified	PD-1/PD-L1 inhibitor	2-80 weeks	Subepidermal blistering eruption; linear IgA deposition on direct immunofluorescence; classified under immunobullous cirAEs	Systemic corticosteroids ± immunomodulators; ICI interruption	Clinical improvement reported
Mucous Membrane Pemphigoid (MMP)	Zumelzu et al. (2018)	Case report	1	83	Female	Melanoma	Pembrolizumab	6 mo after cessation	Gingival MMP	Doxycycline	Complete remission
	Lagos-Villaseca et al. (2023)	Case report	1	84	Male	Urothelial carcinoma	Pembrolizumab	During treatment	Laryngeal MMP	Immunosuppression; ICI stopped	Improvement
	Bezinelli et al. (2019)	Case report	1	70s	Female	Ovarian adenocarcinoma	Pembrolizumab	During treatment	Severe multi-mucosal MMP	Systemic immunosuppression	Refractory
	Triantafillou & Leahy (2025)	Case report	1	69	Male	Not specified	Pembrolizumab	After 2 mo symptoms	Laryngeal + BP lesions	Steroids + dupilumab	Resolution
	Zumelzu et al. (2018) cited in Nadelmann et al. (2022)	Case report	1/56	Elderly	Female	Metastatic melanoma	Pembrolizumab	Not reported	Predominantly mucosal involvement; immunobullous features; DIF with antibody deposition	Doxycycline + topical steroids mouthwashes	Resolution with minimal therapy
Paraneoplastic Pemphigus (PNP)	Yatim et al. (2019)	Case report	1	64	Male	Cutaneous SCC	Pembrolizumab	3 weeks	ICI-unmasked PNP	Steroids; ICI stopped	Remission; flare on rechallenge
	Nadelmann et al. (2022)	Systematic review	1/56	Not specified	Not specified	Various	PD-1/PD-L1	2–80 weeks	PNP	Immunosuppression	ICI stopped/held

Dermatitis Herpetiformis	Mochel et al. (2016)	Case series	2	63 27	Male Female	Melanoma Melanoma	Pembrolizumab Iplimumab	During therapy During therapy	DH-like eruption; granular IgA Granular IgA deposition within the dermal papillae	Oral prednisone + topical corticosteroids. Pembrolizumab was stopped 3 months later, given the near complete response of his melanoma to the PD-1 inhibitor Not specified	No active disease 30 months after beginning pembrolizumab 21 months following initiation of ipilimumab treatment, the patient has had no evidence of melanoma recurrence.
Lichen Planus Pemphigoides (LPP)	Boyle et al. (2022)	Case series	3	66	Female	Metastatic urothelial cancer	Anti-PD-1 (nivolumab, relatilimab, after 14 cycles nivolumab and sitravatinib)	4 weeks	LP → BP features; anti-BP180+	Prednisone	Progression of metastatic urothelial cancer and the patient was referred to radiation oncology for stereotactic body radiation therapy.
				59	Male	Metastatic hepatocellular carcinoma	Nivolumab	After 12 cycles of nivolumab	Orthokeratosis, epidermal acanthosis, vacuolar interface dermatitis with dyskeratotic keratinocytes at the basal epidermis, and superficial to deep perivascular and interstitial inflammation with lymphocytes and numerous eosinophils within the	Topical clobetasol 0.05% ointment with some improvement and nivolumab was eventually discontinued by his oncologist	Transitioned to hospice care because of progression of cirrhosis and hepatocellular carcinoma and eventually passed away.

									dermis. Diagnosed as LPP		
				57	Female	Metastatic non-small cell lung cancer	Pembrolizumab	After 2 cycles of Pembrolizumab	LPP - Elevated anti BP	High-dose oral prednisone taper and topical clobetasol 0.05%	Died 4 months after discontinuing pembrolizumab from complications of her metastatic disease.
	Wat et al. (2022)	Case series	3	80	Female	Lung adenocarcinoma and cerebral metastasis	Pembrolizumab	During therapy (10 months after starting pembrolizumab)	Lichenoid + bullous lesions	Topically with clobetasol	Pembrolizumab was subsequently discontinued, and she improved on intravenous corticosteroids followed by prednisone.
				77	Male	Non-small cell lung cancer	Pembrolizumab	During therapy (6 months after starting pembrolizumab)	Lichenoid tissue reaction	Steroids	Discontinued pembrolizumab
				63	Female	Metastatic breast cancer	Pembrolizumab	During therapy	Lichenoid tissue reaction with a lymphocytic infiltrate that approximated the dermal-epidermal junction and associated vacuolar alteration and dyskeratosis	Topical steroids, Doxycycline and nicotinamide	Resumed pembrolizumab later with control of her eruption.
	Shah et al. (2022)	Case report	1	58	Female	Renal cell carcinoma	Nivolumab	During treatment	Overlap BP + LP	Not specified	Not specified
	Mueller et al. (2023)	Case report	1	12	Male	Spitzoid melanoma	Nivolumab	During treatment	Severe bullous lichenoid eruption	IV steroids, MTX; ICI stopped	Required hospitalization
	Wang et al. (2024)	Case report	1	53	Female	Stage IV vaginal malignant melanoma	Anti-PD-1	During treatment	Isolated oral LPP	Topical therapy	Excellent response
	Liu et al. (2023)	Case report	1	60	Male	Not specified	Nivolumab	During treatment	Lichen planopilaris pemphigoides	Not specified	At the 1-week follow-up, the patient reported significant improvement of the

											rash with 40 mg dose of prednisone in the morning and 20 mg in the evening. At the 1-month follow-up, there was complete resolution of the previously seen bullous reaction.
	Sugawara et al. (2021)	Case report	1	72	Female	Not specified	Pembrolizumab	3 months	LP-like eruption → BP	Oral prednisolone	BP improved; death unrelated

Supplementary Table S2. Comparison of ICI-associated vs conventional autoimmune bullous diseases: target antigens, blister level, and key immunologic distinctions

ICI-AIBD phenotype	Conventional target antigen(s)	ICI-associated target antigen findings	Blister level (conventional vs ICI)	Key immunologic / inflammatory distinctions in ICI-associated disease*	References
Bullous pemphigoid (BP)	BP180 (type XVII collagen); BP230 in 50-70%	BP180 remains dominant antigen; BP180 NC16A Ab detected in 81.8%; BP230 typically absent (91.9% negative in pembrolizumab-BP cohort); restricted profile with no epitope spreading to BP230/Dsg1/Dsg3/COL7; rare anti-LAD-1 variant reported	Subepidermal, dermal-epidermal junction (same in both)	Enhanced T-cell involvement; inflammatory patterns include eosinophilic infiltrate (common); gene-expression overlap with classic BP (IL-4/IL-13 signature) but with subtle DEGs distinguishing ICI-BP; upregulation of TLR4/complement-driven innate immune response; increased density of Th1 cells in dermis; decreased Tregs in blister floor	Saffuri et al., 2025[1]; Wang et al., 2023[2]; Sadik et al., 2019[3]; Marques-Piubelli et al., 2023[4]; Asdourian et al., 2022[5]
Pemphigus (PV/PF)	Dsg3 (PV), Dsg1 (PF)	Limited data suggest same antigen targets (Dsg1/Dsg3), but with more restricted autoantibody profile (less epitope diversity)	Intraepidermal (suprabasal acantholysis) (same in both)	Autoantibody profile potentially narrower compared with conventional pemphigus; limited published data on immunologic distinctions	Zhao et al., 2018[6]; NCCN Guidelines, 2025[7]
Mucous membrane pemphigoid (MMP)	BP180 (~75%); laminin 332 (18-31%); BP230 (10-30%); COL7 (5%)	ICI- MMP reported with laminin 332 reactivity; clinically important given malignancy association of anti-laminin 332 MMP (25-35%) and need for screening	Subepidermal, dermal-epidermal junction (same in both)	Anti-laminin 332 antibodies may represent important subtype in ICI context; limited data on IgA prevalence in ICI-MMP; cancer screening recommended for anti-laminin 332 cases	Zumelzu et al., 2018[8]; Lagos-Villaseca et al., 2023[9]; Patzelt Schmidt, 2023[10]; Bernard et al., 2013[11]
Lichen planus pemphigoides (LPP)	BP180-related pemphigoid spectrum	ICI-LPP targets BP180 (serology positive in tested cases), but requires correlation with lichenoid/interface dermatitis in addition to subepidermal blistering	Subepidermal, dermal-epidermal junction (same in both)	Concomitant lichenoid/interface dermatitis with dyskeratosis supports LPP phenotype rather than isolated BP; median onset 24.4 weeks after ICI initiation; histopathology shows lichenoid or vacuolar interface dermatitis with eosinophils and subepidermal bullae	Boyle et al., 2022[12]; Wat et al., 2022[13]; Shah et al., 2022[14]; Wang et al., 2024[15]

*ICI-associated AIBDs generally share the same cleavage plane/blister level localization as conventional disease; distinctions relate primarily to autoantibody profiles, inflammatory patterns, and restricted antigenic spreading rather than a change in blister level.